

GLOBAL JOURNAL

OF MEDICAL RESEARCH: F

Diseases

Cancer, Ophthalmology & Pediatric



Role of Triphala Parishek

Peripheral Precocious Puberty

Highlights

Synchronous Brain Metastasis

Detection of Intron22 Mutations

Discovering Thoughts, Inventing Future

VOLUME 17 ISSUE 1 VERSION 1.0



GLOBAL JOURNAL OF MEDICAL RESEARCH: F
DISEASES
CANCER, OPHTHALMOLOGY & PEDIATRIC



GLOBAL JOURNAL OF MEDICAL RESEARCH: F
DISEASES
CANCER, OPHTHALMOLOGY & PEDIATRIC

VOLUME 17 ISSUE 1 (VER. 1.0)

© Global Journal of Medical Research. 2017.

All rights reserved.

This is a special issue published in version 1.0 of "Global Journal of Medical Research." By Global Journals Inc.

All articles are open access articles distributed under "Global Journal of Medical Research"

Reading License, which permits restricted use. Entire contents are copyright by of "Global Journal of Medical Research" unless otherwise noted on specific articles.

No part of this publication may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopy, recording, or any information storage and retrieval system, without written permission.

The opinions and statements made in this book are those of the authors concerned. Ultraculture has not verified and neither confirms nor denies any of the foregoing and no warranty or fitness is implied.

Engage with the contents herein at your own risk.

The use of this journal, and the terms and conditions for our providing information, is governed by our Disclaimer, Terms and Conditions and Privacy Policy given on our website <http://globaljournals.us/terms-and-condition/menu-id-1463/>

By referring / using / reading / any type of association / referencing this journal, this signifies and you acknowledge that you have read them and that you accept and will be bound by the terms thereof.

All information, journals, this journal, activities undertaken, materials, services and our website, terms and conditions, privacy policy, and this journal is subject to change anytime without any prior notice.

Incorporation No.: 0423089
License No.: 42125/022010/1186
Registration No.: 430374
Import-Export Code: 1109007027
Employer Identification Number (EIN):
USA Tax ID: 98-0673427

Global Journals Inc.

(A Delaware USA Incorporation with "Good Standing"; Reg. Number: 0423089)

Sponsors: *Open Association of Research Society*
Open Scientific Standards

Publisher's Headquarters office

Global Journals® Headquarters
945th Concord Streets,
Framingham Massachusetts Pin: 01701,
United States of America
USA Toll Free: +001-888-839-7392
USA Toll Free Fax: +001-888-839-7392

Offset Typesetting

Global Journals Incorporated
2nd, Lansdowne, Lansdowne Rd., Croydon-Surrey,
Pin: CR9 2ER, United Kingdom

Packaging & Continental Dispatching

Global Journals
E-3130 Sudama Nagar, Near Gopur Square,
Indore, M.P., Pin: 452009, India

Find a correspondence nodal officer near you

To find nodal officer of your country, please
email us at local@globaljournals.org

eContacts

Press Inquiries: press@globaljournals.org
Investor Inquiries: investors@globaljournals.org
Technical Support: technology@globaljournals.org
Media & Releases: media@globaljournals.org

Pricing (Including by Air Parcel Charges):

For Authors:

22 USD (B/W) & 50 USD (Color)
Yearly Subscription (Personal & Institutional):
200 USD (B/W) & 250 USD (Color)

GLOBAL JOURNALS CONSTITUTIONAL EDITORIAL BOARD

~INTEGRATED~

Dr. Charles A. Rarick

Ph.D.
Professor of International Business
College of Business
Purdue University Northwest
Hammond, Indiana USA

Dr. Osman Balci, Professor

Department of Computer Science
Virginia Tech, Virginia University
Ph.D. and M.S. Syracuse University, Syracuse, New York
M.S. and B.S. Bogazici University, Istanbul, Turkey
Web: manta.cs.vt.edu/balci

Dr. A. Heidari

Ph.D, D.Sc, Faculty of Chemistry
California South University (CSU),
United Stated

Dr. Miklas Scholz

B.Eng. (equiv), PgC, MSc, Ph.D, CWEM, C.Env., CSci,
C.Eng.
Nigeria Health, Wellness and Fitness
University of Lund

Dr. Maria Gullo

Ph.D, Food Science and Technology
University of Catania
Department of Agricultural and Food Sciences
University of Modena and Reggio Emilia, Italy

Dr. Qiang Wu

Ph.D University of Technology, Sydney
Department of Mathematics,
Physics and Electrical Engineering
Northumbria University

Dr. Bingyun Li

Ph.D Fellow, IAES
Guest Researcher, NIOSH, CDC, Morgantown, WV
Institute of Nano and Biotechnologies
West Virginia University, US

Dr. Audeh Ahmad Ahmad

Amman Arab University For Higher Education
Ph.D, Accounting-Ais
Faculty of Business Administration
Alalbyt University, Jordan, Amman

Dr. Lucian Baia

Ph.D Julius-Maximilians University Würzburg, Germany
Associate professor
Department of Condensed Matter Physics and
Advanced Technologies, Babes-Bolyai University,
Romania

Dr. Sahraoui Chaieb

PhD Physics and Chemical Physics
M.S. Theoretical Physics
B.S. Physics, École Normale Supérieure, Paris
Associate Professor, Bioscience
King Abdullah University of Science and Technology

Dr. Houfa Shen

Ph.D Manufacturing Engineering,
Mechanical Engineering, Structural Engineering
Department of Mechanical Engineering
Tsinghua University, China

Dr. Arshak Poghossian

Ph.D Solid-State Physics
Leningrad Electrotechnic Institute, Russia
Institute of Nano and Biotechnologies
Aachen University of Applied Sciences, Germany

Dr. A. Stegou-Sagia

Ph.D Mechanical Engineering, Environmental
Engineering School of Mechanical Engineering
National Technical University of Athens

Giuseppe A Provenzano

Irrigation and Water Management, Soil Science,
Water Science Hydraulic Engineering
Dept. of Agricultural and Forest Sciences
Universita di Palermo, Italy

Dr. Ciprian LĂPUȘAN

Ph. D in Mechanical Engineering
Technical University of Cluj-Napoca
Cluj-Napoca (Romania)

Dr. Haijian Shi

Ph.D Civil Engineering Structural Engineering
Oakland, CA, United States

Dr. Yogita Bajpai

Ph.D Senior Aerospace/Mechanical/
Aeronautical Engineering professional
M.Sc. Mechanical Engineering
M.Sc. Aeronautical Engineering
B.Sc. Vehicle Engineering
Orange County, California, USA

Dr. Abdurrahman Arslanyilmaz

Computer Science & Information Systems Department
Youngstown State University
Ph.D., Texas A&M University
University of Missouri, Columbia
Gazi University, Turkey
Web:cis.yzu.edu/~aarslanyilmaz/professional_web

Dr. Chao Wang

Ph.D. in Computational Mechanics
Rosharon, TX, USA

Dr. Adel Al Jumaily

Ph.D Electrical Engineering (AI)
Faculty of Engineering and IT
University of Technology, Sydney

Kitipong Jaojaruek

B. Eng, M. Eng D. Eng (Energy Technology, Asian
Institute of Technology).
Kasetsart University Kamphaeng Saen (KPS) Campus
Energy Research Laboratory of Mechanical Engineering

Dr. Mauro Lenzi

Ph.D, Biological Science, Pisa University, Italy
Lagoon Ecology and Aquaculture Laboratory
Orbetello Pesca Lagunare Company

Dr. Omid Gohardani

M.Sc. (Computer Science), FICCT, U.S.A.
Email: yogita@computerresearch.org

Dr. Yap Yee Jiun

B.Sc.(Manchester), Ph.D.(Brunel), M.Inst.P.(UK)
Institute of Mathematical Sciences,
University of Malaya,
Kuala Lumpur, Malaysia

Dr. Thomas Wischgoll

Computer Science and Engineering,
Wright State University, Dayton, Ohio
B.S., M.S., Ph.D.
(University of Kaiserslautern)
Web:avida.cs.wright.edu/personal/wischgol/index_eng.html

Dr. Baziotis Ioannis

Ph.D. in Petrology-Geochemistry-Mineralogy
Lipson, Athens, Greece

Dr. Xiaohong He

Professor of International Business
University of Quinnipiac
BS, Jilin Institute of Technology; MA, MS, Ph.D,
(University of Texas-Dallas)
Web: quinnipiac.edu/x1606.xml

Dr. Burcin Becerik-Gerber

University of Southern Californi
Ph.D in Civil Engineering
DDes from Harvard University
M.S. from University of California, Berkeley
M.S. from Istanbul Technical University
Web: i-lab.usc.edu

Dr. Söhnke M. Bartram

Department of Accounting and Finance
Lancaster University Management School
Ph.D. (WHU Koblenz)
MBA/BBA (University of Saarbrücken)
Web: lancs.ac.uk/staff/bartras1/

Dr. Söhnke M. Bartram

Ph.D, (IT) in Faculty of Engg. & Tech.
Professor & Head,
Dept. of ISE at NMAM Institute of Technology

Dr. Balasubramani R

Department of Accounting and Finance
Lancaster University Management School
Ph.D. (WHU Koblenz)
MBA/BBA (University of Saarbrücken)
Web: lancs.ac.uk/staff/bartras1/

M. Meguellati

Department of Electronics,
University of Batna, Batna 05000, Algeria

Dr. T. David A. Forbes

Associate Professor and Range Nutritionist
Ph.D Edinburgh University - Animal Nutrition
M.S. Aberdeen University - Animal Nutrition
B.A. University of Dublin- Zoology.
Web: essm.tamu.edu/people-info/faculty/forbes-david

Dr. Bassey Benjamin Esu

B.Sc. Marketing; MBA Marketing; Ph.D Marketing
Lecturer, Department of Marketing, University of Calabar
Tourism Consultant, Cross River State Tourism
Development Department
Co-rdinator , Sustainable Tourism Initiative, Calabar,
Nigeria

Dr. Maciej Gućma

Asistant Professor,
Maritime University of Szczecin Szczecin, Poland
Ph.D. Eng. Master Mariner
Web: www.mendeley.com/profiles/maciej-gucma/

Dr. Shun-Chung Lee

Department of Resources Engineering,
National Cheng Kung University, Taiwan

Dr. Fotini Labropulu

Mathematics - Luther College, University of Regina
Ph.D, M.Sc. in Mathematics
B.A. (Honours) in Mathematics, University of Windsor
Web: luthercollege.edu/Default.aspx

Dr. Vesna Stanković Pejnović

Ph. D. Philosphy , Zagreb, Croatia
Rusveltova, Skopje, Macedonia

Dr. Miguel Angel Ariño

Professor of Decision Sciences
IESE Business School
Barcelona, Spain (Universidad de Navarra)
CEIBS (China Europe International Business School).
Beijing, Shanghai and Shenzhen
Ph.D. in Mathematics, University of Barcelona
BA in Mathematics (Licenciatura)
University of Barcelona
Web: web.iese.edu/MAArino/overview.axd

Dr. Philip G. Moscoso

Technology and Operations Management
IESE Business School, University of Navarra
Ph.D in Industrial Engineering and Management,
ETH Zurich , M.Sc. in Chemical Engineering,
ETH Zurich Link: Philip G. Moscoso personal webpage

Dr. Mihaly Mezei

Associate Professor
Department of Structural and Chemical Biology
Mount Sinai School of Medical Center
Ph.D., Etsv Lornd University, Postdoctoral Training,
New York University, MSSM home:
<https://www.mountsinai.org/Find%20A%20Faculty/profile.do?id=0000072500001497192632>
Lab home - software,
publications: <https://inka.mssm.edu/~mezei>
Department: <https://atlas.physbio.mssm.edu>

Dr. Vivek Dubey (HON.)

MS (Industrial Engineering),
MS (Mechanical Engineering)
University of Wisconsin
FICCT
Editor-in-Chief, USA

Dr. Carlos García Pont

Associate Professor of Marketing
IESE Business School, University of Navarra
Doctor of Philosophy (Management),
Massachusetts Institute of Technology (MIT)
Master in Business Administration, IESE,
University of Navarra
Degree in Industrial Engineering,
Universitat Politècnica de Catalunya
Web: iese.edu/aplicaciones/faculty/facultyDetail.asp

Dr. Sanjay Dixit, M.D.

Director, EP Laboratories, Philadelphia VA Medical Center
Cardiovascular Medicine - Cardiac Arrhythmia
University of Penn School of Medicine
Web: pennmedicine.org/wagform/MainPage.aspx?

Dr. Pina C. Sanelli

Associate Professor of Radiology
Associate Professor of Public Health
Weill Cornell Medical College
Associate Attending Radiologist
NewYork-Presbyterian Hospital
MRI, MRA, CT, and CTA
Neuroradiology and Diagnostic Radiology
M.D., State University of New York at Buffalo,
School of Medicine and Biomedical Sciences
Web: weillcornell.org/pinasanelli/

Er. Suyog Dixit

(M.Tech), BE (HONS. in CSE), FICCT
SAP Certified Consultant
CEO at IOSRD, GAOR OSS
Technical Dean, Global Journals Inc.(US)
Website: www.suyogdixit.com
Email: suyog@suyogdixit.com

Er. Pritesh Rajvaidya

Computer Science Department
California State University
BE (Computer Science), FICCT
Technical Dean, USA
Email: pritesh@computerresearch.org,
deanusa@globaljournals.org

Dr. Apostolos Ch. Zarros

DM, Degree (Ptychio) holder in Medicine,
National and Kapodistrian University of Athens
MRes, Master of Research in Molecular Functions in
Disease,
University of Glasgow
FRNS, Fellow, Royal Numismatic Society
Member, European Society for Neurochemistry
Member, Royal Institute of Philosophy
Scotland, United Kingdom

Dr. Han-Xiang Deng

MD., Ph.D
Associate Professor and Research Department
Division of Neuromuscular Medicine
Davee Department of Neurology and Clinical
Neurosciences
Northwestern University Feinberg School of Medicine
Web: neurology.northwestern.edu/faculty/deng.html

Dr. Roberto Sanchez

Associate Professor
Department of Structural and Chemical Biology
Mount Sinai School of Medicine
Ph.D., The Rockefeller University
Web: mountsinai.org/

Jixin Zhong

Department of Medicine,
Affiliated Hospital of Guangdong Medical College,
Zhanjiang, China Davis Heart and Lung Research Institute,
The Ohio State University, Columbus, OH 43210, USA

Dr. Wen-Yih Sun

Professor of Earth and Atmospheric Sciences
Purdue University, Director
National Center for Typhoon and Flooding Research,
Taiwan
University Chair Professor
Department of Atmospheric Sciences,
National Central University, Chung-Li, Taiwan
University Chair Professor
Institute of Environmental Engineering,
National Chiao Tung University, Hsin-chu, Taiwan.
Ph.D., MS The University of Chicago, Geophysical Sciences
BS National Taiwan University, Atmospheric Sciences
Web: event.nchc.org.tw/2009

Dr. Michael R. Rudnick

M.D., FACP
Associate Professor of Medicine
Chief, Renal Electrolyte and Hypertension Division (PMC)
Penn Medicine, University of Pennsylvania
Presbyterian Medical Center, Philadelphia
Nephrology and Internal Medicine
Certified by the American Board of Internal Medicine
Web: uphs.upenn.edu/

Dr. Aziz M. Barbar, Ph.D.

IEEE Senior Member
Chairperson, Department of Computer Science
AUST - American University of Science & Technology
Alfred Naccash Avenue - Ashrafieh

Dr. Minghua He

Department of Civil Engineering
Tsinghua University
Beijing, 100084, China

Anis Bey

Dept. of Comput. Sci.,
Badji Mokhtar-Annaba Univ.,
Annaba, Algeria

Chutisant Kerdvibulvech

Dept. of Inf.& Commun. Technol.,
Rangsit University, Pathum Thani, Thailand
Chulalongkorn University, Thailand
Keio University, Tokyo, Japan

Dr. Wael Abdullah

Elhelece Lecturer of Chemistry,
Faculty of science, Gazan Univeristy,
KSA. Ph. D. in Inorganic Chemistry,
Faculty of Science, Tanta University, Egypt

Yaping Ren

School of Statistics and Mathematics
Yunnan University of Finance and Economics
Kunming 650221, China

Ye Tian

The Pennsylvania State University
121 Electrical Engineering East
University Park, PA 16802, USA

Dr. Diego González-Aguilera

Ph.D. Dep. Cartographic and Land Engineering,
University of Salamanca, Ávila, Spain

Dr. Hai-Linh Tran

PhD in Biological Engineering
Department of Biological Engineering
College of Engineering Inha University, Incheon, Korea

Dr. Tao Yang

Ph.D, Ohio State University
M.S. Kansas State University
B.E. Zhejiang University

Dr. Feng Feng

Boston University
Microbiology, 72 East Concord Street R702
Duke University
United States of America

Shengbing Deng

Departamento de Ingeniería Matemática,
Universidad de Chile.
Facultad de Ciencias Físicas y Matemáticas.
Blanco Encalada 2120, piso 4.
Casilla 170-3. Correo 3. - Santiago, Chile

Claudio Cuevas

Department of Mathematics
Universidade Federal de Pernambuco
Recife PE Brazil

Dr. Alis Puteh

Ph.D. (Edu.Policy) UUM
Sintok, Kedah, Malaysia
M.Ed (Curr. & Inst.), University of Houston, USA

Dr. R.K. Dixit(HON.)

M.Sc., Ph.D., FICCT Chief Author, India
Email: authorind@globaljournals.org

Dr. Dodi Irawanto

PhD, M.Com, B.Econ Hons.
Department of Management,
Faculty of Economics and Business, Brawijaya University
Malang, Indonesia

Ivona Vrdoljak Raguz

University of Dubrovnik, Head,
Department of Economics and Business Economics,
Croatia

Dr. Prof Adrian Armstrong

BSc Geography, LSE, 1970
PhD Geography (Geomorphology)
Kings College London 1980
Ordained Priest, Church of England 1988
Taunton, Somerset, United Kingdom

Thierry FEUILLET

Géolittomer – LETG UMR 6554 CNRS
(Université de Nantes)
Institut de Géographie et d'Aménagement
Régional de l'Université de Nantes.
Chemin de la Censive du Tertre – BP, Rodez

Dr. Yongbing Jiao

Ph.D. of Marketing
School of Economics & Management
Ningbo University of Technology
Zhejiang Province, P. R. China

Cosimo Magazzino

Roma Tre University
Rome, 00145, Italy

Dr. Shaoping Xiao

BS, MS, Ph.D Mechanical Engineering,
Northwestern University
The University of Iowa
Department of Mechanical and Industrial Engineering
Center for Computer-Aided Design

Dr. Alex W. Dawotola

Hydraulic Engineering Section,
Delft University of Technology,
Stevinweg, Delft, Netherlands

Dr. Luisa dall'Acqua

PhD in Sociology (Decisional Risk sector),
Master MU2, College Teacher in Philosophy (Italy),
Edu-Research Group, Zürich/Lugano

Xianghong Qi

University of Tennessee
Oak Ridge National Laboratory
Center for Molecular Biophysics
Oak Ridge National Laboratory
Knoxville, TN 37922, United States

Gerard G. Dumancas

Postdoctoral Research Fellow,
Arthritis and Clinical Immunology Research Program,
Oklahoma Medical Research Foundation
Oklahoma City, OK
United States

Vladimir Burtman

Research Scientist
The University of Utah, Geophysics
Frederick Albert Sutton Building, 115 S 1460 E Room 383
Salt Lake City, UT 84112, USA

Jalal Kafashan

Mechanical Engineering, Division of Mechatronics
KU Leuven, BELGIUM

Zhibin Lin

Center for Infrastructure Engineering Studies
Missouri University of Science and Technology
ERL, 500 W. 16th St. Rolla,
Missouri 65409, USA

Dr. Lzzet Yavuz

MSc, PhD, D Ped Dent.

Associate Professor,

Pediatric Dentistry Faculty of Dentistry,

University of Dicle, Diyarbakir, Turkey

Prof. Dr. Eman M. Gouda

Biochemistry Department,

Faculty of Veterinary Medicine, Cairo University,

Giza, Egypt

Della Ata

BS in Biological Sciences

MA in Regional Economics

Hospital Pharmacy

Pharmacy Technician Educator

Dr. Muhammad Hassan Raza, PhD

Engineering Mathematics

Internetworking Engineering, Dalhousie University,

Canada

Dr. Asunción López-Varela

BA, MA (Hons), Ph.D (Hons)

Facultad de Filología.

Universidad Complutense Madrid

29040 Madrid, Spain

Dr. Bondage Devanand Dhondiram

Ph.D

No. 8, Alley 2, Lane 9, Hongdao station,

Xizhi district, New Taipei city 221, Taiwan (ROC)

Dr. Latifa Oubedda

National School of Applied Sciences,

University Ibn Zohr, Agadir, Morocco

Lotissement Elkhier N°66

Bettana Salé Maroc

Dr. Belen Riverio, PhD

School of Industrial Enigneering

University of Vigo

Spain

CONTENTS OF THE ISSUE

- i. Copyright Notice
- ii. Editorial Board Members
- iii. Chief Author and Dean
- iv. Contents of the Issue
 1. Peripheral Precocious Puberty Causes, Diagnosis and Management. **1-4**
 2. Role of Triphala Parishek in Lid Concretion : A Case Study. **5-7**
 3. Rectal Adenocarcinoma with Synchronous Brain Metastasis and Prolonged Overall Survival (OS). **9-12**
 4. Detection of Intron22 Mutations in Iraqi Female Carriers in Wasit province with Hemophilia A. **13-24**
 5. Chemoradiotherapy or Induction Chemotherapy Followed by Chemoradiotherapy University Hospital Fuenlabrada: Our Experience in 10 Years. **25-29**
 6. Assessment of Self Care Management and its Associated Factors among Type 2 Diabetes Patients in Mekelle Hospital and Ayder Referral Hospitals, Mekelle City, Tigray, Northern Ethiopia, 2012/13. **31-48**
- v. Fellows
- vi. Auxiliary Memberships
- vii. Process of Submission of Research Paper
- viii. Preferred Author Guidelines
- ix. Index



Peripheral Precocious Puberty Causes, Diagnosis and Management

By Nasir AM. AL. Jurayyan & Huda A. Osman

King Khalid University Hospital

Abstract- Background: Precocious puberty (PP) is a common pediatric endocrine problem. It is a complex and a multifactorial.

Design and settings: A retrospective hospital based study was conducted at King Khalid University Hospital (KKUH), Riyadh Saudi Arabia, during the period January 1990 and December 2016.

Materials and Methods: During the period under review, all patients with the diagnosis of peripheral precocious puberty were reviewed for age, sex, clinical characteristics, hormonal and radiological investigations.

Results: During the period under review; 19 patients were evaluated for PPP. Elevated levels of estradiol or testosterone levels with suppressed gonadotropin levels on GnRH stimulation test. Various etiological causes were noted, with congenital adrenal hyperplasia (8 patients) and hypothyroidism (5 patients) being the commonest. Adrenal tumors in 3 patients, ovarian pathology in two and McCune-Albright Syndrome was the diagnosis in one.

Keywords: *diagnosis, etiology, management, peripheral, precocious, puberty.*

GJMR-F Classification: NLMC Code: WS 450



Strictly as per the compliance and regulations of:



Peripheral Precocious Puberty Causes, Diagnosis and Management

Nasir AM. AL. Jurayyan ^α & Huda A. Osman ^σ

Abstract- Background: Precocious puberty (PP) is a common pediatric endocrine problem. It is a complex and a multifactorial.

Design and settings: A retrospective hospital based study was conducted at King Khalid University Hospital (KKUH), Riyadh Saudi Arabia, during the period January 1990 and December 2016.

Materials and Methods: During the period under review, all patients with the diagnosis of peripheral precocious puberty were reviewed for age, sex, clinical characteristics, hormonal and radiological investigations.

Results: During the period under review; 19 patients were evaluated for PPP. Elevated levels of estradiol or testosterone levels with suppressed gonadotropin levels on GnRH stimulation test. Various etiological causes were noted, with congenital adrenal hyperplasia (8 patients) and hypothyroidism (5 patients) being the commonest. Adrenal tumors in 3 patients, ovarian pathology in two and McCune-Albright Syndrome was the diagnosis in one.

Conclusion: Peripheral precocious puberty wasn't that rare in our series. Variety of causes with congenital adrenal hyperplasia and hypothyroidism were the commonest.

Keywords: diagnosis, etiology, management, peripheral, precocious, puberty.

I. INTRODUCTION

Precocious puberty (pp) is a common problem seen in pediatric endocrinology practice. It is a complex and can be classified into, central precocious puberty, gonadotropin dependent or true PP which results from early maturation of hypothalamo-pituitary- gonadal (HPG) axis, and peripheral (pseudo) precocious puberty which is also known as gonadotropin independent puberty, is the result of autonomous peripheral secretion of excess sex hormones independent of the HPG axis.(1-5)

The aim of this article was to discuss peripheral precocious puberty and its diagnosis and management.

II. MATERIALS AND METHODS

All patients diagnosed to have peripheral (pseudo) precocious puberty at the pediatric endocrine

Author α: MD, Professor and Senior Endocrinologist, Department of Pediatrics (39), College of Medicine and KKUH, Po box: 2925 Riyadh 11461, Saudi Arabia. e-mail: njurayyan@gmail.com

Author σ: MRCPCH (UK), Senior Registrar in Endocrinology, Division of Endocrinology, department of pediatric, Medical College and King Khalid University Hospital (KKUH), King Saud University Riyadh, Saudi Arabia.

series of the King Khalid University Hospital (KKUH), Riyadh, Saudi Arabia in the period January 1990 and December 2016, were retrospectively reviewed. Data included age, sex, clinical demographic data, hormonal and radiological investigations. The diagnosis was based on history, clinical examination, hormonal and radiological findings. Gonadotropin releasing hormone (GnRH) stimulation testing is considered as the gold standard for diagnosis (6-8). Radiological investigations (Pelvic Ultra Sonography), computed tomography (CT), and magnetic resonance imaging (MRI) were performed when indicated.

III. RESULTS

During the period under review a total of 19 patients were diagnosed to have peripheral (pseudo) precocious puberty.

Fifteen girls and 4 boys. Their mean age was 3.5 (range; 0.5-7 years). Laboratory investigations revealed elevated Oestradiol level, mean: 110 ng/ ml (normal; up to 35) and testosterone mean: 2.1 nanomol/ L (normal; 0.1-0.4) with suppressed gonadotropin levels on GnRH stimulation test. The etiological diagnosis showed variety of causes (Table).

Congenital adrenal hyperplasia and chronic hypothyroidism were the commonest found in eight and five patients respectively.

Tumors of the adrenal may cause virilization or feminization depending on whether androgens or estrogens are secreted, one estrogen secreting adenoma presented with feminization in a boy and two were due to adrenal carcinoma (figure).

Ovarian cyst and granulosa cell tumor were present in one patient each. The classic triad of polyostotic fibrous dysplasia, Café/ au/ lait macules of the skin and precocious puberty indicates McCune-Albright syndrome, found in one girl.

IV. DISCUSSION

Precocious puberty is defined as development of secondary sex characteristics before the age of eight years in girls and nine years in boys. Two types of precocious puberty are recognized; central (true) precocious puberty (CPP) and peripheral (pseudo) precocious puberty (PPP). CPP is caused by early activation of the hypothalamic-pituitary axes (HPA), with gonadotropin- releasing hormone (GnRh). Stimulated

gonadotropin secretion causing gonads maturation. In PPP, serum sex steroids are elevated independent of gonadotropin secretion, and because gonadotropin levels are low the gonads do not undergo maturation. Precocious puberty may be isosexual (involving secondary sex characteristics that are gender matched) or heterosexual (involving sex characteristics of the opposite gender). CPP is always isosexual, whereas PPP may be isosexual or heterosexual.

In Saudi Arabia where the prevalence of consanguinity increased (9,10), congenital adrenal hyperplasia commonly causes virilization without testicular enlargement in boys, and girls will not have breast enlargement, unless secondary central precocious occurred. Approximately 40% of our patients in this series were due to congenital adrenal hyperplasia (21- α -hydroxylase or 11- β hydroxylase deficiency which is a common occurrence in Saudi Arabia and easily diagnosed. The treatment includes glucocorticoids, usually hydrocortisone 12-15 mg/m²/day(11,12). Severe chronic hypothyroidism rarely results in precocious puberty, and unlike other causes, is associated with skeletal and growth delay. The pathophysiology is uncertain, but it may be due to the intrinsic FSH activity if very high TSH levels. The signs of puberty is usually reversible with thyroxine therapy (13,14). Tumors of adrenal glands, ovary, or testes may cause virilization or feminization depending on whether androgen or estrogen are secreted. These rare neoplasia require surgery or chemotherapy both. Also, Human Chorionic gonadotropin (hCG) secreting tumors can cause precocious puberty in boys by stimulating Leydig cells to secrete testosterone. Unlike boys, girls with HCG secreting tumors generally do not develop precocious puberty. Both LH and FSH stimulation are necessary for ovarian activation. Rapid virilization suggests the possibility of an endocrine secreting tumor. In adrenal tumors, both testosterone and Dehydroepiandrosterone are usually markedly elevated. A raised serum HCG suggests an hCG secreting tumor. α -fetoprotein and carcinoembryonic antigen (CEA) are potentially useful markers of non germinomatous germ cell tumors. Ultrasonography helps in delineating the different causes (15-17) ovarian cysts occur in 2.5% of pre pubertal girls. Imaging studies (ultrasound help in differentiating benign/ malignant lesions. Cysts having few internal echoes suggestive of hemorrhages with separation/calcification is most benign and requires observation with follow up ultrasound in 1 to 2 months. Surgery may be required for large ovarian cyst (>20 ml) because of the risk of adnexal torsion. Aromatase inhibitors are used in the management of persistent cyst. Recurrent or persistent ovarian cyst with a solid component in imaging suggest ovarian tumors. Juvenile granulosa cell tumor was the most common ovarian neoplasia to present with precocious puberty (17-22). The McCune-

Albright Syndrome causes precocious puberty, primarily in girls. The classic disorder comprises the triad of polyostotic fibrous dysplasia, café-au-lait pigmentation, and gonadotropin independent precocious puberty. The disorder results from an activating somatic mutation in Gs, the protein that transduces the signal of many 7-transmembrane domain receptors, including gonadotropin receptors. Testolactone and other anti-estrogen like Fudrozole and Tamoxifen are effective in treating girls with McCune-Albright syndrome. Unfortunately, escaping from the effects of treatment may occur after one to three years. After years of exposure to estrogen, many of these girls enter central precocious puberty and require treatment with LHRH analogue (23-26).

V. ACKNOWLEDGEMENT

The authors would like to thank Mr Mooath N Al-Jurayyan for his help in preparing this manuscript.

Conflict of interest

The authors have no conflict of interest to declare.

Funding None

REFERENCES RÉFÉRENCES REFERENCIAS

1. Sultan C (ed): Pediatric and Adolescent Gynecology. Evidence-Based Clinical Practice. 2nd, revised and extended edition. Endocr Dev. Basel, Karger, 2012, vol 22, pp 84–100.
2. Pouw IS, Drop SL, Ladée-Levy JV, Slijper FM. Tijdschr Kindergeneesk 1986; 54(3): 77-83.
3. Eugster EA: peripheral precocious puberty causes and current management hormone research 2007; 71(supp1); 64-7.
4. Carel JC1, Léger J. Clinical practice. Precocious puberty. N Engl J Med. 2008 29; 358(22): 2366-77.
5. Muir A. Precocious puberty. Pediatr Rev. 2006; 27(10): 373-81.
6. Oerter KE1, Uriarte MM, Rose SR, Barnes KM, Cutler GB Jr. Gonadotropin secretory dynamics during puberty in normal girls and boys. J Clin Endocrinol Metab. 1990; 71(5): 1251-8.
7. Resende EA1, Lara BH, Reis JD, Ferreira BP, Pereira GA, Borges MF. Assessment of basal and gonadotropin-releasing hormone-stimulated gonadotropins by immunochemiluminometric and immunofluorometric assays in normal children. J Clin Endocrinol Metab. 2007; 92(4):1424-9. Epub 2007 Feb 6.
8. Pasternak Y1, Friger M, Loewenthal N, Haim A, HersHKovitz E. The utility of basal serum LH in prediction of central precocious puberty in girls. Eur J Endocrinol. 2012 Feb; 166(2): 295-9. doi: 10.1530/EJE-11-0720. Epub 2011 Nov 14.

9. Saedi-Wong S, Al-Frayh A, Wong H.Y.H. Socio-Economic. Journal of Asian and African Studies 1989; 24: 247-252.
10. AL-Jurayyan NAM, Osman H The increased prevalence of congenital adrenal hyperplasia in Saudi Arabia.
11. The role of consanguinity and multiple siblings involvement. European journal for research and medical science 2015; 3(11): 31-34.
12. Al-Jurayyan NA1, Al-Herbish AS, Abo Bakr AM, Al-Rabeeah AA, Al-Samarrai Al, Jawad AJ, Patel PJ, Abdullah MA.
13. Congenital adrenal hyperplasia in a referral hospital in Saudi Arabia: Epidemiology, pattern and clinical presentation. Ann Saudi Med. 1995 Sep; 15(5): 447-50.
14. Al-Jurayyan NA. Congenital adrenal hyperplasia due to 11 beta-hydroxylase deficiency in Saudi Arabia: clinical and biochemical characteristics. Acta Paediatr. 1995 Jun; 84(6): 651-4.
15. Radaideh AM1, Nusier M, El-Akawi Z, Jaradat D. Precocious puberty with congenital hypothyroidism. Neuro Endocrinol Lett. 2005 Jun; 26(3): 253-6.
16. Anasti JN1, Flack MR, Froehlich J, Nelson LM, Nisula BC A potential novel mechanism for precocious puberty in juvenile hypothyroidism. J Clin Endocrinol Metab. 1995 Jan; 80(1): 276-9.
17. Chowdhuri S1, Dharmalingam M, Kumar KM. Adrenal tumor presenting as precocious puberty. Indian J Pediatr. 2001 Apr; 68(4): 351-2.
18. AL-Jurayyan NA Estrogen-Secreting adrenocortical adenoma causing gynecomastia in a pre pubertal boy. Saudi Medical Journal 1995; (6,2), 75-78.
19. Jean CC, Juliane L Precocious puberty N Eng JM 2008 358: 2366-77.
20. De Sousa G1, Wunsch R, Andler W. Precocious pseudopuberty due to autonomous ovarian cysts: a report of ten cases and long-term follow-up. Hormones (Athens). 2008; 7(2): 170-4.
21. Gideon DS, Rainer W, Werner A. Precocious pseudo puberty due to autonomous ovarian cyst. A report of ten cases and long term follow up. Hormones 2008; 7: 170-4.
22. Sekkate S1, Kairouani M, Serji B, Tazi A, Mrabti H, Boutayeb S, Errihani H. Ovarian granulosa cell tumors: a retrospective study of 27 cases and a review of the literature. World J Surg Oncol. 2013 Jun 18; 11: 142. doi: 10.1186/1477-7819-11-142.
23. Haroon NN, Agarwal G, Pardey R, Dabadgha P, juvenile granulosa cell tumor presenting as isosexual precocious puberty a case report and review of literature. Indian J Endocrinology Metal 2012 17: 157-9.
24. Eugster EA. Peripheral precocious puberty: causes and current management. Horm Res. 2009 Jan; 71 Suppl 1: 64-7. doi: 10.1159/000178041. Epub 2009 21.
25. Mobini M, Vakili P, Vakili S McCune-Albright syndrome. A case report and literature review. Int J Pediatrics 2014 2(2): 153-6.
26. Weinstein LS1, Shenker A, Gejman PV, Merino MJ, Friedman E, Spiegel AM.
27. Activating mutations of the stimulatory G protein in the McCune-Albright syndrome. N Engl J Med. 1991; 12; 325(24): 1688-95.
28. Feuillan PP1, Jones J, Cutler GB Jr. Long-term testolactone therapy for precocious puberty in girls with the McCune-Albright syndrome. J Clin Endocrinol Metab. 1993; 77(3): 647-51.
29. Mieszczyk J1, Eugster EA. Treatment of precocious puberty in McCune-Albright syndrome. Pediatr Endocrinol Rev. 2007; 4 Suppl 4: 419-22.

Table 1: Etiology of peripheral, gonadotropin- independent, (pseudo) precocious puberty in 19 patients

Diagnosis	Male	Female
•congenital adrenal hyperplasia		
-21-α hydroxylase deficiency	-	3
-11 B – hydroxylase deficiency	2	3
•Hypothyroidism	1	4
•adrenal tumors		
-oestrogen- secreting adreno-cortical adenoma	1	-
-adreno- carcinoma	-	2
•ovarian cyst	-	1
•Granulosa cell tumor	-	1
•Mc Cune-Albright syndrome	-	1
Total	4	15

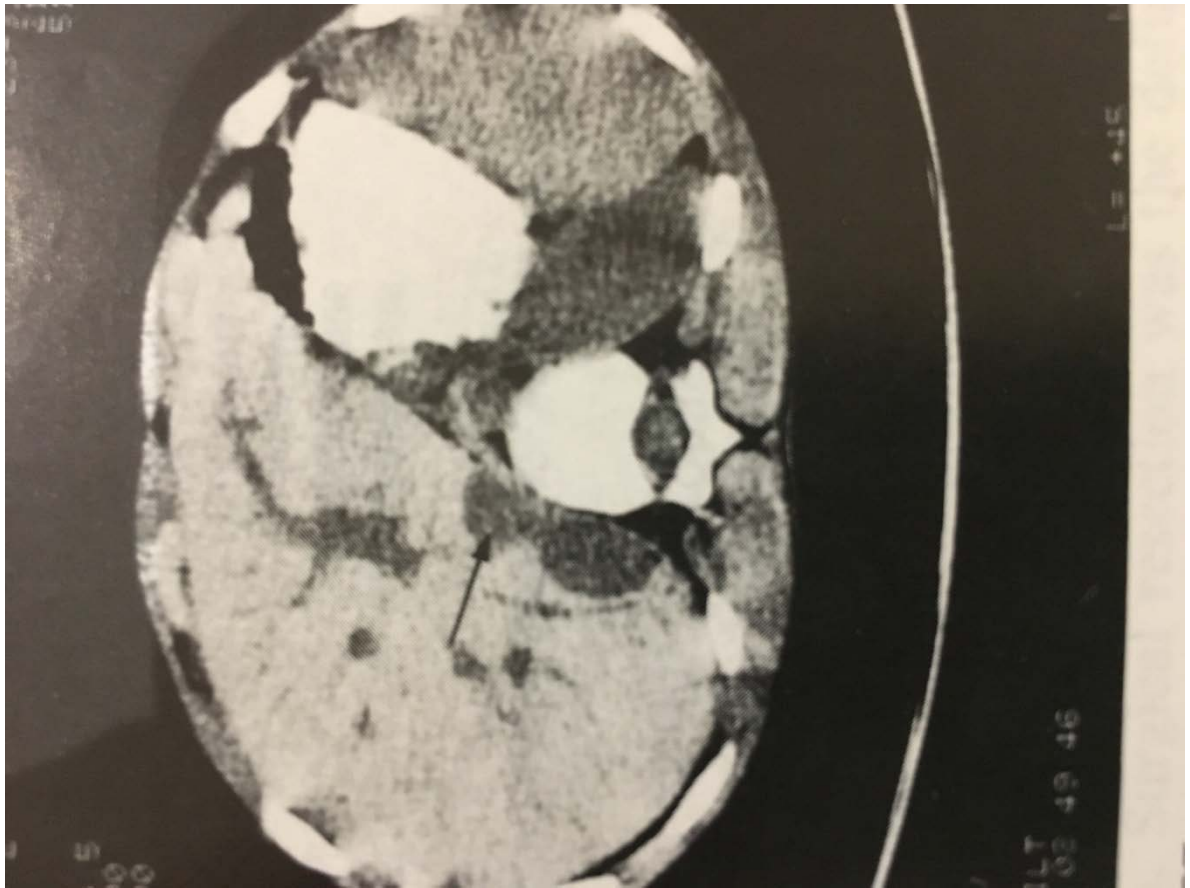


Figure 1: Computed tomography (CT) scan of abdomen reveals right adrenal mass which proved to be estrogen secreting abdomen.





GLOBAL JOURNAL OF MEDICAL RESEARCH: F DISEASES

Volume 17 Issue 1 Version 1.0 Year 2017

Type: Double Blind Peer Reviewed International Research Journal

Publisher: Global Journals Inc. (USA)

Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Role of Triphala Parishek in Lid Concretion : A Case Study

By Dr. Pratibha Upadhyay, Dr. Shamsa Fiaz & Shalakyia Tantra

Abstract- Concretions are small white or yellowish dots, usually less than 1mm in diameter, commonly seen on the undersides of the eyelids. They contain cell debris and calcium. They may be the result of past inflammation. Occasionally they cause irritation. If concretions are causing symptoms, the ophthalmologist intend to remove them. After using anaesthetic drop, concretions can usually be teased out with the tip of a hypodermic needle. In the case chosen in our study the patient has been suffering from ocular discomfort BE since 5 yrs gradually that patients complaint has been increasing in spite of using all the allopathic medicines as prescribed by the doctor. So here in our study triphala parishek is tried for 10 days in three sittings with gap of 10 days and patient got complete and gradual relief from the symptoms in duration of 2 months.

Keywords: *vartma sharkara, conjunctival concretions, netra parisheka, rasayana.*

GJMR-F Classification: *NLMC Code: WW 212*



Strictly as per the compliance and regulations of:



Role of Triphala Parishek in Lid Concretion : A Case Study

Dr. Pratibha Upadhyay ^α, Dr. Shamsa Fiaz ^ο & Shalakyia Tantra ^ρ

Abstract- Concretions are small white or yellowish dots, usually less than 1mm in diameter, commonly seen on the undersides of the eyelids. They contain cell debris and calcium. They may be the result of past inflammation. Occasionally they cause irritation. If concretions are causing symptoms, the ophthalmologist intend to remove them. After using anaesthetic drop, concretions can usually be teased out with the tip of a hypodermic needle. In the case chosen in our study the patient has been suffering from ocular discomfort BE since 5 yrs gradually that patients complaint has been increasing in spite of using all the allopathic medicines as prescribed by the doctor. So here in our study triphala parishek is tried for 10 days in three sittings with gap of 10 days and patient got complete and gradual relief from the symptoms in duration of 2 months.

Keywords: *vartma sharkara, conjunctival concretions, netra parisheka, rasayana.*

I. INTRODUCTION

Conjunctival concretions are of common occurrence and appear as minute hard yellow or white spots in the palpebral conjunctiva. They represent the inspissated degenerative products of leucocytes that wandered from epithelium and of cast off epithelial cells. Usually they cause no symptoms., however, they give rise to irritation and a foreign body sensation in eye. In ayurvedic texts there is immense description regarding various lid disorders of eye under the vartamagata roga in susruta uttar tantra.

Vartma Sharkara is among Vartmagata Roga (disorders in eyelids) that is explained among the twenty one types of Vartma Rogas described in Susruta Samhitha¹. All the three Doshas are involved in this disease (Sannipataja)² and is curable by Lekhana Karma (scraping procedures). Vartma Sharkara is characterized by a hard large Pidaka³ (eruption) with surrounding small densely arranged number of Pidakas inside the eyelid. As per Vagbhata⁴, Vartma Sharkara is described as Sikata Vartma. He described Sikata Vartma as Pidaka (eruptions) which are hard, rough, dry and resembling sand appearing inside the lids. Thus it can be said that it is a kind of small, hard, whitish or yellowish brown (resembling sand-Sikata eruptions in the posterior surface of the eyelids without any discharge. artificial tears during day time and lubricating eye ointments at bedtime are prescribed. Whereas if it gives symptoms like foreign body sensation, irritation it

should be removed by hypodermic needle under topical anaesthesia. This concretion removal by hypodermal needle almost all the time causes conjunctival damage and bleeding. Thus this study was planned to overcome this problem and to evolve a sustainable treatment modality to treat conjunctival concretions ^{5,6,7,8,9}.

a) Aim of the study

To develop a successful, safe and sustainable line of treatment in the management of conjunctival concretion according to the principles of Ayurveda.

II. MATERIAL AND METHODS

A Male patient having age 60yrs attended to eye OPD in the National Institute of Ayurveda, Jaipur, Rajasthan, with conjunctival concretion were selected as per the inclusion and exclusion criterias.

a) Inclusion Criteria

Patient with conjunctival concretions who complained of eye discomfort or eye irritation, lacrimation and foreign body sensation and who was willing to participate was selected for the present study irrespective of their age, race, religion, sex, caste and socio-economic status.

b) Exclusion Criteria

Patients having asymptomatic conjunctival concretion was excluded.

c) Diagnosis Criteria

Patients were diagnosed by using diffuse torch light and findings were further verified by the slit lamp examination.

d) Assessment Criteria

The assessment was done before treatment and after treatment. Also the follow up was done after one month after the treatment. The signs and symptoms were assessed by self-designed scoring system, described in the table No.1

Author α ρ: Phd scholar, Asso. Proff & Head, NIA, Jaipur.
e-mail: dr.pratibha5685@gmail.com

Table No. 1: Scoring system for the assessment

Symptom	Scoring System			
	1. Absent	2. Mild	3. Moderate	4. Severe
1. Foreign body sensation of the eye	No foreign body sensation	Occasionally present and not disturbing daily routine	Frequently present and disturbing daily routine	Present continuously disturbing daily routine
2. Eye discomfort or irritation	No discomfort or irritation	Occasionally present and not disturbing daily routine	Frequently present and disturbing daily routine	Present throughout the day and disturbing daily routine
3. Excessive lacrimation	No excessive lacrimation	Occasionally present, no need to wipe with handkerchief	Frequently present, needs to wipe with handkerchief and not disturbing daily routine	Present throughout the day, needs to wipe with handkerchief disturbing daily routine

Treatments: Thriphalādi Netra Parisheka contains equal quantity of powder of *Terminalia berelica* (Vibhitaka), *Terminalia chebula* (Haritaki), *Phyllanthus embilica* (Āmla), *Glycyrrhiza glabra* (Yashtimadhu) and

Symplocos racemosa (Lodhra) which is a commonly used formula in eye OPD of the National Institute of Ayurveda.

e) Data analyzing and Statistical methods

All the data was analyzed by Microsoft Excel-2007 and presented as percentages.

 Table No.3: Pharmacological properties of Thriphaladi Parisheka^{10,11,12,13,14,15,16,17,18.}

Name of the drug	Rasa	Guna	Virya	Vipaka	Dosha karma
<i>Terminalia chebula</i> (Haritaki)	Pancha rasa	Laghu Ruksha	Ushna	Madhura	Chakshushya, Rasayana
<i>Terminalia berelica</i> (Vibhitaka)	Kashaya	Laghu Ruksha	Ushna	Madhura	Chakshushya, Kapha-pitta Nashaka
<i>Phyllanthus embilica</i> (Āmla)	Pancha rasa	Laghu Ruksha	Sita	Madhura	Chakshushya, Rasayana Thridoshajit
<i>Glycyrrhiza glabra</i> (Yashtimadhu)	Madhura	Guru Snigdha	Sita	Madhura	Chakshushya, Balya Vata-pittajit
<i>Symplocos racemosa</i> (Lodhra)	Kashaya	Laghu	Sita	Katu	Chakshushya Kapha-pitta nashaka, Grahi

It is responsible for the purification action and pacifying of Kapaha Dosha. Maximum of them have Madhura Vipaka which is important for pacifying Pitta Dosha¹⁹. All of the ingredients contain Chakshushya property and Kashaya rasa.

III. DISCUSSION

According to the signs and symptoms mentioned in Ayurvedic classics Vartma Sharkara or Sikara Varma can be correlated with conjunctival concretion which is a degenerative condition of the conjunctiva. Old age and anterior segment chronic inflammations are the main causative factors of concretion. The present study also confirmed those

factors and another etiological factors also i.e. exposure to heat or sunlight frequently and long term exposure to near work which are the causative factors of eye diseases mentioned in Ayurvedic authentic texts. Concretions are more common in upper lids and present study also confirmed it.

Treatments are not essential if it is asymptomatic. However if it is present with symptoms should be removed by hypodermic needle under topical anaesthesia. The concretion removal by hypodermal needle almost all the time causes conjunctival damages with bleeding and most of the time it may be a cause for following conjunctival inflammations unless treated with a topical antibiotic. Ayurveda also advised to perform

Lekhana Karma or remove by scraping. Triphaladi Netra Parisheka with lukewarm decoction was performed to better purification of the eye. It was also helpful for the eliminating the irritation or foreign body sensation. Also it increases blood circulation inside the lids which increases drug absorption. Further Triphaladi Netra Parisheka consists with Chakshushya properties which are beneficial for the healthy maintenance of eye and has anti inflammatory and antimicrobial properties too.

IV. CONCLUSION

Hence it can be concluded that the above mentioned line of treatment is ideal remedy for the management of Varma Sharkara or conjunctival concretion because it completely cure almost all the signs and symptoms without any adverse effects. It was further proved that the treatment had a sustained effect even after one month of follow up period. This study can be evaluated on a large sample size to effectively access the treatment.

REFERENCES RÉFÉRENCES REFERENCIAS

- Susruts samhitha of Susruta, Uttara tantra 3/5-9, English translation by P V Sharma, Vol III, 1st edition, Chaukhambha Vishvabharati, Varanasi, 2010, pp 118.
- Susruts samhitha of Susruta, Uttara tantra 8/9, English translation by P V Sharma, Vol III, 1st edition, Chaukhambha Vishvabharati, Varanasi, 2010, pp 149.
- Susruts samhitha of Susruta, Uttara tantra 3/12, English translation by P V Sharma, Vol III, 1st edition, Chaukhambha Vishvabharati, Varanasi, 2010, pp 119.
- Ashtanga Hridayam of Vagbhata, Uttara sthana 8/18, English Translation by K R Srikantha Murthy, Vol III, 6th edition, Chowkhamba Krishnadas Academy, Varanasi, 2012, pp 77.
- Khurana A. K., Comprehensive Ophthalmology, 5th edition, New Age International (P) Limited Publishers, New Delhi, 2012, pp-81.
- Samar K Basak, Essentials of Ophthalmology, 5th edition, Current Books International, Kolkata, 2013, pp-153.
- http://eyewiki.aao.org/Conjunctival_concretions, access date 11/06/2016.
- <file:///C:/Users/User/Desktop/Conjunctival%20concretions%20-%20EyeWiki.htm>, access date 11/06/2016.
- http://www.eastlancseyecare.co.uk/eyecare_conditions_concretions.php, access date 11/06/2016.
- Ministry of Health and Family Welfare, AYUSH, Government of India, Ayurveda Pharmacopoeia of India, Vol I, Part IV/52, 1st edition, The Controller of Publications Civil Lines, Delhi, 2004, pp-128.
- Bhavaprakasha of Bhavamishra, MadhuVarga, Vidyotini Hindi Commentary, Edited by Brahmashankara Mishra, Part I, 11th edition, Chaukhambha Sanskrit Sansthan, Varanasi, 2004, pp- 788.
- Ministry of Health and Family Welfare, AYUSH, Government of India, Ayurveda Pharmacopoeia of India, Vol VIII, Part I/ 29, 1st edition, The Controller of Publications Civil Lines, Delhi, 2011, pp-93.
- Ministry of Health and Family Welfare, AYUSH, Government of India, Ayurveda Pharmacopoeia of India, Vol I, Part I / 17, 1st edition, The Controller of Publications Civil Lines, Delhi, 2011, pp-34.
- Ministry of Health and Family Welfare, AYUSH, Government of India, Ayurveda Pharmacopoeia of India, Vol VIII, Part I/ 1, 1st edition, The Controller of Publications Civil Lines, Delhi, 2011, pp-5.
- Ministry of Health and Family Welfare, AYUSH, Government of India, Ayurveda Pharmacopoeia of India, Vol VIII, Part I/57, 1st edition, The Controller of Publications Civil Lines, Delhi, 2011, pp-177.
- Ministry of Health and Family Welfare, AYUSH, Government of India, Ayurveda Pharmacopoeia of India, Vol I, Part I / 53, 1st edition, The Controller of Publications Civil Lines, Delhi, 2011, pp-112.
- Ministry of Health and Family Welfare, AYUSH, Government of India, Ayurveda Pharmacopoeia of India, Vol VIII, Part I/9, 1st edition, The Controller of Publications Civil Lines, Delhi, 2011, pp-32.
- Ministry of Health and Family Welfare, AYUSH, Government of India, Ayurveda Pharmacopoeia of India, Vol VIII, Part I/45, 1st edition, The Controller of Publications Civil Lines, Delhi, 2011, pp-143.
- Susruts samhitha of Susruta, Sutrasthana 45/51, English translation by P V Sharma, Vol I, Chaukhambha Vishvabharati, Varanasi, 2013, pp-426.



This page is intentionally left blank



Rectal Adenocarcinoma with Synchronous Brain Metastasis and Prolonged Overall Survival (OS)

By Losada Vila B, Gutiérrez Abad D, De Torres Olombrada MV & Pereira Pérez F

Fuenlabrada University Hospital

Abstract- A 61 years old woman with dizziness and gait disturbance in relation to brain metastases of a rectal adenocarcinoma (cT3N1M1). CT showed an unique frontal lesion and no further disease in other organs. Performance Status 1, so Digestive Tumors Committee decides surgical treatment of frontal brain metastasis and the histologic postsurgical examination showed microscopic affected margins.

Then, radiation therapy (RT) of brain with radiosurgery and short course 5x5 of the primary tumor with low anterior resection was completed. After 2 months of brain RT, liver progression was discovered and then we decided neoadjuvant chemotherapy mFOLFOX6 and bevacizumab x 5 cycles with stable liver metastases and no other lesions. Following, limited liver resection and adjuvant chemotherapy was performed with the same schedule.

No signs of tumor recurrence and more than 13 and 24 months of disease-free survival (DFS) and overall survival (OS) respectively was achieved in a metastatic cancer (brain metastasis) with usually OS 3 months.

Keywords: *brain metastases, rectal adenocarcinoma, radiosurgery.*

GJMR-F Classification: *NLMC Code: WB 344*



Strictly as per the compliance and regulations of:



Rectal Adenocarcinoma with Synchronous Brain Metastasis and Prolonged Overall Survival (OS)

Losada Vila B ^α, Gutiérrez Abad D ^σ, De Torres Olombrada MV ^ρ & Pereira Pérez F ^ω

Abstract- A 61 years old woman with dizziness and gait disturbance in relation to brain metastases of a rectal adenocarcinoma (cT3N1M1). CT showed an unique frontal lesion and no further disease in other organs. Performance Status 1, so Digestive Tumors Committee decides surgical treatment of frontal brain metastasis and the histologic postsurgical examination showed microscopic affected margins.

Then, radiation therapy (RT) of brain with radiosurgery and short course 5x5 of the primary tumor with low anterior resection was completed. After 2 months of brain RT, liver progression was discovered and then we decided neoadjuvant chemotherapy mFOLFOX6 and bevacizumab x 5 cycles with stable liver metastases and no other lesions. Following, limited liver resection and adjuvant chemotherapy was performed with the same schedule.

No signs of tumor recurrence and more than 13 and 24 months of disease-free survival (DFS) and overall survival (OS) respectively was achieved in a metastatic cancer (brain metastasis) with usually OS 3 months.

Keywords: brain metastases, rectal adenocarcinoma, radiosurgery.

I. INTRODUCTION

Colorectal cancer is the second leading cause of death in Spain and up to 20% is diagnosed in an advanced stage, normally with hepatic or lung metastasis. Brain metastases are an uncommon complication of colorectal cancer (1.8-5% of all BM), even more unusual in the beginning (<1%). Overall survival(OS) after diagnosis of BM is 2.6 to 7.4 months. However, we try to perform metastesectomies whenever possible.

We submit a rare case which unique frontal brain metastases of rectal adenocarcinoma without affecting other organs. Emphasize on a multidisciplinary approach to achieve a prolonged survival.

II. CASE PRESENTATION

A 61 year-old woman, with no personal previous history who debut with dizziness, gait disturbance and

Author α: Department of Medical Oncology, Fuenlabrada University Hospital, Madrid, Spain. e-mail: beatriz.losada@salud.madrid.org

Author σ: Department of Medical Oncology, Fuenlabrada University Hospital, Madrid, Spain. e-mail: dgutierrez@salud.madrid.org

Author ρ: Department of Radiation Oncology, Fuenlabrada University Hospital, Madrid, Spain.

e-mail: mariavictoria.detorres@salud.madrid.org

Author ω: Department of Digestive Surgery, Fuenlabrada University Hospital, Madrid, Spain. e-mail: fernando.pereira@salud.madrid.org

memory loss. Performance Status 1. Occasional bleeding tools. No fever.

First of all, brain CT showed a single lesion in left frontal lobe, so she was admitted to complete the study. To better qualify the lesion, brain MRI showed the same nodule, suggesting a metastatic disease (figure 1). As digestive disorders were recent too, colonoscopy was the third test: mass occupying lesión 100% of the circumference and medium rectum location. PA: low-grade colorectal adenocarcinoma. (figure 2)

CT chest-abdom-pelvis: no further disease. Pelvis MRI: 7cm tumor from anal margin.

Clinical ststage: cT3N1M1 (single brain metastasis). According to give a treatment with a curative intention, Tumor Committee decided brain surgery followed by short course rectal RT and low anterior resection (LAR).

III. DIFFERENTIAL DIAGNOSIS

Approaching to a brain lesion discovered with no previous recent trauma, bleeding or halo images suggesting infection or abscess; first possibilities are malignancies and the most frequent ones are lymphoma, metastasis and astrocytoma / glioblastoma multiforme. Less common are ependymoma, tumors of the pineal gland or choroid plexus.

In primary malignancies with brain metastases such as melanoma, lung, kidney or thyroid, brain lesions bleeding would be usual and MRI should be hyperintense on T2 lesion if bleeding was within 6 hours or hypointense on T2 if bleeding was after 24 hours.

Central view for MRI is hyperintense with abscess, while in the tumor is hypointense.

Definitive diagnosis is based on histology, and when the lesion is technically resectable, surgery resection must be performed with intraoperative confirmation.

IV. TREATMENT

Digestive Tumor Committee decided neurosurgery because it was an unique and resectable lesion (10.09.2013). Performance Status 1.

Definitive Histological diagnosis was a 3.1 x 2.2 x 2 cm metastasis of colorectal adenocarcinoma (CK20 +, CK7 - and CEA +) with extensive tumor necrosis. Microscopical surgical margin affected.

RT of primary tumor including pelvis and rectum in short course 5 sessions of 5Gy and subsequent LAR was accomplished on 25/11/13.

Definitive Histological diagnosis: rectum adenocarcinoma ypT4b N2a (4/39) L0V1 R1 (radial margin) Wild KRAS type and mutated NRAS.

Because of surgery infection, no possible "adjuvant" chemo. As brain margin affected and no chance of chemo, radiosurgery treatment in Central Nervous System (total dose of 35 Gy) was completed from 02/05/14 to 02/17/14.

PET-CT reassessment at 2 months (figure 3): liver metastatic spread in both lobes (Sg II 6 mm, 19 mm Sg III, VIII 7 mm Sg, Sg V 20 mm) without other evidence of disease.

Not seen in previous CT, probably present.

Performance Status 1. Chemotherapy treatment mFOLFOX6 + Bevacizumab schedule (25/02/14) was proposed due the new metastatic liver lesions. CEA normalization achieved after 5 cycles and CT showed stable disease and resectable liver metastases. Limited hepatic resection (06.18.14) in those segments with lateral ileostomy closure. Definitive Histologic Diagnoses was liver metastases sg II, III, V and VIII with 0.2 cm of clear margin.

Adjuvant treatment was mFOLFOX6 + Bevacizumab x 3 cycles and final toxicity was diarrhea and neuropathy. CT showed no signs of tumor recurrence at the end of treatment on 24/09/14. Actually Performance Status 0 and no neurologic symptoms.

Outcome and Follow-Up

More than 26 months of DFS and more than 36 months of OS.

V. DISCUSSION

Initial presentation as cerebral involvement is unusual, being 1-4% the incidence of brain metastases associated to colorectal cancer. According to Ko Chu Fang, 3773 patients with colorectal cancer were reviewed, which 37 (1.03%) developed metastases between 1970 and 1996. 55% had a solitary lesion while 45% were multiple. Regarding location, 62% were in temporoparietal lobes, 13% in cerebellum, 13% cerebellum and cerebrum, 8% frontal lobe and 4% in posterior fossa brain. Rectal origin occurs in 56.4%. [1]

This case is unusual in rectal cancer disease because of the synchronous diagnosis and absence of metastatic disease in other organs (liver and lung as usual). In Kye series, 39 patients presented with colorectal brain metastases, 79.5% presented with pulmonary metastases and only 1% as an exclusive involvement in brain. [2] In E Magni serie of 41 patients, 4.9% did not involve other extracranial metastatic locations [3]

Diagnosis of brain metastases appear after a mean of 36 +/- 19 months and diagnosis of colorectal cancer in 77% of reported cases, with just a remaining 23% present in the beginning. In E Magni serie, 17.1% was synchronous too.

According to the treatment, a literature review only describes very few cases treated with radiosurgery, being this indication increasing in those patients with multiple lesions <35 mm, minimum mass effect and affected margins.

Results in NCCTG N0574 (Alliance) demonstrated better OS and quality of life with radiosurgery + RT [4]. Recently, a literature review of 80 patients with brain metastasis reported OS of 6 months in patients who received gamma knife radiosurgery (22 patients), 3 months in whole radiotherapy and 13 months in 10 patients on gamma knife + whole radiotherapy. [5]

Among a serie of 41 patients (E Magni) OS after diagnosis of brain metastases was 5 months: 4.2 months in patients treated with radiotherapy (29.3%), 11.9 months in those with radio and chemotherapy (21.9%), and 21.4 months in those with surgery +/- radio or chemotherapy (29.3%).

We emphasize our case with OS 24 months, never published.

Also, prognostic factors in colorectal cancer has been studied to determine the best therapeutic approach. KRAS mutated patients use to present more common pulmonary and CNS involvement (62 and 56.5%), and liver metastasis are less common. [6].

Regarding primary tumor treatment, Shin et al published the results of RT short course schedule (5 days x 5 Gy) and it seems to be effective in local control and "down-staging" with 85% R0 resections. [7,8]

However, when hepatic progression is demonstrated, chemo is the preferred treatment. Adam showed a survival benefit after surgery in liver tumors in response, however this benefit was lower in progression disease. In the case, we decided initially neoadjuvant CT (ESMO Guidelines) with Bevacizumab (KRAS mutated) (Cairo-2, ARTIST): 45-55% RR, PFS 9-12 months. [9,10,11]. As a partial response was achieved after chemo and liver resection was feasible too, liver surgery was performed because of the impact on survival. [12]

And our last point: chemo maintenance? OPTIMOX trial showed no difference in survival compared to maintenance treatment until progression, so both options are a good idea and depends on the tolerability and performance status of each patient [13]

Learning Points/Take Home Messages

- ✓ Debut of rectal cancer with synchronous single and unique frontal brain metastasis is unusual.
- ✓ Overall survival in brain metastases from colorectal cancer is less than 6 months; achieving with

radiosurgery + radiotherapy up to 11 months in literature and in our case >24 months.

- ✓ Differential diagnosis of single brain lesion by image is inconclusive. Definitive diagnosis can be achieved with surgery.
- ✓ Radical surgery treatment of metastatic brain lesion improves prognosis and quality of life. Thinking in isolated brain metastasis as oligometastatic disease.
- ✓ In this case we demonstrate liver progression with PET-CT. This technique is useful for surgical decisions.
- ✓ Overall survival > 2 years from the debut despite poor prognostic factors (KRAS mutated, brain and liver metastases).
- ✓ Benefit of multidisciplinary approach.

REFERENCES RÉFÉRENCES REFERENCIAS

1. Ko FC, Liu JM, Chen WS et al. Risk and patterns of brain metastases in colorectal cancer: 27-year experience. *Dis Colon Rectum*. 1999 Nov; 42(11): 1467-71.
2. Kye BH, Kim HJ, Kang WK, et al. Brain metastases from colorectal cancer: the role of surgical resection in selected patients. *Colorectal Dis*. 2012 Jul; 14(7): e378-85.
3. E Magni, L Santoro, P Ravenda et al. Brain metastases from colorectal cancer: main clinical factors conditioning outcome. *Int J Colorectal Dis*. 2014; 29: 201-208.
4. Brown PD, Asher AL, Ballman KV et al. NCCTG N0574 (Alliance): a phase III randomized trial of whole brain radiation therapy (WBRT) in addition to radiosurgery (SRS) in patients with 1 to 3 brain metastases. *J Clin Oncol* 2015; (suppl; abstr LBA4).
5. Morovic JA, Chang SD (2011). Literature review of various treatment plans and outcomes for Brain Metastases from colorectal cancer *World Neurosurg* 79 (3-4): 435-436.
6. Sahgal A, Aoyama H, Kocher M et al. Phase 3 trials of stereotactic radiosurgery with or without whole-brain radiation therapy for 1 to 4 brain metastases: individual patient data meta-analysis. *Int J Radiat Oncol Biol Phys*. 2015 Mar 15; 91(4): 710-7.
7. Tie J, Lipton L, Desai J et al. KRAS mutation is associated with lung metastasis in patients with curatively resected colorectal cancer. *Clin Cancer Res*. 2011 Mar 1; 17(5): 1122-30.
8. Shin SJ, Yoon Hii, Kim NK et al. Upfront systemic chemotherapy and preoperative short-course radiotherapy with delayed surgery for locally advanced rectal cancer with distant metastases. *Radiat Oncol*. 2011 Aug 24; 6: 99.
9. Pettersson D, Cedermark B, Holm T et al. Interim analysis of the Stockholm III trial of preoperative radiotherapy regimens for rectal cancer. *Br J Surg*. 2010 Apr; 97(4): 580-7.
10. Adam R, Pascal G, Castaing D et al. Tumor progression while on chemotherapy: a contraindication to liver resection for multiple colorectal metastases? *Ann Surg*. 2004 Dec; 240(6): 1052-61.
11. Schmoll HJ, Van Cutsem E, Stein A et al. ESMO Consensus Guidelines for management of patients with colon and rectal cancer. a personalized approach to clinical decision making. *Ann Oncol*. 2012 Oct; 23(10): 2479-516.
12. Chu E. Dual biologic therapy in the first-line mCRC setting: implications of the CAIRO2 study. *Clin Colorectal Cancer*. 2008 Jul; 7(4): 226.
13. Poultsides GA. Reassessing the need for primary tumor surgery in unresectable metastatic colorectal cancer: overview and perspective. *Ther Adv Med Oncol*. 2011 Jan; 3(1): 35-42.
14. Chau, Cunningham D. Treatment in advanced colorectal cancer: what, when and how?. *Br J Cancer* 2009 Jun 2; 100(11): 1704-19.

FIGURE CAPTIONS

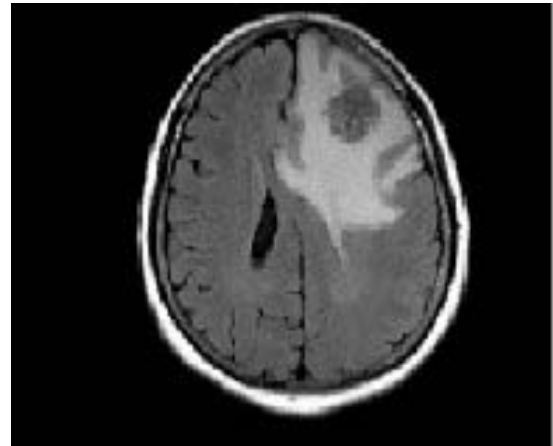


Figure 1: Unique frontal brain metastases



Figure 2: Low-grade colorectal adenocarcinoma

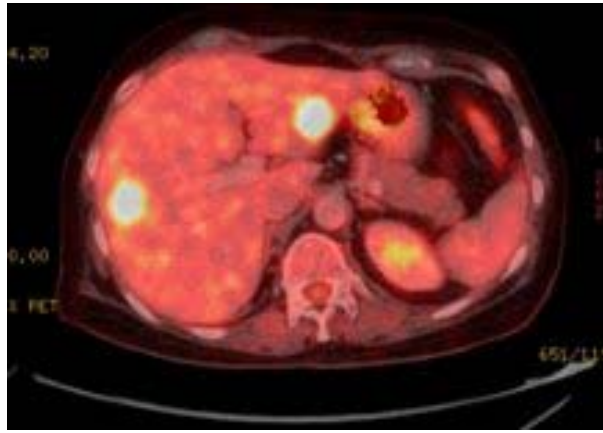


Figure 3: Liver metastatic spread in both lobes (Sg II 6 mm, 19 mm Sg III, VIII 7 mm Sg, Sg V 20 mm)





Detection of Intron22 Mutations in Iraqi Female Carriers in Wasit Province with Hemophilia A

By Maysoon Mohammed Hassan

Wasit University

Abstract- *The background:* One of the prevalent main concerns in the medical world is the identification of Intron22 mutations in the Factor VIII gene carried by Iraqi patient in Wasit town, in Iraq suffering Hemophilia A (classical hemophilia) which is related to a X-chromosome recessive haemorrhage afflictions as the result of a flaw in the coagulation factor VIII (FVIII). It is essentially related with F8 mutations of Intron22 inversion which forms the most typical kind of mutations of blood afflictions worldwide involving half the patients suffering from severe Hemophilia A that possesses mutations, in addition to Intron 1 inversion suffered by 5% of severe Hemophilia A patients. All of the inversion mutations are suffered mainly by males, and uncommonly by females due to the intrachromosomal recombination among the homologous areas, in inversion 1 or 22, with extragenic copy posited the telomeric to the Factor VIII gene. Unfortunately, there is an absence in Iraq on researches pertaining blood affliction gene identification in persons who carries the Intron22 mutations exception in the current research.

Aims of study: The objectives of the research is to to analyze through the detection mechanisms, the existence of Intron 22 mutations in the Factor VIII gene of 10 Hemophilia A Iraqi carriers cohort families. The hypothesis and anticipated result is that there will be a minimal margin of hazardous possibility for the recurrence. The hereditary F8 mutation is unknown to be present on the maternal side of the patient sufferer due to the possibility of germline mosaics that exists within the community.

Keywords: *Hemophilia A, Factor 8 gene, Carriers, Intron 22 mutations.*

GJMR-F Classification: *NLMC Code: WH 325*



DETECTION OF INTRON22 MUTATIONS IN IRAQI FEMALE CARRIERS IN WASIT PROVINCE WITH HEMOPHILIA A

Strictly as per the compliance and regulations of:



RESEARCH | DIVERSITY | ETHICS

Detection of Intron22 Mutations in Iraqi Female Carriers in Wasit Province with Hemophilia A

Maysoon Mohammed Hassan

Abstract- *The background:* One of the prevalent main concerns in the medical world is the identification of Intron22 mutations in the Factor VIII gene carried by Iraqi patient in Wasit town, in Iraq suffering Hemophilia A (classical hemophilia) which is related to a X-chromosome recessive haemorrhage afflictions as the result of a flaw in the coagulation factor VIII (FVIII). It is essentially related with F8 mutations of Intron22 inversion which forms the most typical kind of mutations of blood afflictions worldwide involving half the patients suffering from severe Hemophilia A that possesses mutations, in addition to Intron 1 inversion suffered by 5% of severe Hemophilia A patients. All of the inversion mutations are suffered mainly by males, and uncommonly by females due to the intrachromosomal recombination among the homologous areas, in inversion 1 or 22, with extragenic copy posited the telomeric to the Factor VIII gene. Unfortunately, there is an absence in Iraq on researches pertaining blood affliction gene identification in persons who carries the Intron22 mutations exception in the current research.

Aims of study: The objectives of the research is to to analyze through the detection mechanisms, the existence of Intron 22 mutations in the Factor VIII gene of 10 Hemophilia A Iraqi carriers cohort families. The hypothesis and anticipated result is that there will be a minimal margin of hazardous possibility for the recurrence. The hereditary F8 mutation is unknown to be present on the maternal side of the patient sufferer due to the possibility of germline mosaics that exists within the community.

Patients and Methods: The current research involved 10 Iraqi Hemophilia A carrier, and 5 healthy sampling to act as the control. This study had utilized medicine and science school labs, with the inclusion of AL Karama Teaching Hospital over a time period from November, 2016 up to January, 2017. The aforementioned respective carriers have a previous history of diagnosed case history and DNA testing.

Results: During the whole of the screening duration for Inv22 (intron twenty two inversions) amongst the Hemophilia A carriers, the outcomes indicated that 4 out of the 10 carriers (40%) suffer from these mutations.

Discussion: The research findings highlights on the significance of the Inv22 analysis and their relationship with positive hereditary case history within the Hemophilia A carriers, in addition to our ongoing pursuit of seeking for Inv1 mutations.

Conclusions: The outcomes defines the detrimental influence of a diagnosed positive family case history and the proximal affinity lineage in marriage. There is a dire necessity

for Hemophilia A carriers to be given specialized and dedicated obstetrical attention with close contact with the haemophilia centre, in addition the management processes concerning the case should be available ought and identified.

The outcome manifests the pathway towards a genetic guideline. Having the information pertaining the gender of the foetus gender is significantly crucial to assist in the supervision of labor, in addition to diagnostic processes.

Keywords: Hemophilia A, Factor 8 gene, Carriers, Intron 22 mutations.

I. INTRODUCTION

Hereditary haemorrhage afflictions are specifically challenging and impacts on the majority of ladies and young females due to the monthly discharge of menses, thus impacting on the wellbeing of the reproductive system(1). On another note, males globally are susceptible to be sufferers of Hemophilia A (HA) due to the hereditary X-chromosome related to haemorrhage afflictions, in the majority part is related to Factor VIII gene mutations, which leads to the inadequacy of clotting Factor VIII (FVIII) which plays a significant role in hemostatic system (2). This condition inflicts one per 5,000 males globally. The natality incidences worldwide is homologous regardless of ethnicity, perhaps due to the great impetuous degree of mutation in F8 and its presence situated on the X chromo-some(3). Hemophilia A (HA) is manifested in a limited diverse range of clinical acuteness, with the respective diversity which are parallel to the type and locus of the induced genetic flaw (4:5). Hence, Hemophilia A is the result of a heterogeneous range of flaws that occur at the molecular level in Factor VIII alongside the elisions, huge intron inversions, nonsense mutations, ins/del-frame shifts, splice variants, in addition to an extensive scope of missense point mutations. The aforementioned elements have the possibility to result in flaws within the expression, secretion, and/or half-life of Factor 8 in the flow (6).

The identification of the carrier and symptomatic process might be delivered straight through the evaluation on the diverse ascertained mutations or evasively according to case (lineage) history through analyzing the relationship (7).

The remnant functioning of plasmatic Factor 8 in heterozygous carrier females of severe F8 mutations is identified as a non-dominant X-linked disorder, which is typically found at fifty percent of a person who is not a carrier. Although extremely uncommon, homozy-

Author: (MSc). Zoology-Biotechnic-Genetic, Department of Biology, College of Dentistry, Researcher in Medicine college, Research Laboratory- Wasit University. e-mail: mayalsaraf@gmail.com

gous females who were offsprings of afflicted paternal parent, in cases of marriages with close next-of-kin have a higher potential to be inflicted with blood disorder (Hemophilia) in a likewise situation to hemizygous male patients, and alternatively in Turner Syndrome cases ($45,X^0$) (8). Nevertheless, typical hemophilia (blood disorder) cases of expression in females are caused by the presence of biased Lyonization (biased X chromosome inactivation), in addition to the heterozygous carrier situation (Morris syndrome, 46,XY) (9).

A majority of female are commonly asymptomatic, nonetheless, females have the possibility to be symptomatic (10). According to Haldane's formula (Haldane, 1935) it is anticipated that one-sixth of hemophilia genes are dominant in each generation. Hemophilia A, hence, manifest an extremely great level of mutational heterogeneity which conceals the carrier and prenatal diagnoses which are essential for genetic advisory (11).

The Factor VIII gene embed the code plasma protein VIII, a huge plasma glycoprotein that operates in the clotting cascade, being a cofactor for the factor IXa-dependent that activates the factor X(12).The Factor 8 gene consists of 26 exons, that has a wide diversity from 69 to 3,106 base pairs (bp), with 25 introns encompassing the range of 186-kb genomic DNA, which are plotted to the remote end of X-chromosome (Xq28) long arm. Intron arrangement order is 177.9 kb, and are separated from the initial transcript product through the entire splicing towards the generation of a mature Factor VIII mRNA of approximately 9 kilobytes in length which exhibits a precursor protein containing 2,351 amino acids.

From the more extensive intron arrangement orders, there is an inclination to discover six which is more extensive than fourteen kilobyte (introns-1, 6, 13, 14, 22 and 25), having intron 22 being largest at 32.8 kilobyte in terms of length (13), with Intron twenty two inversion (Inv22) entailing the typical public type in approximately forty to forty-five percent of acute hemophiliacs, in addition from two up to five percent of acute Hemophilia A incidences are full of Intron one inversion (Inv1) (14:15).

According to the work by Rossiter et al. (1994), they discovered that Inv22 stemmed largely and significantly from the male germ cells. They conjectured the existence of another X chromosome in female meiosis could inhibit the intrachromosomal non-allelic pairing required for Intron twenty two inversion (16). Every individual inversions is the resultant from the non-allelic meiotic intrachromosomal recombination among the int22h-1 region within the Factor VIII site, with either int22h-2 or int22h-3, within the male germ cells (16). Int22h-1 recombines with the ultimate telomeric duplicate which is normally is mutually inclined to int22h-1, and commonly it entails int22h-3. The aforementioned

int22h-1/int22h-3 recombination results in the inv22 sort I. Furthermore, a minority of incidences, the inversion was disclosed to be caused by the two recombination occurrences. The beginning stage involved a recombination between the arms of the palindrome inv22h-2/ inv22h-3, which was identified as a public non-deleterious inversion polymorphism. The event altered the locations and inclinations of int22h-2 and located it at the optimal telomeric and inverse location to inv22h-1. The next recombination between inv22h-1 and inv22h-2 terminates in inv22 sort II (17). Moreover, the recombination among the int22h-1 with the equally leaning duplicate of either int22h, int22h-2 or int22h-3 is anticipated to be the cause for huge harmful deletions (Del22), in addition to the possible non-deleterious duplications (Dup22), in contrast with the typical inversions (18). The inversions that occur in individuals with two distal or two proximal estrogenic duplicates are known as type3 inversions (19).

The serial arrangement order of the human X chromosome manifests the int22h-2 and int22h-1 to have an exact positioning, meanwhile the int22h-3 is located at the opposite position to them; where int22h-2 and int22h-3 are part of defective palindrome possessing a central single loop of 67,3 kilobytes, with arms of 50,5 kb (20).The recombination involving the int1h-1 and int1h-2 copies from sister chromatids or homologous chromatids with the chromosomes, would result in dicentric chromosomes and acentric portions. Thus, it would not result in potential embryos. The inv1 and inv22 inhibited the construction of a complete length of the Factor VIII messenger RNA (mRNA), and terminates in the inadequate Factor VIII proteins causing acute HA)(21:14).

Based on the latest to proof, intron22 segregates the exons 22 and 23 (IVS22) consisting of the incidences of a bidirectional (CpG island) which initiates the transcription of a duo of expressed genes (nested genes, F8A and F8B). It is a part of an extensive GC sequence of 9.5 kilobytes (int22h-1) which recur at two locations oriented at the the Xqtelomere (int22h-2 and int22h-3)(20). According to the the opinion of Youssoufian et al. (1986), the statements showed that CpG dinucleotides areal areas of mutation. It was conjectured that methylated cytosines is equally critical areas for mutations caused by 5-methylcytosine will spontaneously deaminate to thymine, resulting in a C-to-T transition in DNA (22). This CpG island was associated to a 1.8 kilobyte transcript elevated to A gene (F8A). The nested Factor VIII associated A gene was positioned in an opposite orientation to that of Factor VIII, comprising of non-intervening arrangements (23;24). From the work by Freije and Schlessinger (1992), the subsequently indicated that the X-chromosome comprises three replications of Factor 8A and its adjacent areas, one in intron 22 and two telomeric and approximately five

hundred kilobyte up the F8 gene transcription initiation site(25).

Meanwhile the F8B transcription of 2.5 kb originates from identical F8 intron22 CpG island, due to the F8A and transcribes in the same orientation as F8. The CpG island functions to encourage bidirectional acts for the F8A and F8B genes, which are jointly manifested universally all over in diverse tissues.

The varying F8A and F8B transcripts initiates from within the 122 bases of each starting point(24).

The codification of a forty kD huntingtin-linked protein was indicated to originate from the F8A gene, known as HAP40 and is assumed to be related inside the abnormal nuclear local positioning of the hunting-tin protein in Huntington ailment(26). From the study by Lakich et al. (1993), they disclosed the rare occurrence of intron 22 in many ways. Comprising 32.8 kb, it is the most expansive intron in the Factor VIII gene. The two mutations that resulted in diseases and neutral polymorphisms appear renewed in each new generation. In the case of a world population of $7 \cdot 10^9$ people and a mean mutation frequency of 10-8 for each base pair and generation. It is obvious that

entire transformations associated with life will undergo mutation recurrence once(27).

The mutation (intron 22 inversion) happen approximately 4×10^{-6} for each gene, for each gamete, and for each generation (15,28). (29). Inv22-positive patients manifest heightened potential towards the hazard of raising the inhibitors in comparison with patients resonating alternative acute mutations (30).

II. THE AIMS OF STUDY

The objective of the current study is to identify the presence of intron 22 mutations in the non-coding FVIII gene of 10 gender-associated afflictions (hemophilic) Iraqi carrier kinship group by Polymerase Chain Reaction (PCR) through Multigene Optimax (Thermo Cycler) device, in addition to and direct sequencing in analyzing inversion. Intron 22 primer with 1916 base pairs generations indicated in figures no.(1),(2),(3) through the utilization of various differing programs for the mutations analysis that consist of NTI vector Pro., Clustal W technique of MEGA4 pro., NCBI/BIAST program, Chromos Pro, Mutation Surveyor.

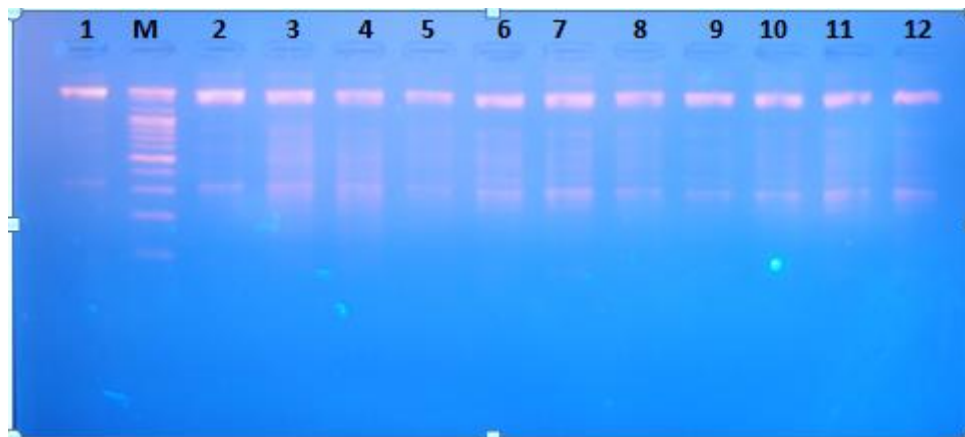


Figure 1: PCR products of FVIII gene on 2% agarose gel at 70 voltages for one hour. Intron22.

Lane 1T: Lane-M-standard molecular weights: Lane 2, 3, 4, 5, 6, 7, 8, 9, 10, C, 11: Lane 12T. Gel was stained with Ethidium bromide staining. *C for carriers; T for control

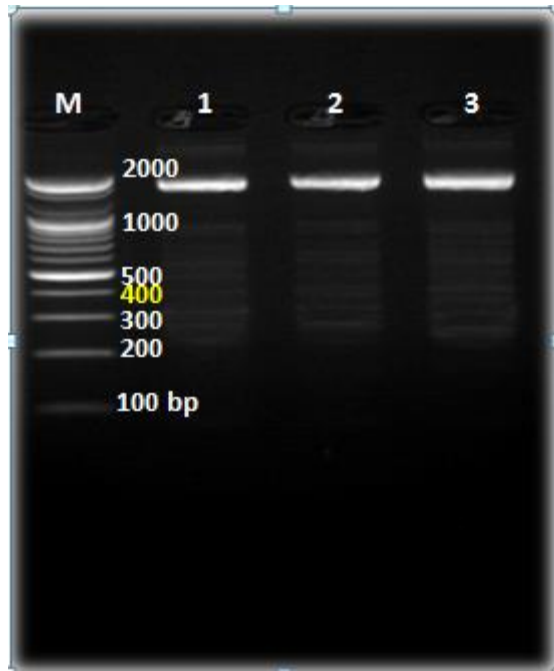


Figure 2: PCR products of FVIII gene on 2% agarose gel at 70 voltages for one hour. Intron22.

Lane-M-standard molecular weights: Lane 1T: Lane 2, 3, C. Gel was stained with Ethidium bromide staining.

*C for carriers; T for control

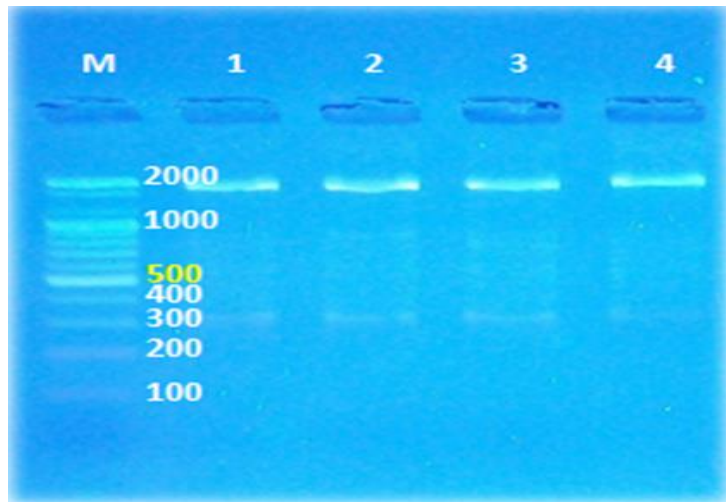


Figure 3: PCR products of FVIII gene on 2% agarose gel at 70 voltages for one hour.

Intron22 - Lane-M-standard molecular weights: Lane 1T: Lane 2, 3, C. Gel was stained with SYBER Green staining.

*C for carriers; T for control.

Collection of samples

This study has enclosed ten Iraqi carriers with classical hemophilia (hemophilia A) from unrelated families and five healthy members as control, were collected from Al-Karama teaching hospital, in Wasit province- kut-city. The age of carriers were ranged from twenty four to sixty four year.

III. METHODS

All samples study of hemophilia A completed in medicine, science college and of AL-Karama Teaching

Hospital laboratories .These carriers formerly identified based on family history, DNA testing. and a few information like age, sex, relative state. After checking the extracted DNA for its purity and concentration, its being subjected to amplification to choose area of F VIII, which has intron 22 then Sequencing has being Conducted for intron22 for all carriers and control for molecular analysis that detection of mutation of commonest segment of FVIII gene. Figure (4) shown PCR product of intron 22 for carrier sand control.

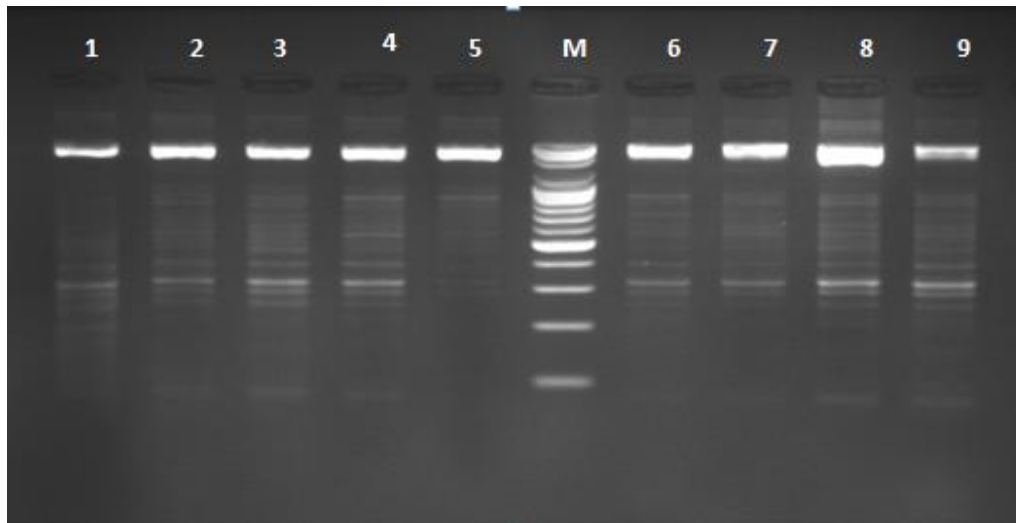


Figure 4: PCR products of FVIII gene on 2% agarose gel at 70 voltages for one hour. Intron22

Lane 1, 2, 3, 4, 5 C: Lane-M-standard molecular weights: Lane 6, 7, 8, 9 T. Gel was stained with Ethidiumbromide staining. *C for carriers; T for control.

IV. CARRIER DETECTION

Approximately 10 percent of females with one F8 pathogenic variant and one normal allele have a factor VIII clotting activity under than thirty percent a bleeding disorder; mild bleeding can take place in carriers with low-normal coagulation factor 8 activity (38).

In this study all carrier females are asymptomatic because of the lyonization phenomenon and FVIII activity is over fifty percent that genetic defects are known by family history assess men (39; 40).

Carrier testing by molecular genetic testing is feasible for utmost at-risk females if the pathogenic variant has been known within the family. Factor VIII clotting activity, or its ratio to von Willebr and factor level, isn't a reliable check for determinant carrier status: it will solely be suggestive if low, because factor VIII

coagulation activity in plasma is augmented with pregnancy, aerobics exercise, oral contraceptive use, and chronic inflammation. factor VIII coagulation activity in plasma is just about twenty five percent lower in people of blood group O than in people of blood groups A,B, or AB and therefore the majority of obligate carriers, even of severe hemophilia A, have normal factor VIII clotting activities.

V. RESULTS

a) DNA Isolation

The genomic DNA extracted from blood of Hemophilia A patients showed good single band when fractionated by gel electrophoresis as show in figure no. (5) then checked for their purity and by using spectrophotometer device.

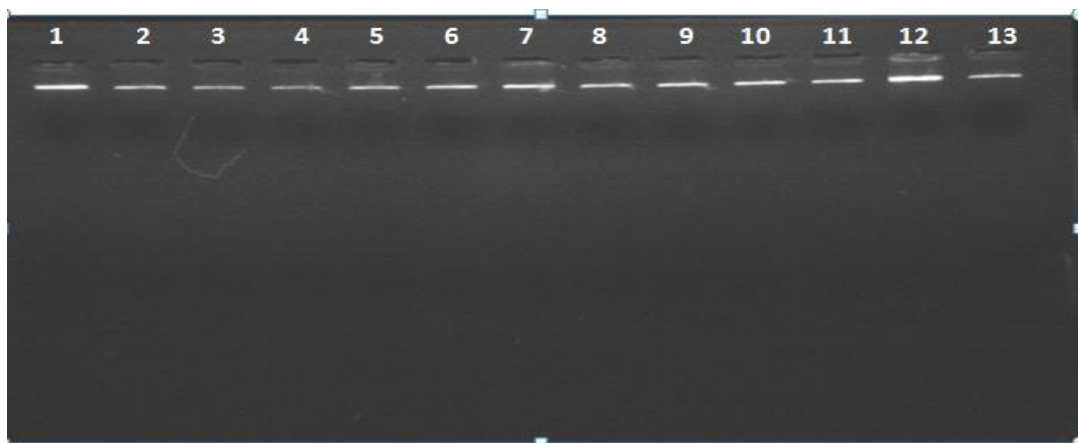


Figure 5: Chromosomal DNA electrophoresis showing bands on 2 % agarose gel at 70 volt/ cm² for 1 hour.

Lane (1) -C, Lane 2 C, Lane 3 C, Lane 4 -C, Lane 5 C, Lane 6 C, Lane 7 C, Lane 8 C, Lane 9 C, Lane 10 C, Lane 11 T, Lane 12 T, Lane 13 T. Gel was stained with Ethidium bromide staining and using loading dye.

*C for carriers; T for control

b) DNA sequence analysis

Sequencing has been run for all the exons and intron 22 for all patients and control for process of determining the exact order of nucleotides within a DNA molecule. It includes any method or technology that is used to determine the order of the four bases (adenine, guanine, cytosine, and thymine) in a strand of DNA. The analysis of nucleotide sequencing was done by using NCBI/Blast computer program, Nucleotide sequences were translated into amino acid sequences also by using the Blast program. Each DNA sequence obtained was aligned with reference F VIII gene sequence that means reference Genomic DNA for intron22 then, same sequence being aligned with Mutation Surveyor software

to check the normal variation and checking amino acid change.

The study was done for 10 hemophiliac carriers (mothers), and 5 control samples, to detect intron 22 inversion which responsible for hemophilia disease. All control samples were obtained from female gender. We found Inv22 mutations in 4 from 10 carriers. During the screening for Inv22 mutations among the HA carriers and controls, we did not find this mutation or gene abnormality in all controls. family history and consanguinity state of haemophilia was recorded in some carriers. Percentage of Hemophiliac carriers group data is depicted in (Table1).

Table 1: Percentage of Hemophiliac Carriers Group Data

Carriers sample no.	Mutation segment	Mutation\Genome		Mutation type	Family history		Consanguinity state	
		Yes	No		Positive	Negative	Positive	Negative
1	Intron 22	nill		-	negative		positive	
2	Intron 22	nill		-	negative		negative	
3	Intron 22	Inth22		Inversion	negative		negative	
4	Intron 22	Inth22		Inversion	positive		negative	
5	Intron 22	Inth22		Inversion	positive		negative	
6	Intron 22	nill			positive		positive	
7	Intron 22	Inth22		Inversion	positive		positive	
8	Intron 22	nill		-	negative		negative	
9	Intron 22	nill		-	positive		positive	
10	Intron 22	nill		-	positive		negative	
Total								
		4	6		60%	40%	40%	60%
		10						

Mutations screening conducted throughout the study shows that most common mutations and located in, intron 22. Carrier no.3 appears in this study aligned was regarded as first carrier detect with intron 22 inversion of the FVIII gene reveal with no family history and consanguinity state as showed in figures no(6,7).

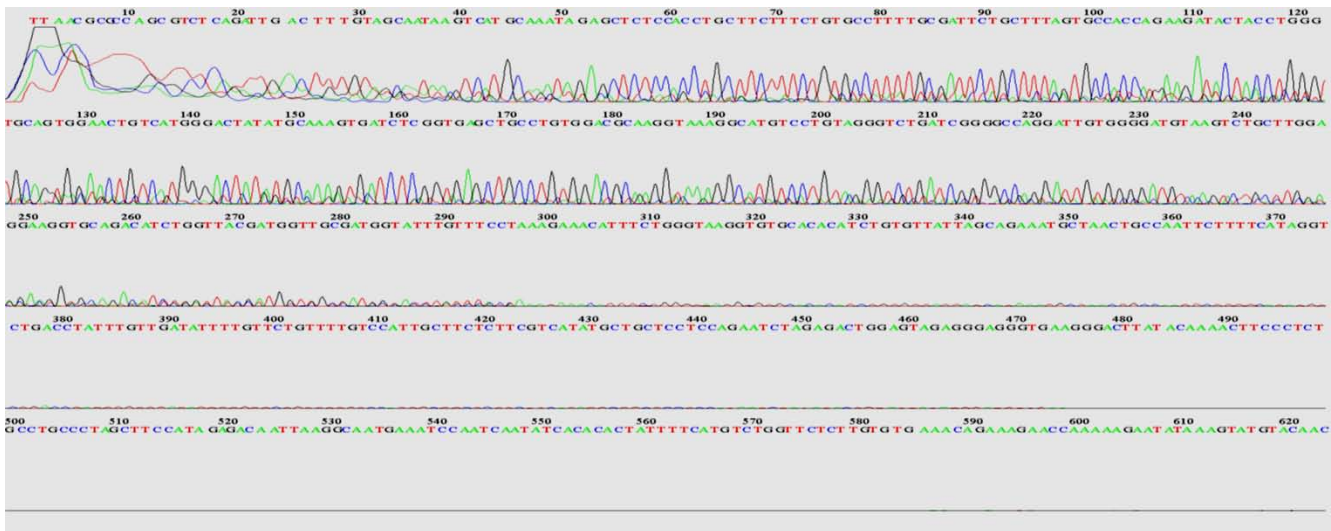


Figure 6: DNA sequencing (forward) for carrier no. 3 detect with Inv22.

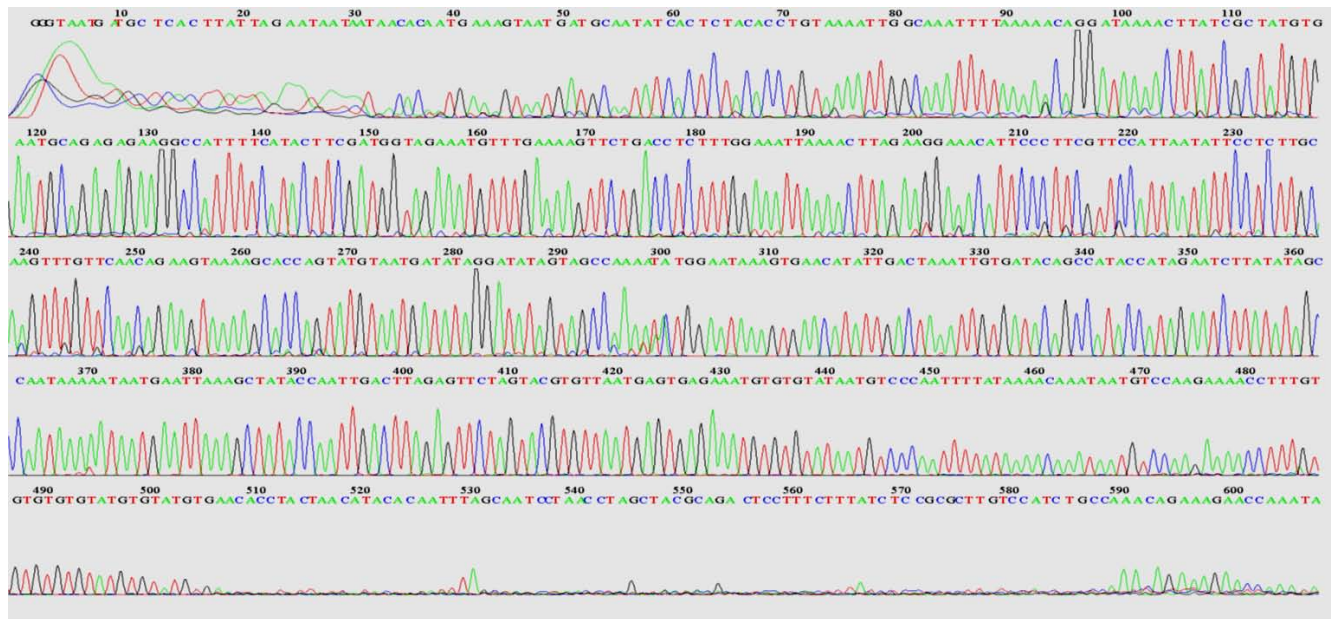


Figure 7: DNA sequencing (reverse) for carrier no. 3 detect with Inv22.

Carrier no.7 appears in this study aligned was regarded as first carrier detect with intron 22 inversion of the FVIII gene reveal with positive family history and consanguinity state as showed in figures no(8,9).

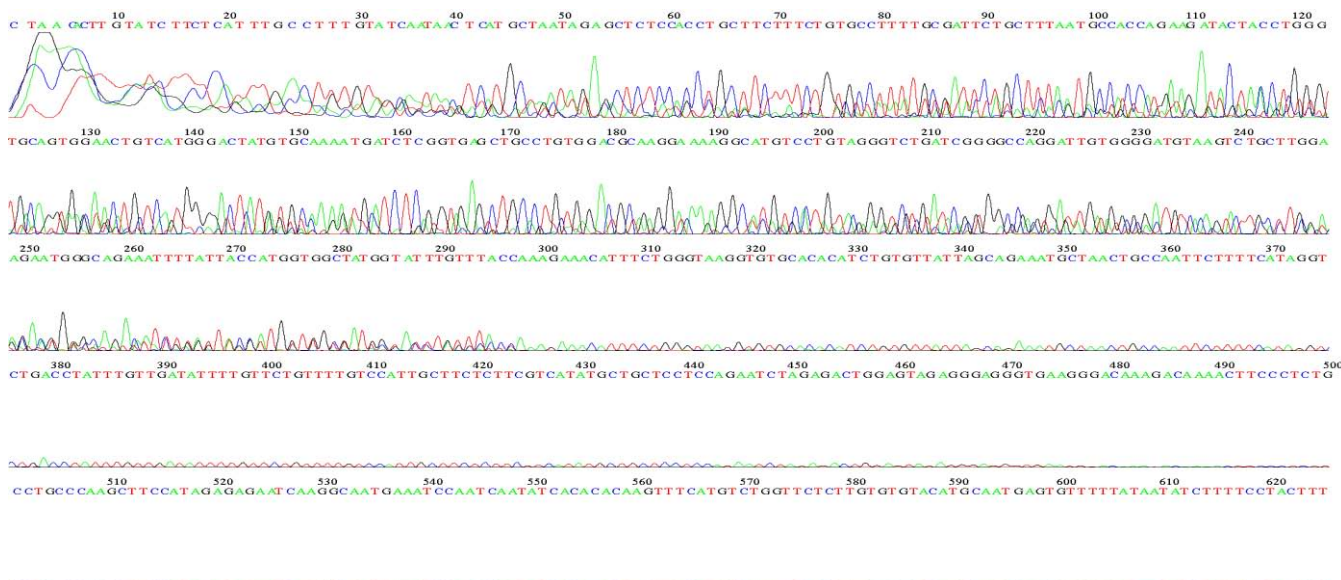


Figure 8: DNA sequencing (forward) for carrier no. 7 detect with Inv22.

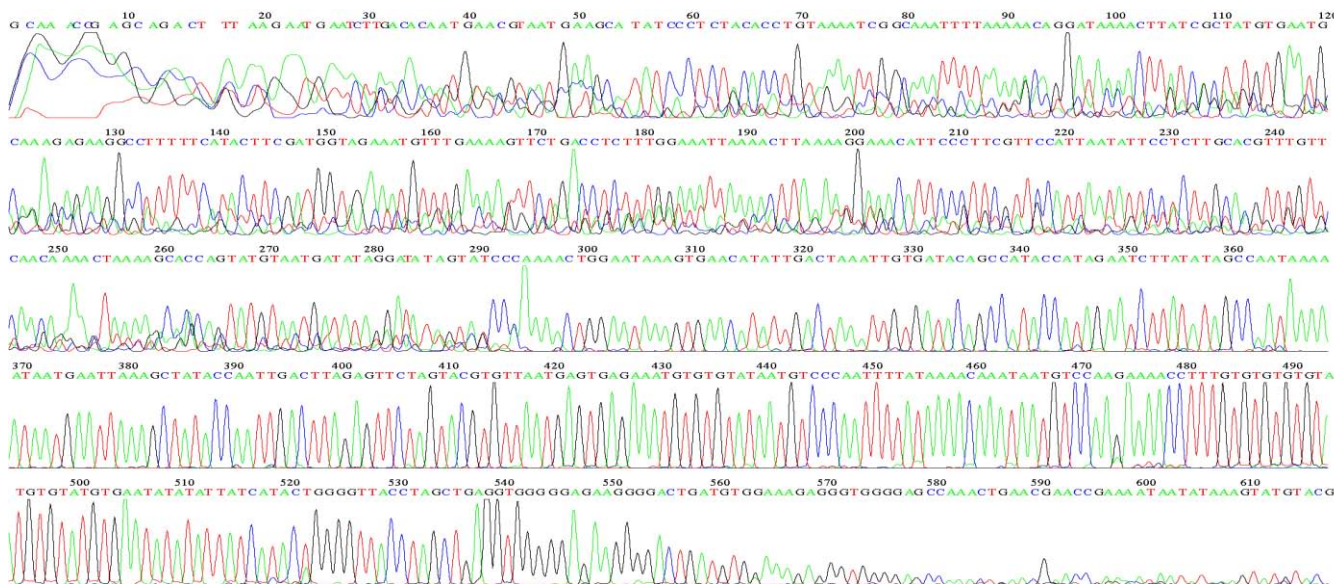


Figure 9: DNA sequencing (reverse) for carrier no. 7 detect with Inv22.

Becker et al. (1996) assessed the male: female ratio of mutation recurrence (k) to be 3.6. By use of the percentages of mutation origin in maternal grandfather to patients' mother or to maternal grandmother, k values were directly estimated as 15 and 7.5, respectively. As each mutation type separately which an inversion of the gene presented a 10-fold-higher mutation rate in male germ cells(31).Although intron 22 segment in the non-coding regions of FVIII gene, intron 22 mutations intermittent the F8 mRNA between exon 22 and23 with large inversion and translocation of nucleotides between these two exons(32).

Inversion of intron 22 (inv22) originates 50% of cases of severe HA and is a major risk factor for inhibitor development and The non-significant risk for developing

inhibitors among inv22-positive patients agrees with the variety of genetic and non-genetic factors involved in such a complication (30).Other normal changes in genomes (normal variants) not indicated in all carriers VIII gene which all intron 22 involved have been aligned and compared the all possible variants.

VI. DISCUSSION

The current study examined different properties of mutations carrying F8 haplotypes. This information was used to infer whether same mutations. Carrier females have a 50% chance of transmitting the F8 pathogenic variant in each pregnancy: sons who inherit the pathogenic variant will be affected; daughters who inherit the pathogenic variant are carriers. Affected

males transmit the pathogenic variant to all of their daughters and none of their sons.

Intron 22 Mutations Frequency Percentage

In this study, four from ten Iraqi carrier females from ten unrelated families were had intron 22 mutations as showed in figure (10).

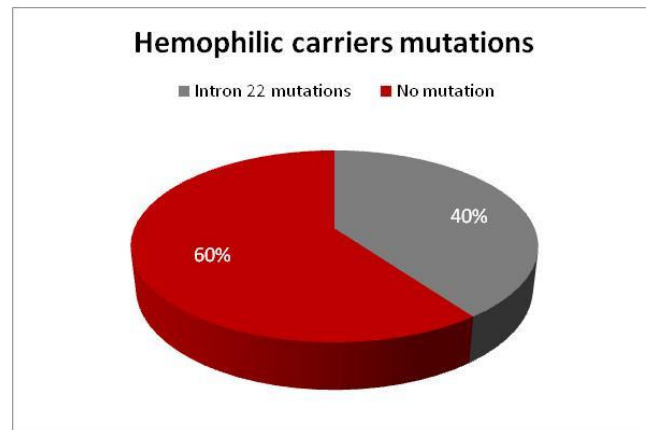


Figure 10: The percentage of intron 22 mutations frequency in hemophilic carriers (mothers).

The mutation is forecast to impair attachment to the factor VIII (FVIII) carrier protein, von Willebrand factor, and thus increased clearance of FVIII from plasma. Clinical and molecular characterization of these carriers is essential to raise follow-up, genetic counseling and treatment of the disease (33). Increased risk are probable if the F8 pathogenic variant has been identified in a family member or if informative (family history) intragenic linked markers have been recognized which genetic counseling deals with genetic risk valuation and the use of family history and genetic testing to explain genetic status for family members. In this study six from ten carriers are with a hemophilia history (60%) which 3 from four carriers have (Inv22) mutations with positive family history represents a major factor for genetic predisposition lead to defective FVIII gene. Carrier no.3 appears in this study aligned was regarded as first carrier detect intron 22 inversion of the FVIII gene reveal with no family history and consanguinity state. There are several clarifications for a hemophilic carrier being identify with inv22 when there is no history of hemophilia in the family which about 30 per cent of these cases arise from spontaneous mutation.

1. The mother is a carrier of a new disease-causing mutation that occurred in one of the following ways:

- As a "germ line mutation" (i.e., in the egg or sperm at the time of her conception so the mother is then the first person in the family to transmit hemophilia. Her children might be influenced either as carriers or as hemophiliacs (34). And thus show in every cell of her body and noticeable in her DNA). Ninety-eight percent of mothers of a simple case with an intron 22 inversion are

carriers because most of these mutations arise in spermatogenesis.

- As a somatic mutation (i.e., a alteration that arisen very early in embryogenesis, subsequent in somatic mosaics in which the pathogenic variant is current in some but not all cells and may or may not be obvious in DNA).
 - As germ line mosaics (in which some germ cells have the pathogenic variant and some do not, and in which the pathogenic variant is not evident in DNA from her leukocytes).
2. The mother is a carrier and has inherited the pathogenic variant either from her mother who has a new disease-producing variant or from her asymptomatic father who is mosaic for the pathogenic variant.
 3. The mother is a carrier of a pathogenic variant that rose in a previous generation and has been send on through the family without manifesting symptoms in female carriers due to the lionization which hemophilia does certainly run in the family but there is no indication of it because no hemophilic boys have been born (35:36)

General, the mother has an roughly 80% chance of being a carrier when her son is the first influenced individual in the family; however, the mother of a severely affected male with an intron 22 inversion has a 98% chance of being a carrier (37) and about 40% of carriers (four) under study with consanguinity marriage that one from four carriers have (Inv22) mutations with positive consanguinity marriage result in concentrated the bad gene copy. Figure no. (12) showed DNA sequencing for carrier no.7 detect with intron 22 mutation in factor 8 gene and represent

positive family history and consanguinity state and Figure no.(11) below showed alignment of hemophilic carrier no.7 detect with intron 22 mutation and control of

selected intron 22 sequence with the genomic DNA reference in deep details and represent positive family history and consanguinity state.

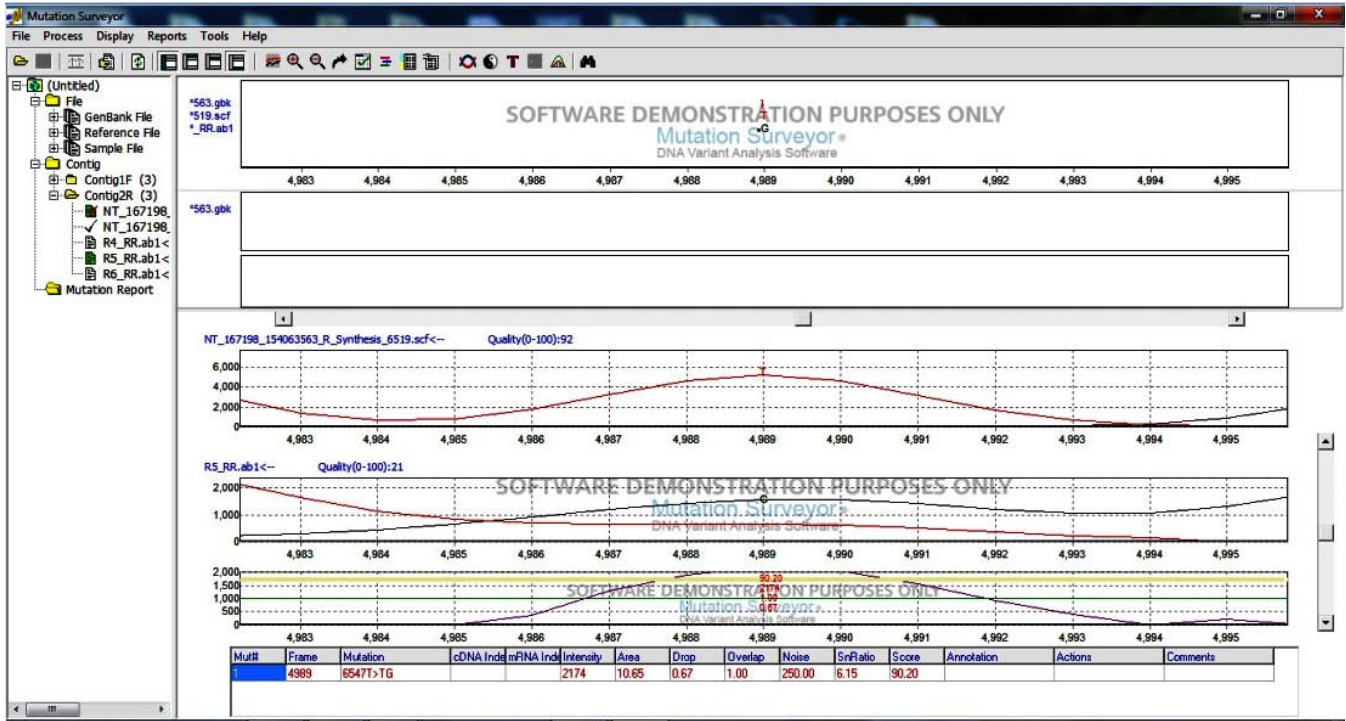


Figure 11: Alignment of hemophilic carrier and control of selected intron 22 sequence with the reference in deep details.

Figure no. (7) Below represents another alignment of hemophilic carrier shown mutations.

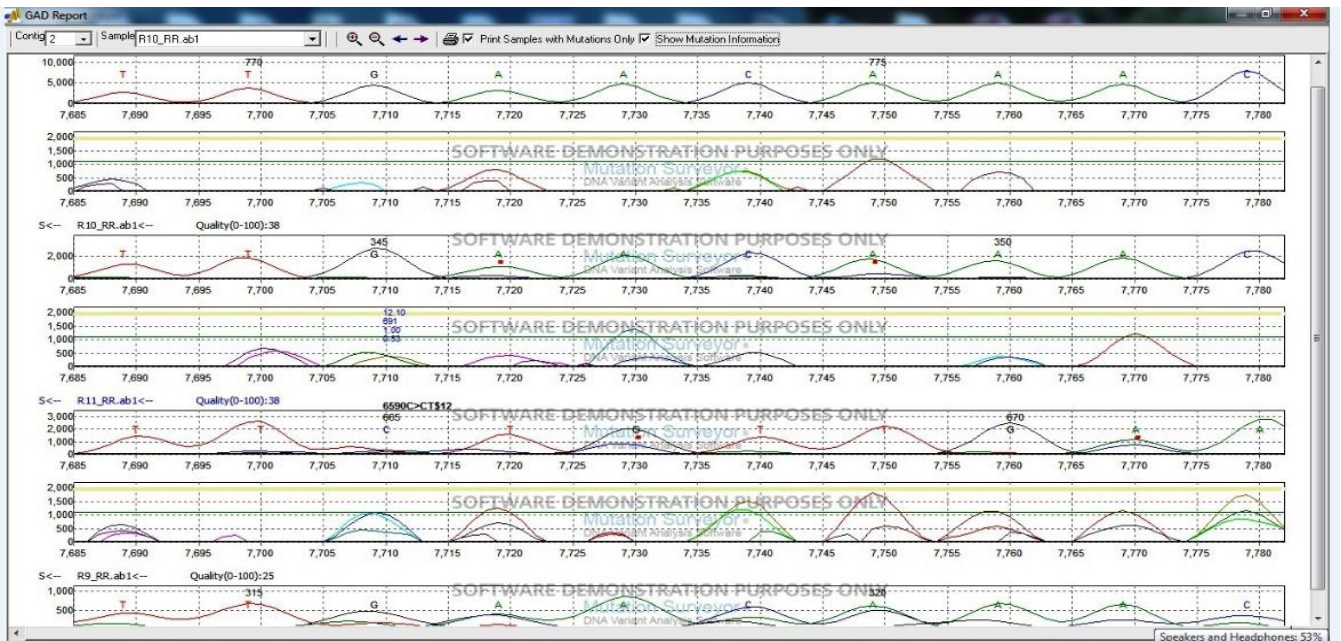


Figure 12: Alignment of hemophilic carrier of selected intron 22 sequence with the reference showing mutations in deep details.

VII. CONCLUSION

Hence present study indicated that detection of Intron 22 mutations in F8 gene is important in identifying female with genetic defects that leads to the birth sons affected with hemophilia A disease and females almost as carriers. This result represents a step for helpfully guide the direction of molecular study in genetic counseling and subsequent for facilitate management in labour and for prenatal diagnosis also for prevention of the inhibitor development which inversion of intron 22 (inv22) is a major risk factor involved in such a complication. This knowledge represents a step. Most of cases are with a family history (60%) represent a major factor for genetic predisposition lead to defective FVIII gene and about 40% of carriers under study with consanguinity marriage result in concentrated the bad gene copy so this is highly suggestive that hemophilia disease is not uncommon. There is an obvious public ignorance about the role of heredity in many disorders in Wasit province.

REFERENCES RÉFÉRENCES REFERENCIAS

- James, A.H.(2005). More than HMB: a review of the obstetric and gynecological manifestations of bleeding disorders. *Hemophilia* ; 11:295–307.
- Salazar-Sánchez L., Jiménez-Cruz G., Mendez M., Chaverri P., Alvarado P., Schröder W, Wulff K., Sandoval M., Herrmann F.H, Pavlova A., Oldenburg J.(2010). Molecular analysis of FVIII gene in severe HA patients of Costa Rica. *Hamostaseologie*. ; 30 Supple 1:S150-2.
- Fogarty P.F., Kessler C.M. Hemophilia A and B. In: Kitchens C.S., Kessler C.M., Konkle BA, eds. *Consultative Hemostasis and Thrombosis*. 3rd ed. Philadelphia, PA: Elsevier Saunders; 2013:45-59.
- Bogdanova, N. ; Markoff, A.; Eisert, R.; Wermes, C.; Pollmann, H.; Todorova, A.; Chlystun, M.; Nowak-Göttl U.; Horst, J. (2007). Spectrum of molecular defects and mutation detection rate in patients with mild and moderate hemophilia A. *Human Mutation Journal*; 28(1):54-60.
- Anjali A. Sharathkumar, Manuel Carcao. (2011). *Clinical Advances in Hemophilia Management*. *Pediatric Blood Cancer*; 57:910-920.
- Fay, P.J.; (1988). Reconstitution of human factor VIII from isolated subunits. *Archives of Biochemistry and Biophysics*; 262 (2):525-531.
- Botton, P.H.; Maggs, K.J.; Hemophilia A and B, *Lancet*, 2003 24,361(2003).
- Graw, J.; Brackmann, H. H.; Oldenburg, J.; Schneppenheim, R.; Spannagl M.; Schwaab, R.(2005). Hemophilia A: From mutation analysis to new therapies. *Nat. Rev. Genet.* 6, 488–501.
- Kasper, C.K.; Buzin, C.H. *Genetics of Hemophilia A and B. An Introduction for Clinicians*, 2009, 1st ed.; Southland Publications: Pasadena, CA, USA, 2009; pp. 27–29.
- V. R. Byams, P. A. Kouides, R. Kulkarni, J. R. Baker, D. L. Brown, J. C. Gill, A. M. Grant, A. H. James, B. A. Konkle, J. Maahs, M. M. Dumas, S. Mcalister, D. Nance, D. Nugent, C. S. Philipp, J. M. Soucie and E. Stange. (2011). Surveillance of female patients with inherited bleeding disorders in United States Haemophilia Treatment Centres. *Hemophilia: Volume 17, Issue Supplement s1 Pages 1–45*.
- Haldane, J.B.S. (1935) the rate of spontaneous mutation of a human gene. *Journal of Genetics*, 31, 317–326.
- Ulla Hedner; David Ginsburg; Jeanne M. Lusher; and Katherine A2000, High, *Congenital Hemorrhagic Disorders: New Insights into the Pathophysiology and Treatment of Hemophilia*. *American Society of Hematology*; 241–65.
- Gitschier, J.; Wood, W.I.; Goralka, T.M.; Wion, K.L.; Chen, E.Y.; Eaton, D.H.; Vehar, G.A.; Capon, D.J.; Lawn, R.M. Characterization of the human factor VIII gene. *Nature* 1984, 312, 326–330.
- Bagnall, R.D.; N. Waseem; P.M. Green; F. Giannelli, (2002). recurrent inversion breaking intron 1 of the factor VIII gene is a frequent cause of severe hemophilia A. *Blood* 99 (1):168–174.
- Lakich, D. ; Kazazian, H. H. Jr. ; Antonarakis, S. E. ; Gitschier, J. (1993) .Inversions disrupting the factor VIII gene are a common cause of severe haemophilia A . *Nature Genetics*; 5(3): 236 – 41.
- Rossiter, J.P.; Young, M.; Kimberland, M.L.; Hutter, P.; Ketterling, R.P.; Gitschier, J.; Horst, J.; Morris, M.A.; Schaid, D.J.; de Moerloose, P.(1994). Factor VIII gene inversions causing severe hemophilia A originate almost exclusively in male germ cells. *Hum. Mol. Genet.*, 3, 1035–1039.
- Bagnall, R.D.; F. Giannelli and P.M. Green. (2005). Polymorphism and hemophilia A causing inversions in distal Xq28: a complex picture. *J Thromb Haemost* 3 (11):2598–2599.
- Bagnall, R.D.; F. Giannelli; P.M. Green (2006): Int22h-related inversions causing hemophilia A: a novel insight into their origin and a new more discriminant PCR test for their detection. *J Thromb Haemost* 4 (3):591–598.
- Antonarakis, S.E.; Rossiter, J.P.; Young, M.; Horst, J.; de Moerloose, P.; Sommer, S.S., et al. (1995). Factor VIII gene inversions in severe haemophilia A: results of an international consortium study. *Blood*; 86:2206-12.
- DE Brasi, C.D. and D.J. Bowen (2008). Molecular characteristics of the intron 22 homologs of the coagulation factor VIII gene: an update. *J Thromb Haemost* 6 (10):1822–1824.
- Miguel Martín Abelleiro, Liliana Carmen Rossetti, Claudia Pamela Radic, Miguel Candela, Irene Beatriz Larripa, Carlos Daniel De Brasi. (2012). *Are*

- int22h-mediated deletions a common cause of hemophilia? *Annals of Hematology*, Volume 91, Issue 4, pp 633–636.
22. Youssoufian, H. ; Kazazian, H.H, Phillips, D.G.; Aronis, S.; Tsiftis, G.; Brown, V.A. ; Antonarakis, S.E. (1986). Recurrent mutations in hemophilia A give evidence for CpG mutation hotspots. *Nature*; 324(6095):380-2.
 23. Levinson, B.; Kenwrick, S.; Lakich, D.; Hammonds, G. Jr.; Gitschier, J. (1990). A transcribed gene in an intron of the human factor VIII gene .*Genomics*; 7(1): 1 – 11.
 24. Levinson, B.; Kenwrick, S.; Gamel, P.; Fisher, K.; Gitschier, J. (1992). Evidence for a third transcript from the human factor VIII gene .*Genomics*; 14(3): 585 – 9.
 25. Freije, D.; Schlessinger, D. A .(1992). 1.6-Mb contig of yeast artificial chromosomes around the human factor VIII gene reveals three regions homologous to probes for the DXS115 locus and two for the DXYS64 locus. *Am. J. Hum. Genet.* 51, 66–80.
 26. Peters, M.F.; Ross, C.A. (2001). Isolation of a 40 k-Da Huntingtin - associated protein. *J. Biol. Chem.*, 276, 3188–3194.
 27. Frazer, K.A.; Murray, S.S.; Schork, N.J.; Topol, E.J. (2009). Human genetic variation and its contribution to complex traits. *Nat Rev Genet*; 10: 241–51.
 28. Naylor, J.; Brinke, A.; Hassock, S.; Green, P.M.; Giannelli, F. Characteristic mRNA abnormality found in half the patients with severe haemophilia A is due to large DNA inversions. *Hum. Mol. Genet.* 1993, 2, 1773–1778.
 29. Preethi, S. N.; Shrimati, D. S.; Chandrakala, S.; Kanjaksha, G. (2014). Mutations in Intron 1 and Intron 22 Inversion Negative Haemophilia A Patients from Western India. *Plos One*: 9 (5): 1-9. e97337.
 30. Mantilla Capacho J.M. Beltrán-Miranda C.P., Luna-Záizar H., Aguilar-López L., Esparza-Flores M.A., López-Guido B., Troyo-Sanromán R., Jaloma-Cruz A.R. (2007). Frequency of intron 1 and 22 inversions of Factor VIII gene in Mexican patients with severe hemophilia A. *American Journal of Hematology*. 82(4):283-7.
 31. J. Becker, R. Schwaab, A. Möller-Taube, U. Schwaab, W. Schmidt, H. H. Brackmann, T. Grimm, K. Olek, and J. Oldenburg. (1996). Characterization of the factor VIII defect in 147 patients with sporadic hemophilia A: family studies indicate a mutation type-dependent sex ratio of mutation frequencies. *Am J Hum Genet*; 58(4): 657–670.
 32. Naylor, J.A.; Green, P.M.; Rizza, C.R.; Giannelli, F. (1992) Factor VIII gene explains all cases of haemophilia A. *Lancet*, 340, 1066–1067.
 33. Martín-Salces M, Venceslá A, Álvarez-Román MT, Rivas I, Fernandez I, Butta N, Baena M, Fuentes-Prior P, Tizzano EF, Jiménez-Yuste V. (2010). Clinical and genetic findings in five female patients with haemophilia A: Identification of a novel missense mutation, p. Phe2127Ser. *Thromb Haemost.*; 104 (4): 718-23.
 34. Mannucci, P. M.; Tuddenham, E. G. D. (2001). The hemophilias from royal genes to gene therapy. *The New England Journal of Medicine*; 344, No. 23:1773-1779.
 35. Ludlam, C.A.; Pasi, K.J.; Bolton-Maggs, P.; Collins, P.W.; Cumming, A.M.; Dolan, G.; Fryer, A.; Harrington, C.; Hill, F.G.; Peake, I.R.; Perry, D.J.; Skirton, H.; Smith, M.(2005). A framework for genetic service provision for haemophilia and other inherited bleeding disorders. *Hemophilia.*; 11 (2): 145-63.
 36. Thomas S, Herbert D, Street A, Barnes C, Boal J, Komesaroff P. Attitudes towards and beliefs about genetic testing in the hemophilia community: a qualitative study. *Haemophilia*. 2007; 13:633–41.
 37. Chi, C.; Shilltagh, N.; Kingman, C.E.; Economides, D.L.; Lee, C.A.; Kadir, R.A.(2006). Identification and management of women with inherited bleeding disorders: a survey of obstetricians and gynaecologists in the United Kingdom. *Hemophilia.* ; 12(4):405-12.
 38. Plug, I.; Mauser-Bunschoten, E.P.; Brocker-Vriends, A.H.; van Amstel, H.K.; van der Bom, J.G.; van Diemen-Homan, J.E.; Willemse, J.; Rosendaal, F.R.(2006). Bleeding in carriers of hemophilia. *Blood*. 108:52–6.
 39. Laurie, A.D.; Hill, A.M.; Harraway, J.R.; Fellowes, A.P.; Phillipson, G.T.; Benny, P.S. ; Smith, M.P.; George, P.M. (2010). Preimplantation genetic diagnosis for hemophilia A using indirect linkage analysis and direct genotyping approaches. *Journals of Thrombosis and Hemostasis*; 8(4): 783-9.
 40. Peake, I.R.; Lillicrap, D.P.; Boulyjenkov, V.; Briët, E.; Chan, V.; Ginter, E.K.; Kraus, E.M.; Ljung, R.; Mannucci, P.M.; Nicolaidis, K. (1993). Report of a joint WHO/WFH meeting on the control of haemophilia: carrier detection and prenatal diagnosis. *Blood Coagulation and Fibrinolysis*; 4(2): 313-344.



Chemoradiotherapy or Induction Chemotherapy Followed by Chemoradiotherapy University Hospital Fuenlabrada: Our Experience in 10 Years

By Beatriz Losada Vila, David Gutiérrez Abad, Maria Victoria de Torres Olombrada,
Blanca Ludeña Martínez & Begoña Caballero Perea

Fuenlabrada University Hospital

Abstract- Head and neck tumors are diagnosed in locally advanced stages up to 60%. The controversy lies in the choice between chemoradiotherapy vs induction chemotherapy.

Retrospective descriptive study with 53 patients undergoing INDUCTION CHEMOTHERAPY + CRT vs CRT alone in which we analyze the tolerability, organ preservation, recurrence rates, overall survival (OS) and disease-free survival (DFS).

Within the group of induction (A), 86% (24/28) received 3 cycles TPF, while 14% (4/28) were treated with a doublet (platinum + taxol), being able to meet the treatment without delay or dose reduction of only 50%. Within non-induction group (B), 80% "RECEIVED all doses and without delay, while 20% (5/25) failed to finish, fell 80 % (4/5) of them.

Keywords: chemoradiotherapy, induction chemotherapy, head and neck, survival, locally advanced.

GJMR-F Classification: NLMC Code: QZ 310



CHEMRADIO THERAPY OR INDUCTION CHEMOTHERAPY FOLLOWED BY CHEMRADIO THERAPY UNIVERSITY HOSPITAL FUENLABRADA OUR EXPERIENCE IN 10 YEARS

Strictly as per the compliance and regulations of:



RESEARCH | DIVERSITY | ETHICS

Chemoradiotherapy or Induction Chemotherapy Followed by Chemoradiotherapy University Hospital Fuenlabrada: Our Experience in 10 Years

Beatriz Losada Vila ^α, David Gutiérrez Abad ^σ, Maria Victoria de Torres Olombrada ^ρ, Blanca Ludeña Martínez ^ω & Begoña Caballero Perea [¥]

Abstract- Head and neck tumors are diagnosed in locally advanced stages up to 60%. The controversy lies in the choice between chemoradiotherapy vs induction chemotherapy.

Retrospective descriptive study with 53 patients undergoing INDUCTION CHEMOTHERAPY + CRT vs CRT alone in which we analyze the tolerability, organ preservation, recurrence rates, overall survival (OS) and disease-free survival (DFS).

Within the group of induction (A), 86% (24/28) received 3 cycles TPF, while 14% (4/28) were treated with a doublet (platinum + taxol), being able to meet the treatment without delay or dose reduction of only 50%. Within non-induction group (B), 80% "RECEIVED all doses and without delay, while 20% (5/25) failed to finish, fell 80 % (4/5) of them.

They are not comparable groups as the most important difference is that those with more advanced (N2 disease) are in group A (92.8% cT3-T4 or N2) versus Group B (32% cT3N0).

Conclusions:

- The Profile of our patients in the group of non-induction have more comorbidities and the earliest stages. Recurrence rates are similar in both groups, with a higher relapse and metastatic disease in the induction group (group A) because of more advanced tumors.
- We have to study new strategies for improving tolerance induction chemotherapy with cetuximab or nab-paclitaxel, and selecting best ones should receive concomitant cetuximab + RT.

Keywords: chemoradiotherapy, induction chemotherapy, head and neck, survival, locally advanced.

I. INTRODUCTION

Head and neck tumors represent in the United States an incidence of 52,610 cases and 60% are diagnosed at locally advanced stage.

Despite treatment aimed at eradicating the disease, the cure rates are still modest, especially in tumors not associated with human papillomavirus (HPV). Chemoradiotherapy (CRT) with Cisplatin 100 mg/m² each 3 weeks showed an improvement in overall

survival (OS) compared to radiotherapy (RT) [1]. Actually the controversy is between CRT vs induction chemotherapy (TPF= docetaxel 75 mg/m², cisplatin 75 mg/m², 5FU 750 mg/m² by continuous infusion days 1-5) prior to CRT because it seems to **reduce distant recurrence without improving overall survival.** [2,3,4,5]

Our objectives are to describe what happens at the University Hospital of Fuenlabrada with 53 patients undergoing induction chemotherapy + CRT vs CRT alone, reflecting tolerability, organ preservation, recurrence rates, overall survival (OS) and disease free survival (DFS).

II. MATERIAL AND METHODS

We present a group of **53 patients**: 28 with induction treatment (cisplatin, 5-fluoracil, docetaxel) + CRT (group A) and 25 CRT or bioRT (group B: B1 cisplatin 100 mg/m²+ RT, B2 cetuximab 250 mg/m²+RT).

We performed a **descriptive retrospective study** and we analyzed tumor stage and nodes, gender, age, comorbidities, rates of relapses/ persistence disease, tolerability to treatment, organ preservation and survival (progression free survival and overall survival). We used SPSS statistic programme for the analyses.

Also **comparing our data** with published studies of induction chemotherapy: TTCC group, PARADIGM, DECIDE and GCTCC.

Author α σ: Medical Oncology Department, Hospital Universitario Fuenlabrada (Madrid). e-mail: beatriz.losada@salud.madrid.org

Author ρ ω: Radiation Oncology Department, Hospital Universitario Fuenlabrada (Madrid).

III. RESULTS

Variables	Induction chemo + CRT (group A) N=28	CRT or bioRT (group B) N=25
Treatment	TPF x 3: 86 % Cisplatin+Taxolx3:14 %	
Induction Chemo		
CRT	Cisplatin: 90% Cetuximab: 10%	Cisplatin: 60% Cetuximab: 40%
Radiotherapy Doses		
66-70 Gy	69%	84%
Unknown	21%	8%
Not finished	10%	8%
Tumor stage		
T2N2M0	7.1%	12%
T3N0M0	3.6%	32%
T3N2M0	21.4%	16%
T4N0M0	10.7%	16%
T4N1M0	10.7%	---
T4N2M0	42.9%	16%
Age(years)	56.9 (range 43-73)	62.2 (range 35-79)
Location		
Oropharynx	16%	46.4%
Larynx	56%	36%
Recurrence	(25%)	(20%)
→Metastasis	14.2%	4%
→Local and metastasis	7%	---
→Local	3.5%	16%
Persistence	35%	20%
Second primary tumours	7%	8%
Not relapsing	33%	48%
Median Survival		
Time to local recurrence (months)	55	21.5
Disease free survival (DFS) (months)	31.4	20
Overall survival(OS) (months)	46.8	32

Figure 1: Comparing analysed variables in induction chemotherapy + CRT vs CRT

a) Treatment

In group A; 86% (24/28) received 3 cycles of TPF, while 14% (4/28) were treated with a doublet (platin + taxol) because of bad tolerance to treatment. After induction, all of them received cisplatin + RT. However even having finished induction chemo, **only 50% completed CRT** without dosis delays.

In group B, the treatment could be cetuximab + RT or cisplatin + RT. **80% receive all doses without delays**, while 20% (5/25) could not finish it, relapsing 80% (4/5) of them.

According to the treatment received, in group B 40% (10/25) were treated with cetuximab, while 60% was cisplatin. The election of cetuximab was in those patients older, with comorbidities or renal impairment who we thought that they are not supporting chemo. In

this group, treatment was even not finished in 3/10, with no relapsing in 2/10 and relapsing/persistence in 5/10.

According to RT, up to 10% could not complete treatment in both groups because of progression or bad tolerance. In group A: doses between 66-70Gy in 69%, 21% missing dates, 10% did not finish treatment or <30 Gy. In group B, 63-70 Gy in 84%, 8% missing dates and 8% 50 Gy.

b) Gender/age

Most of the patients in both groups are males, being younger in group A (media 56.9 years) than group B (media 62.2 years) with a similar age range in the two groups.

c) *Toxic Habits/Comorbidities*

More than 90% have smoking and drinking habit in both groups, with cardiovascular risk factors in 28.6% (group A) and 44% (group B). According to comorbidities (Charlson index), at least one factor was present in 25% of group A vs 44% in group B, being Charlson Index >5 points in most of them because of the tumour which sums 2 points.

d) *Location*

In group A, the first location is larynx (16% vs 56%), although in group B oropharynx is the most frequent organ affected (46.4% vs 36%)

e) *Tumor stage*

Firstly, the most important difference is that those with more advanced stage (N2 lymph node involvement) are in group A (92.8% cT3-T4 or N2) vs Group B (32% cT3N0).

f) *Tumor recurrence*

According to high percentage of advanced stage tumor in group A, it is easily to relapse as metastatic disease (14.2%=4/28 vs 4%=1/25 in group B). Detailing the 4 cases of metastatic relapse, we analysed another factors which could also influence. Initially 100% of them where T4N2, receiving 75% (3/4) of them 70 Gy, with unknown doses the other one (1/4). Persistence tumours are also T4N2-N0, with unknown doses of RT in 10% and less than 70% receive 70Gy, not receiving complete chemoradiotherapy in 20% of them.

In group B, **all of the relapses/persistent tumours** are T3-T4 N0-N2, with unknown RT doses in 10% of them, 50Gy in another 20%, comorbidities, synchronous tumour and older age in most of them.

g) *Response by image*

We have similar response rates (88%) in both groups, however we have more TC than PET in group A because many patients are previously to 2010 and PET/CT was not available in our Hospital. Another important date is that in the beginning we were not used to identify areas of inflammation with this technique, knowing nowadays that we have to wait for 12 weeks to be more exact and decide if what we see is tumor or not.

h) *Survival*

We have no enough patients to conclude, but it seems that our data in group A show a higher rate of metastatic, time to local recurrence (55 months vs 21.5 months), DFS (31.4 months vs 20 months) and OS (46.8 months vs 32 months).

i) *Rescue surgery and organ preservation*

Unable to perform organ preservation is only in 12.5% of cases. Rescue surgery is not need in 60% (A) and 72% (B); with surgery in both cases because of suspicion of tumor persistence. In group A, 25% had neck dissection because of persistence tumour in PET

that was not confirmed with histology. In group B, 20 % had neck dissection without malignancy histology.

We assume that this date is because in the beginning of "PET times", we were not used to identify areas of inflammation, knowing nowadays that we have to wait for 12 weeks to be more exact.

j) *Tolerability*

In group A and B mucositis grade II was achieved in all the patients, improving with dosis relays and topical treatment. In group a neutropenia was avoided with prophylactic G-CSF. As we previously reported, only 50% in group A could finish without doses reduction, while it was 80% in group B.

IV. DISCUSSION

Comparing our results with literature it is well known that neoadjuvant chemotherapy (docetaxel + cisplatin + fluorouracil) (DCF) has achieved a reduction in the rate of distant recurrence [3,4,5], but it seems to not increase overall survival or progression-free survival.

Some important studies on induction QT are the TTCC group (Hitt et al), Boston (Haddad: PARADIGM study), Chicago (Cohen: DECIDE study) and GCTCC (Ghi), where the benefit in overall survival can only be achieved in the last one. [6,7,8,9]

Therefore no scheme is the same. If detailing the recent meta-analysis published in JCO and comparing with ours: [4]

- ✓ *Complete response in TPF group (33%) vs 14% in PF.* In our study, we have many patients valued by TC. In PET we have 10% complete response, adding 32.1% partial response also by PET and 46.4% partial or complete by TC.
- ✓ *Median survival of 43 months.* The dose is kept to 91% of ciplatino, being almost 100% 5FU and paclitaxel. In ours: 46.8 months and dose kept in 86%.
- ✓ *Published DFS is 12.5 months.* Our data is 31.4 months.
- ✓ *Locoregional control 60.9%.* In our study, 33% do not relapse, 7% develop second primary tumours, with 35% persistent tumours (mostly rescued with ganglionar dissection) and only 25% of relapses.

So the question is how to select patients for induction chemotherapy. Data suggest that it would be more useful in those patients who need better locoregional control and have high risk of distant recurrence. As we have described, we have selected for induction chemotherapy those with less comorbities and advanced disease, **achieving good results** but with only 50% of complete treatment and no dosis delay.

Adding to these results, a recent meta-analysis has also described **that organ preservation** is greater in induction arm [9]. In our study, the percentages are similar between groups, needing surgery because of



suspicion of tumor persistence, however in most of surgeries in group a malignancy is not confirmed.

Finally, **we look for what can we do to improve tolerability. Some studies have developed to discern whether cetuximab + RT could be substituted for cisplatin + RT, with no conclusive results:** phase II studies (Pignon and Bonner) highlight HR 0.74 and modest effect on disease control in the distance first (Cisplatin) but not in the second. [1,10] A recent meta-analysis gives better results at 2 years on the arm of cisplatin + RT vs cetuximab + RT (OS 71% vs 60.7%, DFS 61.7% vs 43.1% and locoregional recurrence of 19.6% vs. 32.3%).[10,11]

Studies designed to improve induction tolerability with cetuximab (E1308 study: cetuximab + cisplatin + paclitaxel for 3 cycles) or nab paclitaxel (F II with cetuximab, nab paclitaxel, cisplatin and 5FU) are awaiting for results[12].

V. CONCLUSIONS

The profile of our patients in group B present more comorbidities and earlier stages than induction group. The recurrences rates is similar in both groups, with a higher relapse as metastatic disease in induction group (group A) because of more advanced tumors. Induction group overall survival is also better, however treatment tolerability with dosis delays is worse.

Persistence/Relapsing tumours happen in those patients with advanced stages, comorbidities, older age and not finishing RT (<60 Gy).

In the beginning, we perform neck dissection because of suspicion of persistence tumour in PET/CT (initially not always performed after 12 weeks, which is now the standar to better discern inflammation vs tumor persistence), without confirming malignancy with histology.

Induction chemotherapy has improved distance recurrence rates and organ preservation, with no differences in overall survival. However, in our opinion we must better target the profile of patients who would benefit of this treatment.

It is being studied new strategies for improving tolerance induction chemotherapy with cetuximab or nab-paclitaxel, and selecting better which ones must receive cetuximab + RT concomitant. It is a difficult issue to analyze, because we usually employ cetuximab in more fragile patients, being itself a negative prognostic factor.

BIBLIOGRAPHY

1. Pignon JP, le Maître A, Maillard E Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): An update on 93 randomised trials and 17,346 patients. *Radiother Oncol* 92: 4-14, 2009.
2. Posner MR, Hershock DM, Blajman CR, et al: Cisplatin and fluorouracil alone or with docetaxel in

- head and neck cancer. *N Engl J Med* 357: 1705- 1715, 2007.
3. Vermorken JB, Remenar E, van Herpen C, et al: Cisplatin, fluorouracil, and docetaxel in unresectable head and neck cancer. *N Engl J Med* 357:1695-1704, 2007.
4. Blanchard P, Bourhis J, Lacas B, et al: Taxanecisplatin- fluorouracil as induction chemotherapy in locally advanced head and neck cancers: An individual patient data meta-analysis of the meta-analysis of chemotherapy in head and neck cancer group. *J Clin Oncol* 31:2854-2860, 2013.
5. Ma J, Liu Y, Huang XL, et al: Induction chemotherapy decreases the rate of distant metastasis in patients with head and neck squamous cell carcinoma but does not improve survival or locoregional control: A meta-analysis. *Oral Oncol* 48:1076-1084,2012
6. Hitt R, Grau JJ, Lopez-Pousa A, et al. Final results of a randomized phase III trial comparing induction chemotherapy with cisplatin/ 5FU or docetaxel/ cisplatin / 5FU follow by chemoradiotherapy (CRT) versus CRT alone as first-line treatment of unresectable locally advanced head and neck cancer (LAHNC). *Journal of Clinical Oncology* 2009; 27.
7. Haddad RI, Rabinowits G, Tishler RB et al. The PARADIGM trial: a phase III study comparing sequential therapy (ST) to concurrent chemoradiotherapy (CRT) in locally advanced head and neck cancer (LAHNC). *Journal of Clinical Oncology* 2012: 30. Abstract 5501.
8. Cohen EE, Karrison T, ocherginsky M et al. DeCIDE: a phase III randomized trial of docetaxel (D), Cisplatin (P), 5-Fluoracil (F) (TPF) induction chemotherapy (IC) in patients with N2/N3 locally advanced squamous cell carcinoma of the head and neck (SCCHN). *Journal of Clinical Oncology* 2012: 3, abstr 5500.
9. Ghi et al. A phase II-III study comparing concomitant chemoradiotherapy (CRT) versus cetuximab/RT (CET/RT) with or without induction docetaxel/cisplatin/5-fluorouracil (TPF) in locally advanced head and neck squamous cell carcinoma (LASCCHN): Efficacy results (NCT01086826). *J Clin Oncol* 31, 2013 (suppl; abstr 6003)
10. Bonner JA¹, Harari PM et al. Radiotherapy plus cetuximab for locoregionally advanced head and neck cancer: 5-year survival data from a phase 3 randomised trial, and relation between cetuximab-induced rash and survival. *Lancet Oncol.* 2010 Jan; 11(1): 21-8.
11. Petrelli F¹, Coinu A², Riboldi V³. Concomitant platinum-based chemotherapy or cetuximab with radiotherapy for locally advanced head and neck cancer: a systematic review and meta-analysis

of published studies. Oral Oncol. 2014 Nov; 50(11): 1041-8.

12. Adkins D, Ley J, Nussenbaum B et al. Clinical response rate at primary tumor site (PTS) following a novel induction chemotherapy (IC) regimen of weekly nanoparticle albumin-bound (nab)-paclitaxel and cetuximab with every 3-week cisplatin and 5-FU (ACCF) versus docetaxel, cisplatin, 5FU and cetuximab (TPF+C) in patients with locally advanced head and neck squamous cell carcinoma (HNSCC) Journal of Clinical Oncology 2011; 29, abstract 5560.



This page is intentionally left blank





Assessment of Self Care Management and its Associated Factors among Type 2 Diabetes Patients in Mekelle Hospital and Ayder Referral Hospitals, Mekelle City, Tigray, Northern Ethiopia, 2012/13

By Kalayou K Berhe, Haftu B Gebru, Hailemariam B Kahsay & Alemseged A Kahsay

Mekelle University College of Health Sciences

Abstract- Background: Diabetes is a group of metabolic disorders that affect the body's ability to process and use sugar (glucose) for energy. The success of long-term maintenance therapy for diabetes depends largely on the patients' adherence with self-care practices.

Objective: Was to assess self-management and its associated factors among type 2 diabetes patients in Mekelle hospital and Ayder referral hospitals, Mekelle City, Tigray, Northern Ethiopia, 2012/13.

Method: The research design was institutional based cross sectional method and 343 study subjects were selected using systematic random sampling technique and the data was collected using interviewer administered structured questionnaire, data was analyzed and cleaned using SPSS version 16. Frequencies and proportions were computed. Bivariate and Multivariate logistic regression was computed to assess statistical association between the outcome variable and selected independent variables and significance of statistical association was assured or tested using 95%CI and P-value (<0.05).

Keywords: type 2 diabetic patients, diabetes management, physical exercise & anti diabetes agent.

GJMR-F Classification: NLMC Code: WD 200



Strictly as per the compliance and regulations of:



Assessment of Self Care Management and its Associated Factors among Type 2 Diabetes Patients in Mekelle Hospital and Ayder Referral Hospitals, Mekelle City, Tigray, Northern Ethiopia, 2012/13

Kalayou K Berhe ^α, Haftu B Gebru ^σ, Hailemariam B Kabsay ^ρ & Alemseged A Kabsay ^ω

Abstract- Background: Diabetes is a group of metabolic disorders that affect the body's ability to process and use sugar (glucose) for energy. The success of long-term maintenance therapy for diabetes depends largely on the patients' adherence with self-care practices.

Objective: Was to assess self-management and its associated factors among type 2 diabetes patients in Mekelle hospital and Ayder referral hospitals, Mekelle City, Tigray, Northern Ethiopia, 2012/13.

Method: The research design was institutional based cross sectional method and 343 study subjects were selected using systematic random sampling technique and the data was collected using interviewer administered structured questionnaire, data was analyzed and cleaned using SPSS version 16. Frequencies and proportions were computed. Bivariate and Multivariate logistic regression was computed to assess statistical association between the outcome variable and selected independent variables and significance of statistical association was assured or tested using 95%CI and P-value (<0.05).

Result: A total of 310 male and female adult type 2 diabetes patients were interviewed using standardized structured questionnaire and the response rate was 96.8 %. Of all respondents 57.7% were Male. The majority of the respondents 69% were in the age group of 40 to 69 years. Mean age of patients was 50.02±12.01 years. The mean age in which diabetic disease occurred was 44.53±11.07 years. The mean duration of diabetes was 5.63±7.6 years. More than half respondents 58.7% had multiple injection treatment (two injections per day). Of all respondents only 12.7% had long term diabetic complication confirmed medically.

The majority 86.0% of the study participants were not adhered to Self-Monitoring of Blood Glucose. Those who have glucometer at home were eleven times less risk not to be adhered to the practice when compared with those who didn't have [P<0.001, AOR (95% CI) = 10.722 (4.095-28.075)] and those who are with monthly income of above average were adhered nigh times more than counterpart [P<0.001, AOR (95% CI) = 9.036(1.742-46.879)]. A total of 83.7% respondents were adhered with prescribed anti-diabetic drugs and there

was significant association between prescribed medication adherence condition and monthly income[P=0.015, AOR (95% CI) = 2.761(1.106-6.892)].

From the total respondents 74.0% were reported adhered to physical activity that meet the recommended guidelines and those who were employment and age had statistically significant association with their adherence condition to physical activity [P=0.001, AOR(95% CI)= 4.349(1.191-15.884) and [P=0.453, AOR(95%CI)= 0.375 (0.150-0.940)] respectively. Of all respondents 51.3% were adhered to the recommended diabetic foot care practices and Education, marital status and monthly income were found to have statistically significant association with adherence to diabetic foot care practices [P=<0.001,AOR (95% CI) =10.525 (1.256-3.297)] and [P=<0.001, AOR (95% CI) =2.101 (1.060-4.165)] respectively. Over all Self-care management were reported adhered in 51.0%respondents. Education level, Marital status and diabetes complication were found to have statistically significant association with adherence level to overall diabetes self-care management [P<0.001, AOR (95% CI) = 4.194 (1.213- 14.510), [P<0.001, AOR (95%CI) = 0.343(0.162-0.726)] and [P=<0.004, AOR (95% CI) = 2.860 (1.109-7.375)]

Conclusion: Generally adherence to self-care management was suboptimal among type 2 diabetic patients in Ayder referral hospital endocrinology and Mekelle hospital chronic care unit.

Keywords: type 2 diabetic patients, diabetes management, physical exercise & anti diabetes agent.

I. INTRODUCTION

Diabetes is a general term for a group of metabolic disorders that affect the body's ability to process and use sugar (glucose) for energy. The three most common forms of diabetes are type 1diabetes, type 2 diabetes, and gestational diabetes. Type 2 diabetes mellitus comprises an array of dysfunctions resulting from the combination of resistance to insulin action and inadequate insulin secretion. It is characterized by hyperglycemia and associated with micro vascular (i.e., retinal, renal, possibly neuropathic), macro vascular (i.e., coronary, peripheral vascular), and

Author ^{α σ ρ ω}: Department of Nursing, College of Health sciences, Mekelle University, Tigray, North Ethiopia.
e-mails: kalushaibex@yahoo.com, haftuber@yahoo.com, aidhbk@gmail.com, Alex_aregay@yahoo.com

neuropathic (i.e., autonomic, peripheral) complications (1, 2).

The prevalence of diabetes has reached epidemic proportions. World Health Organization predicts that developing countries will bear the brunt of this epidemic in the 21st century. According to IDF diabetes Atlas, 5th edition 2012 report, currently, more than 80% of people with diabetes live in Low and Middle Income Countries. An estimated 366 million people were living with diabetes in 2011. The number is expected to grow to 552 million by 2030 and the largest age group currently affected by diabetes is between 40-59 years. By 2030 this "record" is expected to move to the 60-79 age groups with some 196 million cases. While the global prevalence of diabetes is 8.3%, the prevalence varies from 10% in the Western Pacific to 4% in the African region. However, the African region is expected to experience the highest increase in coming years with estimated increase in prevalence rates of 98% for sub-Saharan Africa, and 94% for North Africa and the Middle East (1,3,4).

The IDF Atlas 5th edition 2012 report (ARF) revealed that in 2011, 14.7 million adults in the Africa Region are estimated to have diabetes, with a regional prevalence of 3.8%. The top six countries with the highest number of people with diabetes make up just over half of the total number in the region. This would rise to 28 million by 2030 with prevalence of 4.3%, an increase of 80%, as such exceeding the predicted worldwide increase of 55%. Type 2 diabetes is responsible for 85-95% of all diabetes in high-income countries but Type 2 diabetes accounts for well over 90% of diabetes in Sub-Saharan Africa even in other low- and middle-income countries and population prevalence proportions ranged from 1% in rural Uganda to 12% in urban Kenya. Based on the IDF Atlas 5th edition, 2012 report number of cases of diabetes in Ethiopia to be estimated about 1.4 million in 2011. The greatest weapon in the fight against diabetes mellitus is knowledge. Information can help people assess their risk of diabetes, motivate them to seek proper treatment and care, and inspire them to take charge of their disease for their lifetime. In view of the increasingly high incidence of complications in diabetic patients, it would be valid to assess the perception of the primary healthcare patient of his or her actual disease state and the problems that may arise. Proper management requires life style changes and adequate Diabetes Knowledge of which is considered a key component of diabetes management. Differences in knowledge level have been described depending on level of education, gender and social classes (5,6,7,8).

When it is not prevented and properly managed diabetes is one of the major causes of premature illness and death worldwide. Non- communicable diseases including diabetes account for 60% of all deaths worldwide and more than 80% of diabetes deaths occur

in low- and middle-income countries According to IDF Atlas 5th edition 2012 report Diabetes caused 4.6 million deaths in 2011 globally. World Health Organization projects that diabetes deaths will double between 2005 and 2030 (9).

Statistics for medical complications from diabetes are also concerning. Proportions of patients with diabetic complications in sub Saharan region ranged from 7-63% for retinopathy, 27-66% for neuropathy, and 10-83% for nephropathy. Diabetes is likely to increase the risk of several important infections in the region, including tuberculosis, pneumonia and sepsis.

Assessment of the level self-care management among persons with diabetes can assist in targeting public health efforts to reduce complications. and Self-care practices are believed to play an important role in diabetes management this is because there is a significant link between blood glucose control using self-care practices and the later development of diabetes complications and with improved glycemic control the patient could decrease the risk of these complications (5) So the aim of this study was to assess diabetes self-care management and the influence of demographic characteristics and clinical status on their self-care management in patients with type 2 diabetes attending in Mekelle Hospital and Ayder referral hospital diabetes clinic, Mekelle City.

Today's nurse is faced with challenges of providing high quality evidence-based care to clients/patients in traditional as well as new innovative health care settings for both acute and chronic illnesses. Diabetes being a chronic illness requires continues self care practices by sufferers so that they can contribute meaningfully in the management of their lives. An essential ingredient that has been missing from the health care delivery system in Ethiopia is the lack of diabetes self care knowledge by the diabetic patients. Diabetes self care knowledge is considered an essential part of clinical management: simply prescribing the correct amount of insulin and oral agents and drawing up meal plan is not always enough to meet blood glucose targets. Poor patient understanding of diabetes is believed to impede appropriate self-care management, thus accelerating cardiovascular complications, stroke, and kidney failure.

A situation where diabetes patients visit clinics regularly and their blood glucose levels still remain high despite the treatment they receive is a problem that calls for attention. This is a very common observation in many diabetes patients. Sometimes, slight symptoms that these patients could take care of at home bring them back to the hospitals for medical checks. A good number of them, however, report to the hospital with severe complications, like gangrene that may lead to amputation and possible premature death, this might be because of lack of appropriate self care practices, as

cited by Okolie, V. Uchenna and Ehiemere, O. Ijeoma et al. The Behavioral Risk Factor Surveillance System for North Carolina revealed that 83% of respondents with type 2 diabetes mellitus performed blood glucose monitoring and more than 93% had visited a health care provider for diabetes care in the past year. Other researchers have suggested that self-care activities vary extensively according to the nature of the activity itself, with taking of medication often occurring as recommended and exercise frequently falling below recommended levels. For example, results from one study showed that 97% of respondents with diabetes always or usually took their medication, whereas only 41% always or usually exercised, as cited by Nancy E. Schoenberg (10,11).

Because of the importance of self-care activities to achieve and maintain desirable blood glucose levels or glycemic control, researchers increasingly have begun to investigate correlates of perceived barriers to type 2 diabetes self-care behaviors. For example study found that the following personal characteristics were associated with problems in type 2 diabetes mellitus self-care: lower education and socioeconomic status, higher level of depression, male gender, being unmarried and younger age (30-49 years old). However, although it is useful to identify general characteristics that relate to poor self-care behaviors, it may be of greater utility from a public health perspective to identify and understand inconsistent self care practices and associated factors of diabetes patients, as cited by Nancy E. Schoenberg (11).

Furthermore, although the studies cited above have begun to illuminate our understanding of some of the predictors of differences in diabetes self-care, we currently lack an in-depth understanding or information of level and associated factors of type 2 diabetes patients to ward diabetes self-care practices especially this is more obviously true in Ethiopia, Mekelle Hospital and Ayder referral hospital. To promote optimal self-care practices, it is important to understand the level to which adults with type 2 diabetes mellitus integrate self-care recommendations into their lives as well as its associated factors and their knowledge status. The major problematic condition about diabetes self care practices and their knowledge status is that there are limited research findings on patients who are found in sub Saharan Africa especially in Ethiopia, even there is no enough published material and little research is done. To address these deficits, this research explores patients' diabetes self-care management status and its associated factors in Mekelle Hospital and Ayder referral hospital diabetes clinic, Mekelle City.

II. METHODOLOGY

a) *Study area and period*

Mekelle, the capital city of Tigray Region and the largest city in northern Ethiopia. It is located approximately 780 km from the capital, Addis Ababa. It has two governmental and three private hospitals. Ayder referral hospital is the only University Hospital in Mekelle, Tigray region which was established in 2000 E.C with 500 beds. The hospital is one of the major referral & teaching hospital found in the region and the serves gives for patients from every corner of the region, some area of Afar & Amara regions with total annual flow of 32,000 patients. The second one is Mekelle Hospital, a Regional hospital for the area, that serve as a referral and teaching hospital, which was established in 1954 E.C with 162 beds and the total annual flow of 4276 patient. The two governmental hospitals are chosen to the study because the patient flow is significant and both serve to the region as referral and teaching hospital beside to this those hospitals are hospitals with a facility or clinic that serve as follow up clinic for all diabetes patients came from every corner of the region including from neighboring Afar and Amara regions. The study period will be from Sep. 2012 to July 2013.

b) *Study design*

The study design was institutional based cross-sectional study design.

c) *Source population*

The source population was all patients who visit the diabetes clinic of the hospitals during the study period (April 1st week to May 2nd week, 2013).

d) *Study population*

The study population was all Type 2 diabetic patients who visit the hospitals' diabetes clinic at the time of data collection period and fulfilling the inclusion criteria.

e) *Inclusion criteria*

Study subjects included in this study were those who full fill the following inclusion criteria

1. Age greater than 18 years.
2. Diagnosed with type 2 diabetes and made follow up for at least one months and consented.

f) *Exclusion criteria*

Study subjects excluded from this study were those who full fill the following exclusion criteria, they are those who

1. Were unable to answer the questions because of altered mental state or mentally unstable
2. Diagnosed as type 1 and gestational diabetics.

g) *Sample size determination*

The sample size for the study was determined using the following assumptions and single population

proportion formula: where Z^2 . Standard normal score at 95% confidence interval = 1.96, d = degree of accuracy or margin of error 0.02 to get maximum sample size., n_0 - Sample size desired (initial), n_1 - Final sample size, N = Estimated annual patients flow of type II diabetes in the two hospitals: 750, $P = 5.0\%$, which is population proportion prevalence of diabetic in Ethiopia (urban), So initial sample size was calculated as follow. $n_0 = (1.96)^2 * 0.05 * 0.95 / (0.02)^2 = 456$. Since the total population was less than 10,000, correction formula was used to determine The final sample size, as a result the final sample size was 285, Thus by adding 10 % for possible non-response rate, a total sample size of 310 was obtained. Proportion allocation was employed to allocate the sample size among the two hospitals.

h) Sampling procedure

Systematic random sampling technique was utilized for this study. K value was calculated as $K = n_f / N$, where n_f = final sample size = 310 and N = total Number of type 2 diabetes patients who are attending the units per week = 25. X_0 total number of days use for data collection = 48, $K_0 = n_f / X_0 = 310 / 48 = 6$ and $K = N / k_0 = 12 / 6 = 2$. So using the K value, patients was selected using patient registration number in every 2 number intervals and the first study subject was selected by lottery method and averagely 26 study subjects was interviewed weekly.

i) Data collection procedure

Data was collected using standardized structured questionnaire and three diploma completed Nurses with previous experience of data collection and multi lingual ability were recruited. Continuous follow up and supervision were made by the supervisors and principal investigators throughout the data collection period. Data collection was accomplished within twelve weeks duration (April. 1st week to July, 2013).

j) Data collection Tool

Interviewer administered structured questionnaire data collection tool was used, it contains three parts, Part I was used to collect socio demographic data, part II was used to collect clinical status data of the study subjects, part III is the original SDSCA, which was used to measure five areas or domains of diabetes self-care practices: diet, exercise, medication, and self-blood glucose monitoring. Beside to this the revised SDSCA also it contain items on foot care and smoking. SDSCA questionnaires will be adopted contextually (48).

k) Study variables

i. Independent variables

Socio-demographic characteristics: Age, Religion, Marital status, education level, Sex, monthly income, ethnicity, and occupation.

Clinical or disease state: Age of diabetes onset, Duration of the disease, Family history of diabetes, Complications of diabetes, Treatment intensity

ii. Dependent Variable

The outcome variables of the study was self-care managements (Self glucose monitoring, physical exercise, diet management, foot care and overall diabetes self-care management)

l) Pre-test

The questionnaire was pre-tested prior to the actual data collection on 10 respondents outside study area and the respondents were excluded from the actual study.

m) Data quality assurance

To assure data quality, training and orientation was given for the data collectors by the principal investigators. The questionnaire was initially prepared in English and then translated in to Tigrigna version. The Tigrigna version was again translated back to English to check for consistency of meaning. However since the dominant ethnic group is Tigrian with Tigrigna language then the study subjects was interviewed with Tigrigna version questionnaire. Moreover questionnaire was pre-tested and necessary corrections and amendment was considered. The collected data was reviewed and checked for completeness and consistency by principal investigators on daily bases at the spot during the data collection time.

n) Data entry and analysis

The data was recorded, cleaned and analyzed using SPSS version 16 software statistical packages. Frequencies and proportions were used to describe the study population in relation to relevant variables. Logistic regression was computed to assess statistical association via Odds ratio, and significance of statistical association was assured or tested using 95% confidence interval and P-value (<0.05). Bivariate and Multivariate analysis were employed to examine the relationship or statistical association between the outcome variable and selected independent variables. Results were presented using tables, figures and texts.

o) Ethical consideration

Ethical clearance was secured from the Mekelle University, college of health science IRB (research committee). Official letter of permissions was obtained from Tigray regional health Bureau, Ayder referral Hospital and Mekelle hospital medical director office and respondents ware well informed about the purpose of the study, then information was collected after written consent from each participant obtained. Respondents were allowed to refuse or discontinue participation at any time they want. Information was recorded anonymously and confidentiality and beneficence were assured throughout the study period.

p) *Operational definitions*

1. *Self-care management*: is defined as activities that individuals initiate and perform on their own behalf in maintaining life, health, and wellbeing.
2. *Adherence with Physical activity regimen*: was determined as 30 minutes moderate activity for at least 3 days per week or total score of $\geq 50\%$
3. *Foot Care*: was determined as proper care of the foot, including nail and skin care, and the selection of appropriate footwear daily(for 3 days and above per week) or total score of $\geq 50\%$
4. *Adherence with dietary regimen*: was recorded when the patient strictly followed the prescribed dietary regimen for 3 days or more days per week or total score of $\geq 50\%$.
5. *Adherence with anti-diabetic drugs*: was recorded when diabetic patient took all medications, done all self-management in accordance with prescription or total score of $\geq 80\%$.
6. *Adherence with Self measurement of blood glucose*: was recorded when the patient practice for 3 or more days per week or total score of $\geq 50\%$
7. The total score of each item of the questionnaire was calculated out of 100. Considering to the total score, the level of self-care practice was classified into: Not adhered (<49%), adhered (50% and above) .this scoring method is adopted from previously done researches (25, 49)

q) *Dissemination of the results*

The result of this study will be disseminated to ENA, EDA, Ayder referral hospital and Mekelle hospital medical director and nursing service offices and TRHB research unit. Moreover, efforts will be made to publish the paper in scientific journals.

III. RESULTS

a) *Socio-demographic characteristics of the respondents*

A total of 310 male and female adult type 2 diabetes patients were interviewed using standardized structured questionnaire and included in the analysis. Questioners of ten respondents were excluded from the analysis for gross incompleteness and inconsistency of responses, made a response rate of 96.8 %. Of all respondents 173(57.7%) and 127(42.3%) were Male and Female respectively. The majority of the study participants 207(69%) were in the age group of 40 to 69 years. Mean age of patients was 50.02 ± 12.01 years [(95% CI) (38.01-62.03)] with minimum of 30 and maximum of 78 years of age. Majority of respondents 264(88%) were orthodox Christian by religion and Tigrian 286 (95.3%) by ethnicity. A significant number 140 (46.7%) of the respondents did attend formal education. Two hundred twenty (73.3%) of respondents were married at the time of study period. From the total respondents one hundred three (34.3%) were unemployed and majority of the study participants 171(57%) were had very low monthly income (Table 1).

Table 1: Socio demographic data of the respondent

Sr. No	Variable	Category	Frequency	
			NO	%
1	Gender	Female	127	42.3
		Male	173	57.7
2	Age^a	25-39 years	75	25.0
		40-54 years	110	36.7
		55-69 years	97	32.3
		70-84 years	18	6.0
3	Monthly income^b	Very low	171	57.0
		Low	66	22.0
		Average	41	13.7
		Above average	22	7.3
4	Ethnicity	Tigrian	286	95.3
		Amara	14	4.7
5	Educational Level	Illiterate	140	46.7
		Elementary	80	26.7
		High school	37	12.3
		College university	43	14.3
6	Marital Status	Married	220	73.3
		Divorced	10	3.3
		Widowed	7	2.3
		Single/never married	63	21.0
7	Occupation	Employed	87	29.0
		un employed	103	34.3
		Merchant	14	4.7
		House servant	70	23.3
		Daily laborer	26	8.7
8	Religion	OrthodoxChristian	264	88.0
		Muslim	36	12.0

a Age category was adopted from research article (study done in Africa)

b Monthly income category: Very Low <445 Birr, Low=446-1200Birr, Average=1201-2500Birr,

Above Average= 2501-3500Birr and High >3501Birr (Based on the Ethiopian Civil service monthly salary for civil servants)

b) *Health status data of the respondents*

The mean age in which diabetic disease occurred was 44.53 ± 11.07 years [(95% CI) (33.46—55.60)] with minimum age of 27 and maximum age of 69. The mean duration of diabetes was 5.63 ± 7.6 years with minimum of 1 year and maximum of 33 years. More than half respondents 176 (58.7%) had multiple injection

treatment (two injections per day). Of all respondents 124(41.3%) had oral hypoglycemic agent. Two hundred thirty two (77.3%) of the respondents did not have family history of diabetes and only 44 (14.7%) respondents had glucometre at home. Of all respondents only 38 (12.7%) had long term diabetic complication confirmed medically. (Table2).

Table 2: Health status data of respondents research done in Ayder referral hospital and Mekelle hospital Endocrine Unit, Ethiopia, 2012/13 (N=300)

Sr. No	Variable	Category	Frequency	
			NO	%
1	Age in which DM start	25-39 years	114	38.0
		40-54 years	122	40.7
		55-69 years	64	21.3
2	Duration of DM	less than 5 years	207	69.0
		6-10 years	59	19.7
		11 and above years	34	11.3
3	Family History of DM	No	232	77.3
		Yes	68	22.7
4	Treatment intensity	Oral hypoglycemic agent	124	41.3
		Insulin therapy	176	58.7
5	Currently do you have glucometry at home	No	256	85.3
		Yes	44	14.7
6	Diabetes Complication	No	262	87.3
		Yes	38	12.7

c) *All Self-care management Domains Adherence Condition of respondents*

Respondents' self-care management were, the majority 258 (86.0%) respondents were not adhered to SMBG practice. A total of 251(83.7%) respondents were adhered to anti-diabetic medication. The majority 208 (69.3%) respondents were not adhered to recommended diet management practices. From the total respondents two hundred twenty two (74.0%) were reported adhered to physical activity that meet the recommended guidelines. Of all study participants, 154 (51.3%) respondents were adhered to the recommended diabetic foot care practices. Overall self-care practices (SDSCA) were reported as adhered in 153(51.0%) participants. Of all respondents 311(97%) were adhered to prescribed anti-diabetic medications. (Fig1 show the detail).

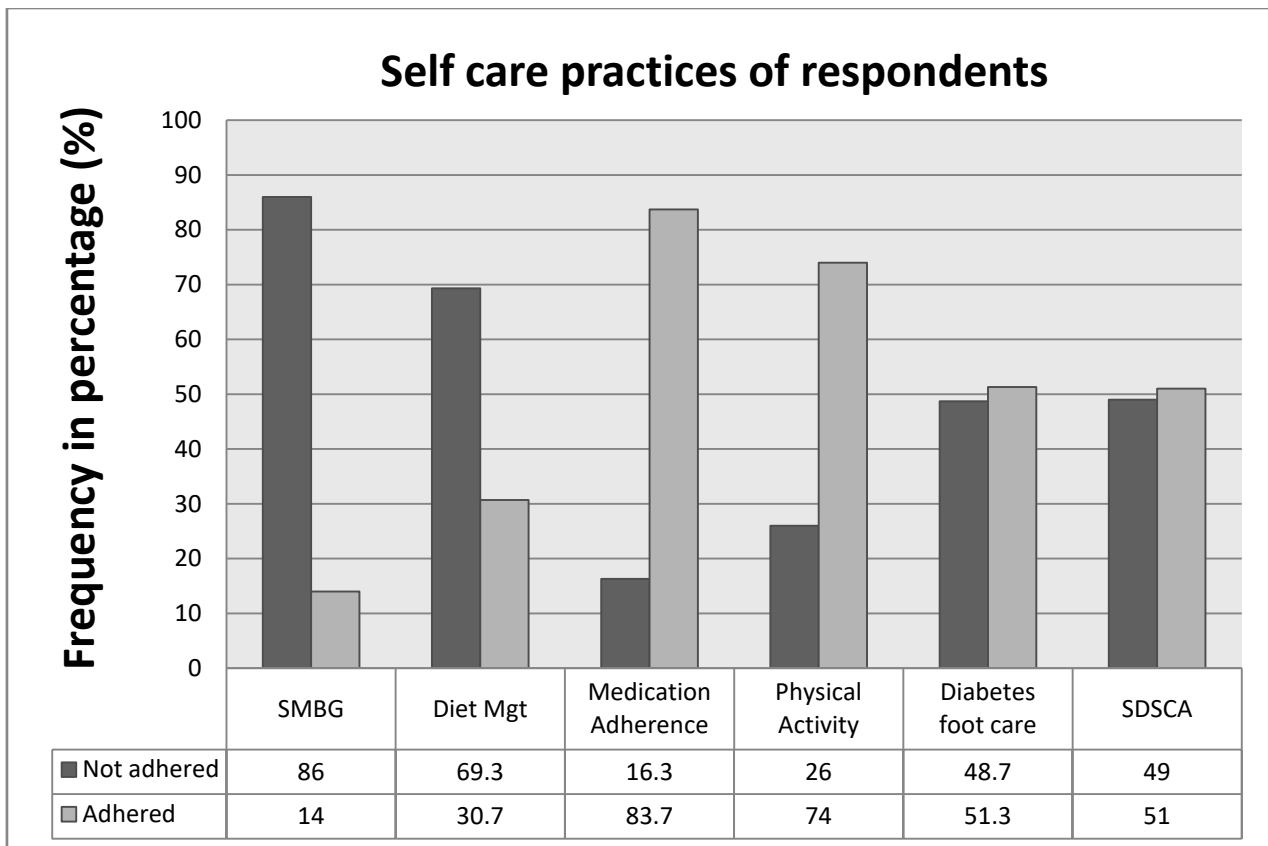


Figure 1: A Bar graph showing Self-care management adherence level of type 2 diabetes Patients in Ayder referral hospital and Mekelle hospital Endocrine Unit, Ethiopia, 2012/13 (N=300)

d) Adherence to Self-Monitoring of Blood Glucose (SMBG) Practice

The majority 258(86.0%) of the study participants were not adhered to Self-Monitoring of Blood Glucose which means, monitored less than 1-2 times per week, even almost all participants said that they did SMBG practices when they had symptoms of hyperglycemia or hypoglycemia or at the time of health care visit and only 42(14.0%) were adhered which means monitored at least 2 times a week. Presence of glucometer at home, and Monthly income was found to have statistically significant association with adherence to SMBG practice. Those who have glucometer at home were eleven times less risk not to be adhered to the practice when compared with those who didn't have [P<0.001, AOR (95% CI) = 10.722 (4.095-28.075)] and those who are with monthly income of above average were adhered high times more than counterpart [P<0.001, AOR (95% CI) = 9.036(1.742-46.879)]. Table 5 shows the details of Logistic regression analysis result of SMBG practice and health status data and demographic characteristics.

Table 3: Logistic regression analysis result of Adherence to SMBG practice and Socio demographic & clinical data among Type 2 diabetic study subjects in Mekelle & Ayder Hospitals, Ethiopia 2012 (N=300)

Factor	SMBG Practices		COR	CI of 95 %	AOR	CI of 95%
	Not adhered	Adhered				
	No. (%)	No. (%)				
Monthly income P-Value=<0.001						
Very low	159(53.0)	12(4.0)	1.00		1.00	
Low	57(19.0)	9(3.0)	2.092	(0.837-5.227)	1.964	(0.637-6.049)
Average	30(10.0)	11(3.7)	4.858	(1.963-12.026)*	2.919	(0.643-13.260)
Above average	12(4.0)	10(3.3)	11.042	(3.966-30.743)*	9.036	(1.742-46.879)**
Total	258(86.0)	42(14.0)				
Level of education P-value=0.001						
Illiterate	129(43.0)	11(3.7)	1.00		1.00	
Elementary	67(22.3)	13(4.3)	2.275	(0.967-5.353)	2.133	(0.711-6.403)
High school	31(10.3)	6(2.0)	2.270	(0.779-6.612)	0.918	(0.187-4.513)
College university	31(10.3)	12(4.0)	4.540	(1.832-11.246)*	0.296	(0.055-1.600)
Total	258(86.0)	42(14.0)				
Occupation: P-Value=0.012						
Employed	67(22.3)	20(6.7)	1.00		1.00	
un employed	92(30.7)	11(3.7)	0.401	(0.180-0.892)*	0.799	(0.235-2.719)
Merchant	10(3.3)	4(1.3)	1.340	(0.379-4.736)	0.679	(0.149-3.100)
House servant	65(21.7)	5(1.7)	0.258	(0.091-0.727)*	0.460	(0.115-1.840)
Daily laborer	24(8.0)	2(0.7)	0.279	(0.061-1.285)*	0.755	(0.107-5.327)
Total	258(86.0)	42(14.0)				
Age in which diabetes started P-Value=0.269						
25-39 years	98(32.7)	16(5.3)	2.449	(0.782-7.671)	1.00	
40-54 years	100(33.3)	22(7.3)	3.300	(1.085-10.037)*	1.283	(0.514-3.200)
55-69 years	60(20.0)	4(1.3)	1.00		0.335	(0.082-1.364)
Total	258(86.0)	42(14.0)				
Family History of Diabetes P-Value=0.030						
No	205(68.3)	27(9.0)	1.00			
Yes	53(17.7)	15(5.0)	2.149	(1.067-4.326)*	0.978	(0.390-2.455)
Total	258(86.0)	42(14.0)				
Diabetes Complication P-Value=0.401						
No	227(75.7)	35(11.7)	1.465	(0.599-3.581)		
Yes	31(10.3)	7(2.3)	1.00			
Total	258(86.0)	42(14.0)				
Diabetes knowledge level P-Value=0.130						
No	149(49.7)	19(6.3)	1.00			
Yes	109(36.3)	23(7.7)	0.604	(0.314-1.164)		
Total	258(86.0)	42(14.0)				
Presence of Glucometre at home P-Value=<0.001						
No	235(78.3)	21(7.0)	1.00			
Yes	23(7.7)	21(7.0)	10.217	(4.870-21.438)*	10.722	(4.095-28.075)**
Total	258(86.0)	42(14.0)				

NB: P-Value is, Value of COR analysis result

** Statistically associated Variable

P=<0.05

*Variable were showed Statistical Association in COR but lost during AOR Analysis,

e) *Adherence to diet management of the respondents*

The majority 208 (69%) of the study participants were not adhered to recommended diet management practices which means, apply the recommended diet management practices for about less than 1-2 times per week, and only 92(30.7%) study participants were Adhered which means follow the recommended diet management practices at least 3-4 times a week. Variables like education level and marital status were showed statistically significant association with adherence to diet management practices. Respondents

with high level of education (college or university graduates) and who are single were about four and two times more likely to be engaged in diet management practices when compared with their counter parts [P<0.001, AOR (95% CI) = 4.481 (1.166-17.222)] and [P=0.002, AOR (95% CI) = 2.416(1.157-5.044)] respectively. Table6 shows the details of Logistic regression analysis result of diet management practice adherence condition and health status data and demographic characteristics.

Table 4: Logistic regression analysis result of Adherence to diet management and Socio demographic & clinical data Among Type 2 diabetic study subjects in Mekelle & Ayder Hospitals, Ethiopia 2012 (N=300)

Factor	Diet management		COR	CI of 95 %	AOR	CI of 95%
	Not adhered	Adhered				
	No. (%)	No. (%)				
Gender P-Value=0.012						
Female	98(32.7)	29(9.7)	1.00		1.00	
Male	110(36.7)	63(21.0)	1.935	(1.154-3.247)*	1.422	(0.750-2.697)
Total	208(69.3)	92(30.7)				
Age P-value=0.08						
25-39 years	45(15.0)	30(10.0)	3.333	(0.888-12.514)		
40-54 years	74(24.7)	36(12.0)	2.432	(0.662-8.943)		
55-69 years	74(24.7)	23(7.7)	1.554	(0.413-5.846)		
70-84 years	15(5.0)	3(1.0)	1.00			
Total	208(69.3)	92(30.7)				
Monthly income P-Value=0.061						
Very low	125(41.7)	46(15.3)	1.00		1.00	
Low	43(14.3)	23(7.7)	1.453	(0.791-2.672)	0.956	(0.431-2.122)
Average	29(9.7)	12(4.0)	1.124	(0.530-2.387)	0.252	(0.075-0.845)
Above average	11(3.7)	11(3.7)	2.717	(1.103-6.694)*	0.945	(0.235-3.796)
Total	208(69.3)	92(30.7)				
Level of Education P-Value= <0.001						
Illiterate	113(37.7)	27(9.0)	1.00		1.00	
Elementary	56(18.7)	24(8.0)	1.794	(0.949-3.389)	1.564	(0.721-3.394)
High school	18(6.0)	19(6.3)	4.418	(2.047-9.535)	4.195	(1.516-11.604)**
College university	21(7.0)	22(7.3)	4.384	(2.112-9.104)*	4.481	(1.166-17.222)**
Total	208(69.3)	92(30.7)				
Marital status P-Value=0.002						
Married	162(54.0)	58(19.3)	1.00		1.00	
Divorced	8(2.7)	20(7)	0.698	(0.144-3.384)	0.840	(0.168-4.202)
Widowed	5(1.7)	2(0.7)	1.117	(0.211-5.917)	1.224	(0.193-7.764)
Single/never married	33(11.0)	30(10.0)	2.539	(1.424-4.527)*	2.416	(1.157-5.044)**
Total	208(69.3)	92(30.7)				
Occupation P-Value=0.037						
Employed	47(15.7)	40(13.3)	1.00		1.00	
un employed	79(26.3)	24(8.0)	0.357	(0.192-0.665)*	0.479	(0.192-1.191)
Merchant	11(3.7)	3(1.0)	0.320	(0.084-1.229)	0.237	(0.048-1.171)
House servant	54(18.0)	16(5.3)	0.348	(0.173-0.701)*	0.455	(0.161-1.286)
Daily laborer	17(5.7)	9(3.0)	0.622	(0.250-1.547)	0.849	(0.250-2.883)
Total	208(69.3)	92(30.7)				
Age in which Diabetes started P-Value=0.006						
25-39 years	70(23.3)	44(14.7)	2.724	(1.310-5.665)*	1.00	
40-54 years	86(28.7)	36(12.0)	1.814	(0.867-3.796)	1.588	(0.773-3.262)
55-69 years	52(17.3)	12(4.0)	1.00		1.158	(0.457-2.932)
Total	208(69.3)	92(30.7)				

** Statistically associated Variable

P= <0.05

*Variable were showed Statistical Association in COR but lost during AOR Analysis,

NB: P-Value is, Value of COR analysis result

f) Adherence to Prescribed medication

A total of 251(83.7%) study participants were adhered with prescribed anti-diabetic drugs but out of the total study subjects 49(16.3%) were non-adhered. Of the total adhered respondents 147(49.0%) and 104 (34.7%) were Male and Female respectively and out of all not adhered respondents 26(8.7%) and 23(7.7%) were male and female respectively. Treatment intensity of the study participants were oral hypoglycemic agent 124(41.3%) and insulin therapy 176(58.7%). Multinomial logistic regression analysis result showed that there was

significant association between prescribed medication adherence condition and monthly income, those who had higher income were three times adhered than those who had very low monthly income[P=0.015,AOR (95% CI) = 2.761(1.106-6.892)]. But no association were shown to other health status data and socio demographic characteristics. Table 7 shows the details of Logistic regression analysis result of adherence to Anti-diabetes medication and health status data and demographic characteristics.

Table 5: Logistic regression analysis result of Adherence to Medication and Socio demographic & clinical data Among Type 2 diabetic study subjects in Mekelle & Ayder Hospitals, Ethiopia 2012 (N=300)

Factor	Medication Adherence		COR	CI of 95 %	AOR	CI of 95%
	Not adhered	Adhered				
	No. (%)	No. (%)				
Monthly income P-Value=0.015						
Very low	37(12.3)	134(44.7)	1.00		1.00	
Low	6(2.0)	60(20.0)	2.761	(1.106-6.892)*	2.761	(1.106-6.892)**
Average	4(1.3)	37(12.3)	2.554	(0.855-7.627)	2.554	(0.855-7.627)
Above average	2(0.7)	20(6.7)	2.761	(0.617-12.355)	2.761	(0.617-12.355)
Total	49(16.3)	251(83.7)				
Level of education P-value=0.019						
Illiterate	28(9.3)	112(37.3)	1.00			
Elementary	15(5.0)	65(21.7)	1.083	(0.539-2.176)		
High school	3(1.0)	34(11.3)	2.833	(0.811-9.899)		
College university	3(1.0)	40(13.3)	3.333	(0.961-11.567)		
Total	49(16.3)	251(83.7)				
Occupation: P-Value=0.123						
Employed	10(3.3)	77(25.7)	2.310	(0.750-7.118)		
un employed	17(5.7)	86(28.7)	1.518	(0.531-4.338)		
Merchant	3(1.0)	11(3.7)	1.100	(0.229-5.282)		
House servant	13(4.3)	57(19.0)	1.315	(0.441-3.925)		
Daily laborer	6(2.0)	20(6.7)	1.00			
Total	49(16.3)	251(83.7)				
Marital status P-Value=0.040						
Married	31(10.3)	189(63.0)	1.905	(0.953-3.810)		
Divorced	0(0.0)	10(3.3)	5.048	(0.000 -).		
Widowed	3(1.0)	4(1.3)	0.417	(0.084-2.075)		
Single/never married	15(5.0)	48(16.0)	1.00			
Total	49(16.3)	251(83.7)				
Family History of Diabetes P-Value=0.608						
No	37(12.3)	195(65.0)	1.00			
yes	12(4.0)	56(18.7)	0.885	(0.433-1.811)		
Total	49(16.3)	251(83.7)				
Diabetes Complication P-Value=0.335						
No	43(14.3)	219(73.0)	0.955	(0.376-2.423)		
yes	6(2.0)	32(10.7)	1.00			
Total	49(16.3)	251(83.7)				
Diabetes knowledge level P-Value=0.923						
Poor	28(9.3)	140(46.7)	1.00			
Good	21(7.0)	111(37.0)	1.057	(0.570-1.962)		
Total	49(16.3)	251(83.7)				
Presence of Glucometre at home P-Value=<0.001						
No	44(14.7)	212(70.7)	1.00			
Yes	5(1.7)	39(13.0)	1.619	(0.604-4.339)		
Total	49(16.3)	251(83.7)				

** Statistically associated Variable P= <0.05

*Variable were showed Statistical Association in COR but lost during AOR Analysis,

NB: P-Value is, Value of COR analysis result

g) Adherence to Physical activity regimen of respondents

From the total respondents two hundred twenty two (74.0%) were reported adhered to physical activity that meet the recommended guidelines and 78 (26.0%) were not adhered. Respondents who were in the age group of 40-54 years and those who were employed had statistically significant association with their adherence condition to physical activity and those who are in the age group of 40-54 years were about four

times more likely to be engaged in physical activity when compared with those who are in the age group of 25-39 years [P=0.001, AOR(95% CI)=4.349(1.191-15.884) and those who are employed were 70 % likely to protected from the risk or be engaged in physical activity as compared to unemployed one [P=0.453, AOR(95%CI)= 0.375(0.150-0.940)]. Table8 shows the details of Logistic regression analysis result of physical Activities regimen adherence condition and health status data and demographic characteristics.

Table 6: Logistic regression analysis result of Adherence to Physical activity and Socio demographic & clinical data Among Type 2 diabetic study subjects in Mekelle & Ayder Hospitals, Ethiopia 2012/13 (N=300)

Factor	Physical Activity		COR	CI of 95 %	AOR	CI of 95%
	Not adhered	Adhered				
	No. (%)	No. (%)				
Age P-Value=0.001						
25-39 years	18(6.0)	57(19.0)	3.958	(1.358-11.541)*	1.00	
40-54 years	14(4.7)	96(32.0)	8.571	(2.894-25.384)*	4.349	(1.191-15.884)**
55-69 years	36(12.0)	61(20.3)	2.118	(0.766-5.855)	1.478	(0.349-6.256)
70-84 years	10(3.3)	8(2.7)	1.00		1.074	(0.165-6.994)
Total	78(26.0)	222(74.0)				
Level of education P-value=0.003						
Illiterate	47(15.7)	93(31.0)	1.00		1.00	
Elementary	19(6.3)	61(20.3)	1.623	(0.870 -3.025)	1.650	(0.800-3.404)
High school	6(2.0)	31(10.3)	2.611	(1.018-6.697)*	2.515	(0.805-7.859)
College university	6(2.0)	37(12.3)	3.116	(1.228-7.908)*	1.963	(0.532-7.247)
Total	78(26.0)	222(74.0)				
Occupation: P-Value=0.453						
Employed	12(4.0)	75(25.0)	0.815	(0.212-3.140)	1.00	
un employed	44(14.7)	59(19.7)	0.175	(0.049-0.620)*	0.375	(0.150-0.940)**
Merchant	5(1.7)	9(3.0)	0.235	(0.046-1.193)	0.294	(0.079-1.095)
House servant	14(4.7)	56(18.7)	0.522	(0.137-1.989)	1.149	(0.407-3.239)
Daily laborer	3(1.0)	23(7.7)	1.00		2.701	(0.559-13.039)
Total	78(26.0)	222(74.0)				
Age in which diabetes started P-Value=0.003						
25-39 years	22(7.3)	92(30.7)	2.861	(1.447-5.659)*	1.00	
40-54 years	30(10.0)	92(30.7)	2.098	(1.099-4.007)*	0.758	(0.211-2.720)
55-69 years	26(8.7)	38(12.7)	1.00		0.927	(0.217-3.964)
Total	78(26.0)	222(74.0)				
Family History of Diabetes P-Value=0.030						
No	65(21.7)	167(55.7)	1.00			
yes	13(4.3)	55(18.3)	1.647	(0.844-3.215)		
Total	78(26.0)	222(74.0)				
Diabetes Complication P-Value=0.043						
No	63(21.0)	199(66.3)	2.060	(1.013-4.188)*	1.00	
yes	15(5.0)	23(7.7)	1.00		0.569	(0.238-1.358)
Total	78(26.0)	222(74.0)				
Diabetes knowledge level P-Value=0.330						
Poor	40(13.3)	128(42.7)	1.00			
Good	38(12.7)	94(31.3)	0.773	(0.461-1.297)		
Total	78(26.0)	222(74.0)				
Gender P-Value=0.290						
Female	37(12.3)	90(30.0)	1.00			
Male	41(13.7)	132(44.0)	1.324	(0.788-2.224)		
Total	78(26.0)	222(74.0)				

** Statistically associated Variable P= <0.05

*Variable were showed Statistical Association in COR but lost during AOR Analysis,

NB: P-Value is, Value of COR analysis result

h) Adherence to Diabetic Foot care of respondents

Among 300 study participants 154(51.3) respondents were adhered to the recommended diabetic foot care practices and 146(48.7%) were not adhered. Education, marital status and monthly income were found to have statistically significant association with adherence to diabetic foot care practices. Respondents who are college graduates and with higher monthly income were about eleven and two times more likely to be engaged in the practices when compared

with the counterpart [P= <0.001, AOR (95% CI) =10.525 (1.256-3.297)] and [P= <0.001, AOR (95% CI) =2.101 (1.060-4.165)] respectively. But single respondents were about 70% protected from not to be adhered to diabetes foot care practices, [P= <0.001, AOR (95% CI) =0.317 (0.146-0.689)]. Table 9 shows the details of Logistic regression analysis result of diabetic foot care practice adherence condition and health status data and demographic characteristics.

Table 7: Logistic regression analysis result of Adherence to diabetes foot care and Socio demographic & clinical data Among Type 2 diabetic study subjects in Mekelle & Ayder Hospitals, Ethiopia 2012 (N=300)

Factor	Diabetes foot care		COR	CI of 95 %	AOR	CI of 95%
	Not adhered	Adhered				
	No. (%)	No. (%)				
Gender P-Value=0.328						
Female	66(22.0)	61(20.3)	0.795	(0.502-1.258)		
Male	80(26.7)	93(31.0)	1.00			
Total	146(48.7)	154(51.3)				
Age P-Value=0.014						
25-39 years	33(11.0)	42(14.0)	6.364	(1.699-23.840)*	0.441	(0.066-2.931)
40-54 years	48(16.0)	62(20.7)	6.458	(1.768-23.593)*	1.041	(0.202-5.374)
55-69 years	50(16.7)	47(15.7)	4.700	(1.278-17.280)*	2.112	(0.505-8.837)
70-84 years	15(5.0)	3(1.0)	1.00			
Total	146(48.7)	154(51.3)				
Level of education P-value=<0.001						
Illiterate	97(32.3)	43(14.3)	1.00			
Elementary	34(11.3)	46(15.3)	3.052	(1.725-5.399)*	2.394	(1.225-4.680)**
High school	9(3.0)	28(9.3)	7.018	(3.053-16.134)*	4.866	(1.736-13.637)**
College university	6(2.0)	37(12.3)	13.911	(5.465-35.411)*	10.525	(2.861-38.728)**
Total	146(48.7)	154(51.3)				
Marital Status P-Value=<0.001						
Married	124(41.3)	96(32.0)	0.286	(0.154-0.530)	0.317	(0.146-0.689)**
Divorced	4(1.3)	6(2.0)	0.554	(0.139-2.208)*	0.574	(0.118-2.794)
Widowed	1(0.3)	6(2.0)	2.217	(0.248-19.791)	3.480	(0.338-35.798)
Single/never married	17(5.7)	46(15.3)	1.00		1.00	
Total	146(48.7)	154(51.3)				
Monthly income P-Value=<0.001						
Very low	105(35.0)	66(22.0)	1.00			
Low	25(8.3)	41(13.7)	2.609	(1.454-4.683)*	2.101	(1.060-4.165)**
Average	11(3.7)	30(10.0)	4.339	(2.037-9.244)*	1.294	(0.457-3.665)
Above average	5(1.7)	17(5.7)	5.409	(1.905-15.358)*	1.869	(0.462-7.559)
Total	146(48.7)	154(51.3)				
Age in which diabetes started P-Value=0.002						
25-39 years	45(15.0)	69(23.0)	2.733	(1.450-5.152)*	2.605	(0.760-8.921)
40-54 years	60(20.0)	62(20.7)	1.842	(0.989-3.431)	1.566	(0.655-3.748)
55-69 years	41(13.7)	23(7.7)	1.00		1.00	
Total	146(48.7)	154(51.3)				
Diabetes Complication P-Value=0.024						
No	121(40.3)	141(47.0)	2.241	(1.099-4.571)*	1.861	(0.743-4.664)
yes	25(8.3)	13(4.3)	1.00		1.00	
Total	146(48.7)	154(51.3)				
Diabetes knowledge level P-Value=0.04						
No	94(31.3)	74(24.7)	1.00		1.00	
yes	52(17.3)	80(26.7)	1.954	(1.230-3.106)*	1.446	(0.831-2.516)
Total	146(48.7)	154(51.3)				

** Statistically associated Variable P=<0.05

*Variable were showed Statistical Association in COR but lost during AOR Analysis,

NB: P-Value is, Value of COR analysis result

i) Adherence to overall self-care management (SDSCA) of respondents

Self-care managements were reported adhered in 153 (51.0%) respondents, and not adhered in 147 (49.0%) respondents. Respondents who are college graduates, Married and diabetes complication were found to have statistically significant association with adherence level to overall diabetes self-care management and about four times more likely to be engaged in overall self-care management when compared with illiterate respondents [P<0.001, AOR (95% CI) =4.194 (1.213- 14.510)and marital status

showed that significant association but it is protective which means respondents who are married had 70% chance to be engaged in the practice as compared with their counterpart [P<0.001, AOR (95%CI)=0.343(0.162-0.726)]. Similarly those respondents who are without diabetes complication were adhered two times more than the counterpart [P=<0.004, AOR (95% CI) =2.860 (1.109-7.375)]. Table10 shows the details Logistic regression analysis result of overall self-care practice adherence condition and health status data and demographic characteristics.

Table 8: Logistic regression analysis result of Adherence to SDSCA and Socio demographic & clinical data Among Type 2 diabetic study subjects in Mekelle & Ayder Hospitals, Ethiopia 2012 (N=300)

Factor	SDSCA		COR	CI of 95 %	AOR	CI of 95%
	Not adhered	Adhered				
	No. (%)	No. (%)				
Gender P-Value=0.041						
Female	71(23.7)	56(18.7)	1.00		1.00	
Male	76(25.3)	97(32.3)	1.618	(1.020-2.567)*	1.244	(0.720-2.150)
Total	147(49.0)	153(51.0)				
Age P-Value=0.001						
25-39 years	31(10.3)	44(14.7)	4.968	(1.493-16.535)*	0.639	(0.108-3.768)
40-54 years	45(15.0)	65(21.7)	5.056	(1.562-16.361)*	1.441	(0.309-6.722)
55-69 years	57(19.0)	40(13.3)	2.456	(0.753-8.013)	1.417	(0.384-5.226)
70-84 years	14(4.7)	4(1.3)	1.00		1.00	
Total	147(49.0)	153(51.0)				
Level of education P-value= <0.001						
Illiterate	93(31.0)	47(15.7)	1.00		1.00	
Elementary	37(12.3)	43(14.3)	2.300	(1.311-4.035)*	1.698	(0.868-3.322)
High school	11(3.7)	26(8.7)	4.677	(2.128-10.279)*	2.471	(0.942-6.478)
College university	6(2.0)	37(12.3)	12.202	(4.809-30.963)*	4.194	(1.213-14.510)**
Total	147(49.0)	153(51.0)				
Marital Status P-Value= <0.001						
Married	124(41.3)	96(32.0)	0.264	(0.141-0.493)*	0.343	(0.162-0.726)**
Divorced	4(1.3)	6(2.0)	0.511	(0.128-2.043)*	0.669	(0.142-3.151)
Widowed	3(1.0)	4(1.3)	0.454	(0.092-2.250)*	0.657	(0.108-3.987)
Single/never married	16(5.3)	47(15.7)	1.00		1.00	
Total	147(49.0)	153(51.0)				
Monthly income P-Value= <0.001						
Very low	100(33.3)	71(23.7)	1.00		1.00	
Low	33(11.0)	33(11.0)	1.408	(0.796-2.491)	1.223	(0.623-2.401)
Average	10(3.3)	31(10.3)	4.366	(2.012-9.477)*	1.374	(0.486-3.880)
Above average	4(1.3)	18(6.0)	6.338	(2.057-19.528)*	2.743	(0.677-11.106)
Total	147(49.0)	153(51.0)				
Age in which diabetes started P-Value= <0.001						
25-39 years	43(14.3)	71(23.7)	3.152	(1.662-5.978)*	2.010	(0.606-6.670)
40-54 years	62(20.7)	60(20.0)	1.848	(0.988-3.456)	1.197	(0.499-2.870)
55-69 years	42(14.0)	22(7.3)	1.00		1.00	
Total	147(49.0)	153(51.0)				
Diabetes Complication P-Value=0.004						
No	120(40.0)	142(47.3)	2.905	(1.383-6.100)*		
yes	27(9.0)	11(3.7)	1.00		1.00	
Total	147(49.0)	153(51.0)			2.860	(1.109-7.375)**
Presence of Glucometre at home P-Value=0.002						
No	135(45.0)	121(40.3)	1.00		1.00	
yes	12(4.0)	32(10.7)	2.975	(1.467-6.036)*	2.324	(0.904-5.977)
Total	147(49.0)	153(51.0)				

** Statistically associated Variable

P= <0.05

*Variable were showed Statistical Association in COR but lost during AOR Analysis,

NB: P-Value is, Value of COR analysis result

SDSCA= means summarized diabetes self-care activities (over all the five domain of self-care management)

IV. DISCUSSION

In Ethiopia, there is limited information about the diabetes self-care managements of patients with type 2 diabetes mellitus. Thus this study has tried to assess the diabetes self-care management level and its associated factors among type 2 diabetes patients in Ayeder

referral Hospital endocrinology unit and Mekelle Hospital chronic care unit, Mekelle City, Ethiopia. In this study the majority of subjects 94.0% were found to be in the age group 25 to 69 years and 6.0% of the respondents were in the age group of 70-84 years. Similarly study done in Ethiopia (Tikur Anbesa specialized hospital), Egypt showed that 73% , 66% respondents in the age group of

30-60 years and 28%, 44% of respondents were 61 and above years respectively. The present study showed that 58.7% and 41.3% of the sample were taking insulin injection and oral hypoglycemic agent respectively compared to 35% and 57% in a study done in Egypt and 64% and 32% in a study done in Tikur Anbesa Specialized hospital, Ethiopia. But study carried out in United States revealed that Three-quarters of the patients received hypoglycemic agents (oral or insulin) (19, 26, 30).

Diabetes outcome depends mainly on the patient's sound self-care management that is dependent upon their health-related behavior and care-seeking which are guided and determined by individually and culturally defined beliefs about health, illness and health-care. As far as we know, this is the first study investigating Self-care management using a validated instrument among diabetes patients who have follow-up in Ayder referral hospital and Mekelle hospital.

Diabetes self-management behaviors such as diet and exercise involve depend on guidance from a health care provider, meal preparation in a family context, exercising with a partner or in a group. Glucose monitoring is a relatively quick and straightforward procedure; diabetes is managed via a regimen of control via self-care management. Health professionals advise adults living with type 2 diabetes to control blood sugar levels by controlling diabetogenic life style like diet management, maintaining regular exercise, and adhered regularly to prescribed medications. The extent to which individuals are able to adhere to such recommendations varies and entirely dependent on various factors like diabetes knowledge level. Despite the increasing prevalence of diabetes, improved understanding of the disease, and a variety of new medications, glycemic control does not appear to be improving. SMBG is one strategy for improving glycemic control; however, patients' adherence is suboptimal and a proper education and follow-up are crucial, cited by Eman M. Mahfouz, and Hala I (19,30).

The finding of this study also showed that only 14% were adhered to SMBG practices. This result is higher than a study done in Ethiopia 5%, India 3% and Nigeria 8% but lower than Pakistan 61%, U.S.A 78% of respondents were check blood glucose regularly. But almost similar with studies done in Ethiopia (TASH) 16%, Malaysia 15%. A study done in Malaysia showed that level of education; family income; duration of diabetes; and treatment regime (insulin) and in Ethiopia (TASH) showed that level of education, monthly income and presence of glucometre at home was significant predictors of SMBG practice. Similarly in this study monthly income and presences of glucometer at home showed that significant association to SMBG practices. Although SMBG is recognized to be useful and effective in achieving diabetes control, this study has found that only a minority of respondents with diabetes were

perform SMBG (Self-Monitoring of Blood Glucose) practices this is probably related to a lack of awareness on its importance in the management of diabetes and there are relevant financial barriers to purchase the device and its strips (8,14,16, 17,18,30,42).

In this study only 16.3% were unable to adhere with prescribed medicine. This result was lower from study result of Ethiopia (3%), Egypt (9%), Malaysia (46%) and Nigeria (46%). This study indicated that there was significant association between medication adherence and monthly income. But study done in Ethiopia showed that type of diabetes medication (injection or pills) had significant association and in Nigeria report that lack of finance, drug side effect, and perceived inefficacy of the prescribed medications had significant association with the practice.. Concerning adherence to the diet management practices; this study showed that only 30.7% of respondents were adhered. This is higher than a study done in Ethiopia(TASH) 21% but lower than a study done in Egypt 81%, India women 52% and men 32% and Iran 96% male and 100% female were followed the recommended diet instructions. Study done in U.A.E indicated that only 24% respondents were read food labeling. 76% reported being unable to distinguish clearly between low and high carbohydrate index food items and no one reported counting calorie intake. 46% reported that they had never been seen by dietician since their diagnosis. Their overall risk profile, notably body weight, lipid profile and blood pressure, was very unfavorable; more than half of the study sample had uncontrolled hypertension and uncontrolled lipid profile and the majority was overweight (36%) or obese (45%). Abdominal obesity was particularly common (59%). Only 31% had an HbA1c of less than 7%. As this study indicated that Similar to the SMBG practice adherence condition, adherence to diet management practices were lower than the other studies, this might be because of financial barrier, Poor perception toward the importance of fruits and vegetables, lack of awareness on the importance of the practices and most respondents had not any idea even how to prepare and follow healthy diet plan at all, Socio-cultural variation and life style difference (16, 19, 20, 23, 30).

A study in Ethiopia (TSAH) and Egypt showed that there was a statistically significant difference between marital status, education and adherence to dietary management of diabetes, nearly one quarter (26%) of illiterates were not adhered to dietary management of diabetes and also revealed that younger age group and shorter disease duration had a positive impact on dietary management practices adherence condition (19, 30).

Similarly this study also showed that subjects with high level of education and who are single were more adhered to dietary management practices than the counterpart but other socio demographic data, health

status data and diabetes knowledge level did not show significant association this might be because of small sample size. In this study 74.0% respondents were adhered to physical activity that meets the recommended guidelines. This result is higher than studies done in Ethiopia (TASH) 53.0%, U.A.E only 3%, in India only 9% of the male and 4% of the women adhered to the practices, it is also higher than studies done in Malaysia 46 % and in Iran 66% male and 46% female respondents were active in daily life, in U.S.A 52% of respondents were exercise once a week or more. The result is higher than the other study this might be because of most patients did not live sedentary life, as they have physical exercise daily at least simple walk for half an hour each day. Study in Malaysia indicated that there was significant association between level of education, Age and anti-hyperglycemic medication type and self-care practices. Study in Ethiopia (TSAH) revealed that there was significant association between marital status, level of education, monthly income and diabetic complication and adherence to physical activities. But this study showed that there is significant association between age, occupation and adherence to physical activities (16, 17, 20, 25, 26, 31).

In this study almost half (51.3%) of all respondents were adhered to the recommended diabetic foot care practices. This result is higher than studies done in Nigeria only 10% had adherence to practices of DM foot care. But lower than studies done in, Ethiopia (TASH) 67%, Chandigarh 63.3%, Pakistan 68%, U.S.A 64% of all respondents had adherence to practices. The result of this study showed that level of education, marital status and monthly income showed that significant association but study done in Ethiopia (TASH) showed that male and older participants were less adherent to diabetic foot care practices, while study in Nigeria revealed that illiteracy and low socioeconomic statuses were significantly associated with poor practices (27, 28, 29,31,40).

In this study almost half 51.0% respondents were adhered to overall self-care management domains. This result is lower than study done in Ethiopia (TASH) 56%, Iran 74%, Finland 81% respondents were adhered to the overall self-care management domains. The result of this study is lower than the other studies this might be because of financial barrier, lack of awareness on the importance of the practices, Socio-cultural variation and life style difference. A study done in Iran indicated that insulin therapy, high educational status, and duration of diabetes had positive effects on level of self-care practice. This study also revealed that educational level, marital status and diabetes complication were an important variable in improving self-care practice or showed that significant association with the overall self-care managements (SDSCA). But study done in Ethiopia indicated that only level of education showed that significant association. Another study in Finland

revealed that poor metabolic control, smoking and living alone were associated with neglect of self-care managements but gender, Co-morbidity and diabetic complication increase the risk, but had no significant association with adherence to or neglect of self-care practice. In contrary this study showed that gender, age and diabetic complication had significant association on adherence condition to overall self-care management domains (18, 20, 31).

V. STRENGTHS AND LIMITATIONS OF THE STUDY

a) *Strength*

1. Use of contextually adopted standardized questionnaire.
2. High response rate.
3. Since there is no similar study conducted in the area, it can contribute a lot as baseline information for future studies.

b) *Limitations*

1. Social desirability bias due to sensitive and personal question related to diabetic self care especially about financial issues.
2. Limitation of related literatures to compare and discuss some of the findings.
3. Because the data are cross-sectional, the direction of causal relationship between variables can't always be determined.

VI. CONCLUSION AND RECOMMENDATION

a) *Conclusion*

Despite the important role of self-care practices in management of diabetes were recognized to be useful and effective in achieving diabetes control and preventing its serious complication, findings of this study confirm previous findings concerning self-care managements among people with type 2 diabetes: Prescribed medications adherence practice was accomplished as recommended in majority respondents, but the other aspects of self-care management domains were more problematic. SMBG practice and diet management practices especially warrants. However self-monitoring of blood glucose and diet management practices are said to be the cornerstone of self-care management activities and glycemic control. Generally adherence to self-care management was suboptimal among type 2 diabetic patients in Ayder referral hospital endocrinology and Mekelle hospital chronic care unit.

b) *Recommendations*

Hence Interventions aiming at improving diabetes control should be multifaceted and should involve more effective measures of awareness creation on the importance of the self-care management and more frequent clinic visits. Family members should be

informed about their important roles in encouraging patients to undergo a glycemic control or self-care practice. Increase access to health education through a multidisciplinary approach via IEC programme this could improve the glycemic control in patients with diabetes mellitus. Policy decisions for improving diabetes outcome should target barriers to health care access and utilization and focus on developing programs to help population groups at high-risk of neglecting their self-care practice.

Similarly healthcare personnel must increase patients' awareness toward the importance of all types of self-care practices domains and strongly promote the practice among diabetic patients via strengthening IEC program and providing quality care at all level and the diabetic association, Staff members of the endocrinology and chronic care units and department of internal medicine need to participate in strengthening the overall awareness of the patients toward their self-care management and providing equitable service to all patients regardless of patients socio-economic status.

As to the adherence to the prescribed diet and SMBG practices, patients should be well informed and the diet regimens are recommended to be simplified. In nursing, we can provide informational and emotional support by planning the care together, listening to the people and respecting their expertise. It is also suggested that nursing research should be carried out to investigate adherence to self-care management in a broader social context and larger sample size. Further studies are needed in order to achieve a deeper understanding about the subjective experience of being chronically ill, but still feeling healthy and doing well.

c) *Practice implications of the Study in nursing profession*

This study should contribute to the development of effective nursing education strategies to promote health for adults with sub-optimal diabetes self-care practices. This study should also contribute to the nurse researcher as a base line data in order to carried out in a broader social context and larger sample size to investigate adherence to self-care and achieve a deeper understanding about the subjective experience of being chronically ill, but still feeling healthy and doing well. Finally this study should contribute to the development of effective Nursing practices in order to promote health and be adhered to self-care practices.

REFERENCES RÉFÉRENCES REFERENCIAS

1. Diabetics. Better medicine. 2011. Retrieved from <http://www.bettermedicine.com/>
2. Romesh Khardori. Type 2 Diabetes Mellitus Workup. Medscape. 2010. retrieved from <http://emedicine.medscape.com/>
3. Diabetic facts. IDA data base. 2011. Retrieved from <http://www.worlddiabetesfoundation.org/>
4. Diabetes in the developing world. Media Backgrounder IDF data base.2011 Retrieved from <http://www.worlddiabetesfoundation.org/media>.
5. Hall V and Thomsen RW et al. Diabetes in Sub Saharan Africa 1999-2011: epidemiology and public health implications. *Journal of Bio Medical Central Public Health*. 2011; 14;11: 564.
6. Moodley LM, BPharm and MMed.Sci. An assessment of the level of knowledge about diabetes mellitus among diabetic patients in a primary healthcare setting. *SA FamPract* 2007;49 (10):16.
7. Khaldon K. Al-Sarihin, Mohammad H. Bani-Khaled and et al. Diabetes Knowledge among Patients with Diabetes Mellitus. *JRMS* March 2012; 19(1): 72-77
8. Yeweyenhareg Feleke, and Fikre Enquselassie. An assessment of the health care system for diabetes in Addis Ababa, Ethiopia. *Ethiopia Journal of Health Development*. 2005;19(3):203-210.
9. WHO Diabetes Fact sheet N°312.2011. Retrieved from <http://www.who.int/mediacentre/factsheets/fs312/en/index.html>
10. Okolie, V. Uchenna and Ehiemere, O. Ijeoma et al. Knowledge of diabetes management and control by diabetic patients. *International Journal of Medicine and Medical Sciences*. 2009 Vol. 1(9), pp. 353-358. retrieved: <http://www.academicjournals.org/ijmms>
11. Nancy E. Schoenberg and Suzanne C. Drungle. Barriers to Non-Insulin Dependent Diabetes Mellitus (NIDDM) Self-Care Practices among Older Women. *Journal of Aging and Health*. 2001.
12. Yeweyenhareg Feleke, and Mphil. Studies on Diabetes Mellitus and other Endocrine diseases in Addis Ababa, Ethiopia.2004. retrieved from www.aau.edu.et/news/inag/Prof.
13. MirkaKneckt. Psychological features characterizing oral health behavior, diabetes self-care health status among IDDM patients. Oulu University Library. 2000. Retrieved from <http://herkules.oulu.fi/isbn9514256301/html/index.html>
14. A Eregie and B C Unadike. Factors associated with self-monitoring of glycaemic control among persons with diabetes in Benin City, Nigeria. *African Journal of Diabetes Medicine*. 2010: Vol 19 No 1.
15. Mastura I and Mimi O, et al. Self-monitoring of blood glucose among diabetes patients attending government health clinics. *Medical Journal of Malaysia*. 2007: 62(2):147-51.
16. J P, Majra and Das Acharya. Awareness Regarding Self Care among Diabetics in Rural India. *Middle east journal of medicine*. 2009: Volume 7, Issue 6.
17. Ming Yeong Tan and Judy Magarey. Self-care practices of Malaysian adults with diabetes and sub-optimal glycaemic control. *International journal for communication in Health care*. 2007. Volume: 72, Issue: 2, Pages: 252-267.

18. G L Beckles, and M MEngelgau. Population-based assessment of the level of care among adults with diabetes in the U.S. *Pub med*. 1998; 21(9):1432-8.
19. Eman M. Mahfouz, and Hala I. Awadalla. Compliance to diabetes self-management in rural El-Mina, Egypt. *Central European Journal of Public Health* 2011; 19 (1): 35–41.
20. Zahra Yekta and Reza Pourali et al. Assessment of Self-Care Practice and Its Associated Factors among Diabetic Patients. *Journal of Research in Health Sciences*. 2011; 11(1): 33-38.
21. Kazeem B. Yusuff, and OlubunmiObe..etal. Adherence to anti-diabetic drug therapy and self management practices among type-2 diabetics. *International Journal of Clinical Pharmacy and Pharmaceutical Care*. 2008: Volume 30, Number 6.
22. Maisa Toljamo and Maija Hentinen .Adherence to self-care and glycaemic control among people with insulin-dependent diabetes mellitus. *Journal of Advanced Nursing*. 2001. Volume 34, Issue 6, pages 780–786.
23. Juma Al-Kaabi and Fatma Al-Maskari. Assessment of Dietary Practice among Diabetic Patients in the United Arab Emirates. *Journal of Society for biomedical diabetes research*.2008.
24. Ruggiero L, and Glasgow R. Diabetes self-management. Self-reported recommendations and patterns in a large population. American Diabetic Association diabetic care data base.1997. Retrieved from <http://care.diabetesjournals.org/content/20/4/568>
25. Juma Al-Kaabi and Fatma Al-Maskari. Physical Activity and Reported Barriers to Activity Among Type 2 Diabetic Patients in the United Arab Emirates. *Journal of the society for Biomedical diabetic research*.2009.
26. Gloria LA Beckles, and Michael MEngelgau, et al. Population-Based Assessment of the Level of Care Among Adults With Diabetes in the U.S. American Diabetic Association diabetic care data base .1998.
27. O ODesalu, and F K Salawu, et al. Diabetic Foot Care: Self Reported Knowledge and Practice Among Patients. *Ghana Medical Journal*. 2011:45 (2):60-65.
28. Moreno Hernández MI, and Trilla Soler M, et al. Self care and risk factors of diabetic foot in patients with type II diabetes mellitus. *Pub med*.1997: 9410141.
29. Seema Hasnain, and Naheed Humayun Sheikh. Knowledge and practices regarding foot care in diabetic patients visiting diabetic clinic in Jinnah Hospital, Lahore. *Journal of Pakistan medical Association*. 2007.
30. Berhe et al. Assesment of diabetes self care practices and associated factors among type 2 diabetic patients in tikuranbessa specialized hospital, Addis Ababa, Ethiopia. *IJPSR*, 2012; Vol. 3(11): 4461-4471)
31. Kalayou Kidanu Berhe, Alemayehu Bayeray and Kahsay, Haftu Berhe Gebru. Assessment of Adherence to Diabetes Self-Management Practices among Type II Diabetic Patients in Tikur Anbesa Hospital, Addis Ababa city, Ethiopia. *Greener Journal of Medical Sciences*.2013.Vol. 3 (6), pp. 211-221.)
32. Viral N. Shah, P. K. Kamdar, and Nishit Shah¹ *Int J Diabetes Dev Ctries*. 2009 Jul-Aug; 29(3) 118–122
33. *J Clin Nurs*. 2013 Jan; 22(1-2): 51-60. doi: 10.1111/j.1365-2702.2012.04273.x.)
34. Al-Maskari F, El-Sadig M, Al-Kaabi JM, Afandi B, Nagelkerke N, et al. (2013) Knowledge, Attitude and Practices of Diabetic Patients in the United Arab Emirates. *PLoS ONE* 8(1): e52857.
35. Chan YM, Molassiotis A. the relationship between diabetes knowledge and compliance among Chinese with non-insulin dependent diabetes mellitus in Hong Kong *J Adv Nurs*. 1999 Aug; 30(2): 431-8
36. HarithKh Al-Qazaz, Syed A Sulaiman, and et al. Diabetes knowledge, medication adherence and glycemic control among patients with type 2 diabetes. *International journal of clinical pharmacy* 11/2011; 33(6):1028-35. DOI:10.1007/s11096-011-9582-2)
37. Esther Mufunda, Kerstin Wikby, Albin Björn, Katarina Hjelm. Level and determinants of diabetes knowledge in patients with diabetes in Zimbabwe: a cross-sectional study. *The Pan African Medical Journal*. 2012;13:78)
38. ShuHui Ng, Kheng Hooi Chan, and et al. Knowledge, Attitude and Practice among Diabetic Patients in Monash University Sunway Campus, Malaysia. Abstracts of 5 th International Online Medical Conference (IOMC 2012)
39. Heather P. WHITLEY, Joli D. FERMO, Kelly RAGUCCI, Elinor C. CHUMNEY. *Pharmacy Practice (Granada) versión On-line ISSN 1885-642X Pharmacy pract. (Granada Ed. impr.) v.4 n. 4 Redondelaoct. -dic. 2006* <http://dx.doi.org/10.4321/S1885-642X2006000400006>)
40. Kaur K, Singh MM, Kumar, Walia I. Knowledge and self-care practices of diabetics in a resettlement colony of Chandigarh. *Indian J Med Sci*. 199, 52(8): 341-7.
41. KetemaAyele, Bisrat Tesfa, Lakew Abebe, et al. Self Care Behavior among Patients with Diabetes in Harari, Eastern Ethiopia. open accessed journal
42. Naheed Gul: knowledge, attitudes and practices of type 2 diabetic patients, *J Ayub Med Coll Abbottabad* 2010; 22(3): <http://www.ayubmed.edu.pk/JAMC/PAST/22-3/Naheed.pdf>
43. Naeema Badruddin, Abdul Basit, and M. ZafarIqbal Hydrie et al. Knowledge, Attitude and Practices of Patients Visiting a Diabetes Care Unit. *pjbs.org: http://www.academia.edu/1296035/Knowledge_*

44. Zachary t and Bloomgarden. Cardiac disease and related topics. American diabetes association annual meeting, 1998. Retrieved from <http://care.diabetesjournals.org/content/>
45. Jacqueline Fawcett. Dorothea Orem's Self-Care Framework. 2008. Retrieved from: <http://www4.desales.edu/~sey0/orem.html>
46. Dorothea Orem's self-care framework. Taber's Cyclopedic Medical, Last updated: 2009.
47. Orem, D.E. Nursing: Concepts of practice 4th edition. St. Louis: Mosbly.1993: p.435.
48. Deborah j. Toobert, and Sarah e. Hampson, et al. The Summary of Diabetes Self-Care activities Measure: Results from 7 studies and a revised scale. Diabetes care. 2000, volume 23, number 7. Retrieved from <http://care.diabetesjournals.org/content/23/7/943.long>



GLOBAL JOURNALS INC. (US) GUIDELINES HANDBOOK 2017

WWW.GLOBALJOURNALS.ORG

FELLOWS

FELLOW OF ASSOCIATION OF RESEARCH SOCIETY IN MEDICAL (FARSM)

Global Journals Incorporate (USA) is accredited by Open Association of Research Society (OARS), U.S.A and in turn, awards “FARSM” title to individuals. The 'FARSM' title is accorded to a selected professional after the approval of the Editor-in-Chief/Editorial Board Members/Dean.



- The “FARSM” is a dignified title which is accorded to a person’s name viz. Dr. John E. Hall, Ph.D., FARSS or William Walldroff, M.S., FARSM.

FARSM accrediting is an honor. It authenticates your research activities. After recognition as FARSM, you can add 'FARSM' title with your name as you use this recognition as additional suffix to your status. This will definitely enhance and add more value and repute to your name. You may use it on your professional Counseling Materials such as CV, Resume, and Visiting Card etc.

The following benefits can be availed by you only for next three years from the date of certification:



FARSM designated members are entitled to avail a 40% discount while publishing their research papers (of a single author) with Global Journals Incorporation (USA), if the same is accepted by Editorial Board/Peer Reviewers. If you are a main author or co-author in case of multiple authors, you will be entitled to avail discount of 10%.

Once FARSM title is accorded, the Fellow is authorized to organize a symposium/seminar/conference on behalf of Global Journal Incorporation (USA). The Fellow can also participate in conference/seminar/symposium organized by another institution as representative of Global Journal. In both the cases, it is mandatory for him to discuss with us and obtain our consent.



You may join as member of the Editorial Board of Global Journals Incorporation (USA) after successful completion of three years as Fellow and as Peer Reviewer. In addition, it is also desirable that you should organize seminar/symposium/conference at least once.

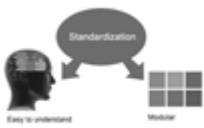
We shall provide you intimation regarding launching of e-version of journal of your stream time to time. This may be utilized in your library for the enrichment of knowledge of your students as well as it can also be helpful for the concerned faculty members.





The FARSM can go through standards of OARS. You can also play vital role if you have any suggestions so that proper amendment can take place to improve the same for the benefit of entire research community.

As FARSM, you will be given a renowned, secure and free professional email address with 100 GB of space e.g. johnhall@globaljournals.org. This will include Webmail, Spam Assassin, Email Forwarders, Auto-Responders, Email Delivery Route tracing, etc.



The FARSM will be eligible for a free application of standardization of their researches. Standardization of research will be subject to acceptability within stipulated norms as the next step after publishing in a journal. We shall depute a team of specialized research professionals who will render their services for elevating your researches to next higher level, which is worldwide open standardization.

The FARSM member can apply for grading and certification of standards of their educational and Institutional Degrees to Open Association of Research, Society U.S.A. Once you are designated as FARSM, you may send us a scanned copy of all of your credentials. OARS will verify, grade and certify them. This will be based on your academic records, quality of research papers published by you, and some more criteria. After certification of all your credentials by OARS, they will be published on your Fellow Profile link on website <https://associationofresearch.org> which will be helpful to upgrade the dignity.



The FARSM members can avail the benefits of free research podcasting in Global Research Radio with their research documents. After publishing the work, (including published elsewhere worldwide with proper authorization) you can upload your research paper with your recorded voice or you can utilize chargeable services of our professional RJs to record your paper in their voice on request.



The FARSM member also entitled to get the benefits of free research podcasting of their research documents through video clips. We can also streamline your conference videos and display your slides/ online slides and online research video clips at reasonable charges, on request.





The FARSM is eligible to earn from sales proceeds of his/her researches/reference/review Books or literature, while publishing with Global Journals. The FARSS can decide whether he/she would like to publish his/her research in a closed manner. In this case, whenever readers purchase that individual research paper for reading, maximum 60% of its profit earned as royalty by Global Journals, will be credited to his/her bank account. The entire entitled amount will be credited to his/her bank account exceeding limit of minimum fixed balance. There is no minimum time limit for collection. The FARSM member can decide its price and we can help in making the right decision.

The FARSM member is eligible to join as a paid peer reviewer at Global Journals Incorporation (USA) and can get remuneration of 15% of author fees, taken from the author of a respective paper. After reviewing 5 or more papers you can request to transfer the amount to your bank account.



MEMBER OF ASSOCIATION OF RESEARCH SOCIETY IN MEDICAL (MARSM)

The ' MARSM ' title is accorded to a selected professional after the approval of the Editor-in-Chief / Editorial Board Members/Dean.

The “MARSM” is a dignified ornament which is accorded to a person’s name viz. Dr. John E. Hall, Ph.D., MARSM or William Walldroff, M.S., MARSM.



MARSM accrediting is an honor. It authenticates your research activities. After becoming MARSM, you can add 'MARSM' title with your name as you use this recognition as additional suffix to your status. This will definitely enhance and add more value and repute to your name. You may use it on your professional Counseling Materials such as CV, Resume, Visiting Card and Name Plate etc.

The following benefits can be availed by you only for next three years from the date of certification.



MARSM designated members are entitled to avail a 25% discount while publishing their research papers (of a single author) in Global Journals Inc., if the same is accepted by our Editorial Board and Peer Reviewers. If you are a main author or co-author of a group of authors, you will get discount of 10%.

As MARSM, you will be given a renowned, secure and free professional email address with 30 GB of space e.g. johnhall@globaljournals.org. This will include Webmail, Spam Assassin, Email Forwarders, Auto-Responders, Email Delivery Route tracing, etc.





We shall provide you intimation regarding launching of e-version of journal of your stream time to time. This may be utilized in your library for the enrichment of knowledge of your students as well as it can also be helpful for the concerned faculty members.

The MARS member can apply for approval, grading and certification of standards of their educational and Institutional Degrees to Open Association of Research, Society U.S.A.



Once you are designated as MARS, you may send us a scanned copy of all of your credentials. OARS will verify, grade and certify them. This will be based on your academic records, quality of research papers published by you, and some more criteria.

It is mandatory to read all terms and conditions carefully.



AUXILIARY MEMBERSHIPS

Institutional Fellow of Open Association of Research Society (USA) - OARS (USA)

Global Journals Incorporation (USA) is accredited by Open Association of Research Society, U.S.A (OARS) and in turn, affiliates research institutions as “Institutional Fellow of Open Association of Research Society” (IFOARS).

The “FARSC” is a dignified title which is accorded to a person’s name viz. Dr. John E. Hall, Ph.D., FARSC or William Walldroff, M.S., FARSC.



The IFOARS institution is entitled to form a Board comprised of one Chairperson and three to five board members preferably from different streams. The Board will be recognized as “Institutional Board of Open Association of Research Society”-(IBOARS).

The Institute will be entitled to following benefits:



The IBOARS can initially review research papers of their institute and recommend them to publish with respective journal of Global Journals. It can also review the papers of other institutions after obtaining our consent. The second review will be done by peer reviewer of Global Journals Incorporation (USA). The Board is at liberty to appoint a peer reviewer with the approval of chairperson after consulting us.

The author fees of such paper may be waived off up to 40%.

The Global Journals Incorporation (USA) at its discretion can also refer double blind peer reviewed paper at their end to the board for the verification and to get recommendation for final stage of acceptance of publication.



The IBOARS can organize symposium/seminar/conference in their country on behalf of Global Journals Incorporation (USA)-OARS (USA). The terms and conditions can be discussed separately.

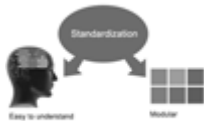
The Board can also play vital role by exploring and giving valuable suggestions regarding the Standards of “Open Association of Research Society, U.S.A (OARS)” so that proper amendment can take place for the benefit of entire research community. We shall provide details of particular standard only on receipt of request from the Board.



The board members can also join us as Individual Fellow with 40% discount on total fees applicable to Individual Fellow. They will be entitled to avail all the benefits as declared. Please visit Individual Fellow-sub menu of GlobalJournals.org to have more relevant details.



We shall provide you intimation regarding launching of e-version of journal of your stream time to time. This may be utilized in your library for the enrichment of knowledge of your students as well as it can also be helpful for the concerned faculty members.



After nomination of your institution as “Institutional Fellow” and constantly functioning successfully for one year, we can consider giving recognition to your institute to function as Regional/Zonal office on our behalf. The board can also take up the additional allied activities for betterment after our consultation.

The following entitlements are applicable to individual Fellows:

Open Association of Research Society, U.S.A (OARS) By-laws states that an individual Fellow may use the designations as applicable, or the corresponding initials. The Credentials of individual Fellow and Associate designations signify that the individual has gained knowledge of the fundamental concepts. One is magnanimous and proficient in an expertise course covering the professional code of conduct, and follows recognized standards of practice.



Open Association of Research Society (US)/ Global Journals Incorporation (USA), as described in Corporate Statements, are educational, research publishing and professional membership organizations. Achieving our individual Fellow or Associate status is based mainly on meeting stated educational research requirements.

Disbursement of 40% Royalty earned through Global Journals : Researcher = 50%, Peer Reviewer = 37.50%, Institution = 12.50% E.g. Out of 40%, the 20% benefit should be passed on to researcher, 15 % benefit towards remuneration should be given to a reviewer and remaining 5% is to be retained by the institution.



We shall provide print version of 12 issues of any three journals [as per your requirement] out of our 38 journals worth \$ 2376 USD.

Other:

The individual Fellow and Associate designations accredited by Open Association of Research Society (US) credentials signify guarantees following achievements:

- The professional accredited with Fellow honor, is entitled to various benefits viz. name, fame, honor, regular flow of income, secured bright future, social status etc.



- In addition to above, if one is single author, then entitled to 40% discount on publishing research paper and can get 10% discount if one is co-author or main author among group of authors.
- The Fellow can organize symposium/seminar/conference on behalf of Global Journals Incorporation (USA) and he/she can also attend the same organized by other institutes on behalf of Global Journals.
- The Fellow can become member of Editorial Board Member after completing 3yrs.
- The Fellow can earn 60% of sales proceeds from the sale of reference/review books/literature/publishing of research paper.
- Fellow can also join as paid peer reviewer and earn 15% remuneration of author charges and can also get an opportunity to join as member of the Editorial Board of Global Journals Incorporation (USA)
- • This individual has learned the basic methods of applying those concepts and techniques to common challenging situations. This individual has further demonstrated an in-depth understanding of the application of suitable techniques to a particular area of research practice.

Note :

//

- In future, if the board feels the necessity to change any board member, the same can be done with the consent of the chairperson along with anyone board member without our approval.
- In case, the chairperson needs to be replaced then consent of 2/3rd board members are required and they are also required to jointly pass the resolution copy of which should be sent to us. In such case, it will be compulsory to obtain our approval before replacement.
- In case of “Difference of Opinion [if any]” among the Board members, our decision will be final and binding to everyone.

//



PROCESS OF SUBMISSION OF RESEARCH PAPER

The Area or field of specialization may or may not be of any category as mentioned in 'Scope of Journal' menu of the GlobalJournals.org website. There are 37 Research Journal categorized with Six parental Journals GJCST, GJMR, GJRE, GJMBR, GJSFR, GJHSS. For Authors should prefer the mentioned categories. There are three widely used systems UDC, DDC and LCC. The details are available as 'Knowledge Abstract' at Home page. The major advantage of this coding is that, the research work will be exposed to and shared with all over the world as we are being abstracted and indexed worldwide.

The paper should be in proper format. The format can be downloaded from first page of 'Author Guideline' Menu. The Author is expected to follow the general rules as mentioned in this menu. The paper should be written in MS-Word Format (*.DOC,*.DOCX).

The Author can submit the paper either online or offline. The authors should prefer online submission.Online Submission: There are three ways to submit your paper:

(A) (I) First, register yourself using top right corner of Home page then Login. If you are already registered, then login using your username and password.

(II) Choose corresponding Journal.

(III) Click 'Submit Manuscript'. Fill required information and Upload the paper.

(B) If you are using Internet Explorer, then Direct Submission through Homepage is also available.

(C) If these two are not convenient, and then email the paper directly to dean@globaljournals.org.

Offline Submission: Author can send the typed form of paper by Post. However, online submission should be preferred.



PREFERRED AUTHOR GUIDELINES

MANUSCRIPT STYLE INSTRUCTION (Must be strictly followed)

Page Size: 8.27" X 11"

- Left Margin: 0.65
- Right Margin: 0.65
- Top Margin: 0.75
- Bottom Margin: 0.75
- Font type of all text should be Swis 721 Lt BT.
- Paper Title should be of Font Size 24 with one Column section.
- Author Name in Font Size of 11 with one column as of Title.
- Abstract Font size of 9 Bold, "Abstract" word in Italic Bold.
- Main Text: Font size 10 with justified two columns section
- Two Column with Equal Column with of 3.38 and Gaping of .2
- First Character must be three lines Drop capped.
- Paragraph before Spacing of 1 pt and After of 0 pt.
- Line Spacing of 1 pt
- Large Images must be in One Column
- Numbering of First Main Headings (Heading 1) must be in Roman Letters, Capital Letter, and Font Size of 10.
- Numbering of Second Main Headings (Heading 2) must be in Alphabets, Italic, and Font Size of 10.

You can use your own standard format also.

Author Guidelines:

1. General,
2. Ethical Guidelines,
3. Submission of Manuscripts,
4. Manuscript's Category,
5. Structure and Format of Manuscript,
6. After Acceptance.

1. GENERAL

Before submitting your research paper, one is advised to go through the details as mentioned in following heads. It will be beneficial, while peer reviewer justify your paper for publication.

Scope

The Global Journals Inc. (US) welcome the submission of original paper, review paper, survey article relevant to the all the streams of Philosophy and knowledge. The Global Journals Inc. (US) is parental platform for Global Journal of Computer Science and Technology, Researches in Engineering, Medical Research, Science Frontier Research, Human Social Science, Management, and Business organization. The choice of specific field can be done otherwise as following in Abstracting and Indexing Page on this Website. As the all Global

Journals Inc. (US) are being abstracted and indexed (in process) by most of the reputed organizations. Topics of only narrow interest will not be accepted unless they have wider potential or consequences.

2. ETHICAL GUIDELINES

Authors should follow the ethical guidelines as mentioned below for publication of research paper and research activities.

Papers are accepted on strict understanding that the material in whole or in part has not been, nor is being, considered for publication elsewhere. If the paper once accepted by Global Journals Inc. (US) and Editorial Board, will become the copyright of the Global Journals Inc. (US).

Authorship: The authors and coauthors should have active contribution to conception design, analysis and interpretation of findings. They should critically review the contents and drafting of the paper. All should approve the final version of the paper before submission

The Global Journals Inc. (US) follows the definition of authorship set up by the Global Academy of Research and Development. According to the Global Academy of R&D authorship, criteria must be based on:

- 1) Substantial contributions to conception and acquisition of data, analysis and interpretation of the findings.
- 2) Drafting the paper and revising it critically regarding important academic content.
- 3) Final approval of the version of the paper to be published.

All authors should have been credited according to their appropriate contribution in research activity and preparing paper. Contributors who do not match the criteria as authors may be mentioned under Acknowledgement.

Acknowledgements: Contributors to the research other than authors credited should be mentioned under acknowledgement. The specifications of the source of funding for the research if appropriate can be included. Suppliers of resources may be mentioned along with address.

Appeal of Decision: The Editorial Board's decision on publication of the paper is final and cannot be appealed elsewhere.

Permissions: It is the author's responsibility to have prior permission if all or parts of earlier published illustrations are used in this paper.

Please mention proper reference and appropriate acknowledgements wherever expected.

If all or parts of previously published illustrations are used, permission must be taken from the copyright holder concerned. It is the author's responsibility to take these in writing.

Approval for reproduction/modification of any information (including figures and tables) published elsewhere must be obtained by the authors/copyright holders before submission of the manuscript. Contributors (Authors) are responsible for any copyright fee involved.

3. SUBMISSION OF MANUSCRIPTS

Manuscripts should be uploaded via this online submission page. The online submission is most efficient method for submission of papers, as it enables rapid distribution of manuscripts and consequently speeds up the review procedure. It also enables authors to know the status of their own manuscripts by emailing us. Complete instructions for submitting a paper is available below.

Manuscript submission is a systematic procedure and little preparation is required beyond having all parts of your manuscript in a given format and a computer with an Internet connection and a Web browser. Full help and instructions are provided on-screen. As an author, you will be prompted for login and manuscript details as Field of Paper and then to upload your manuscript file(s) according to the instructions.



To avoid postal delays, all transaction is preferred by e-mail. A finished manuscript submission is confirmed by e-mail immediately and your paper enters the editorial process with no postal delays. When a conclusion is made about the publication of your paper by our Editorial Board, revisions can be submitted online with the same procedure, with an occasion to view and respond to all comments.

Complete support for both authors and co-author is provided.

4. MANUSCRIPT'S CATEGORY

Based on potential and nature, the manuscript can be categorized under the following heads:

Original research paper: Such papers are reports of high-level significant original research work.

Review papers: These are concise, significant but helpful and decisive topics for young researchers.

Research articles: These are handled with small investigation and applications

Research letters: The letters are small and concise comments on previously published matters.

5. STRUCTURE AND FORMAT OF MANUSCRIPT

The recommended size of original research paper is less than seven thousand words, review papers fewer than seven thousands words also. Preparation of research paper or how to write research paper, are major hurdle, while writing manuscript. The research articles and research letters should be fewer than three thousand words, the structure original research paper; sometime review paper should be as follows:

Papers: These are reports of significant research (typically less than 7000 words equivalent, including tables, figures, references), and comprise:

- (a) Title should be relevant and commensurate with the theme of the paper.
- (b) A brief Summary, "Abstract" (less than 150 words) containing the major results and conclusions.
- (c) Up to ten keywords, that precisely identifies the paper's subject, purpose, and focus.
- (d) An Introduction, giving necessary background excluding subheadings; objectives must be clearly declared.
- (e) Resources and techniques with sufficient complete experimental details (wherever possible by reference) to permit repetition; sources of information must be given and numerical methods must be specified by reference, unless non-standard.
- (f) Results should be presented concisely, by well-designed tables and/or figures; the same data may not be used in both; suitable statistical data should be given. All data must be obtained with attention to numerical detail in the planning stage. As reproduced design has been recognized to be important to experiments for a considerable time, the Editor has decided that any paper that appears not to have adequate numerical treatments of the data will be returned un-refereed;
- (g) Discussion should cover the implications and consequences, not just recapitulating the results; conclusions should be summarizing.
- (h) Brief Acknowledgements.
- (i) References in the proper form.

Authors should very cautiously consider the preparation of papers to ensure that they communicate efficiently. Papers are much more likely to be accepted, if they are cautiously designed and laid out, contain few or no errors, are summarizing, and be conventional to the approach and instructions. They will in addition, be published with much less delays than those that require much technical and editorial correction.



The Editorial Board reserves the right to make literary corrections and to make suggestions to improve brevity.

It is vital, that authors take care in submitting a manuscript that is written in simple language and adheres to published guidelines.

Format

Language: The language of publication is UK English. Authors, for whom English is a second language, must have their manuscript efficiently edited by an English-speaking person before submission to make sure that, the English is of high excellence. It is preferable, that manuscripts should be professionally edited.

Standard Usage, Abbreviations, and Units: Spelling and hyphenation should be conventional to The Concise Oxford English Dictionary. Statistics and measurements should at all times be given in figures, e.g. 16 min, except for when the number begins a sentence. When the number does not refer to a unit of measurement it should be spelt in full unless, it is 160 or greater.

Abbreviations supposed to be used carefully. The abbreviated name or expression is supposed to be cited in full at first usage, followed by the conventional abbreviation in parentheses.

Metric SI units are supposed to generally be used excluding where they conflict with current practice or are confusing. For illustration, 1.4 l rather than $1.4 \times 10^{-3} \text{ m}^3$, or 4 mm somewhat than $4 \times 10^{-3} \text{ m}$. Chemical formula and solutions must identify the form used, e.g. anhydrous or hydrated, and the concentration must be in clearly defined units. Common species names should be followed by underlines at the first mention. For following use the generic name should be constricted to a single letter, if it is clear.

Structure

All manuscripts submitted to Global Journals Inc. (US), ought to include:

Title: The title page must carry an instructive title that reflects the content, a running title (less than 45 characters together with spaces), names of the authors and co-authors, and the place(s) wherever the work was carried out. The full postal address in addition with the e-mail address of related author must be given. Up to eleven keywords or very brief phrases have to be given to help data retrieval, mining and indexing.

Abstract, used in Original Papers and Reviews:

Optimizing Abstract for Search Engines

Many researchers searching for information online will use search engines such as Google, Yahoo or similar. By optimizing your paper for search engines, you will amplify the chance of someone finding it. This in turn will make it more likely to be viewed and/or cited in a further work. Global Journals Inc. (US) have compiled these guidelines to facilitate you to maximize the web-friendliness of the most public part of your paper.

Key Words

A major linchpin in research work for the writing research paper is the keyword search, which one will employ to find both library and Internet resources.

One must be persistent and creative in using keywords. An effective keyword search requires a strategy and planning a list of possible keywords and phrases to try.

Search engines for most searches, use Boolean searching, which is somewhat different from Internet searches. The Boolean search uses "operators," words (and, or, not, and near) that enable you to expand or narrow your affords. Tips for research paper while preparing research paper are very helpful guideline of research paper.

Choice of key words is first tool of tips to write research paper. Research paper writing is an art. A few tips for deciding as strategically as possible about keyword search:



- One should start brainstorming lists of possible keywords before even begin searching. Think about the most important concepts related to research work. Ask, "What words would a source have to include to be truly valuable in research paper?" Then consider synonyms for the important words.
- It may take the discovery of only one relevant paper to let steer in the right keyword direction because in most databases, the keywords under which a research paper is abstracted are listed with the paper.
- One should avoid outdated words.

Keywords are the key that opens a door to research work sources. Keyword searching is an art in which researcher's skills are bound to improve with experience and time.

Numerical Methods: Numerical methods used should be clear and, where appropriate, supported by references.

Acknowledgements: Please make these as concise as possible.

References

References follow the Harvard scheme of referencing. References in the text should cite the authors' names followed by the time of their publication, unless there are three or more authors when simply the first author's name is quoted followed by et al. unpublished work has to only be cited where necessary, and only in the text. Copies of references in press in other journals have to be supplied with submitted typescripts. It is necessary that all citations and references be carefully checked before submission, as mistakes or omissions will cause delays.

References to information on the World Wide Web can be given, but only if the information is available without charge to readers on an official site. Wikipedia and Similar websites are not allowed where anyone can change the information. Authors will be asked to make available electronic copies of the cited information for inclusion on the Global Journals Inc. (US) homepage at the judgment of the Editorial Board.

The Editorial Board and Global Journals Inc. (US) recommend that, citation of online-published papers and other material should be done via a DOI (digital object identifier). If an author cites anything, which does not have a DOI, they run the risk of the cited material not being noticeable.

The Editorial Board and Global Journals Inc. (US) recommend the use of a tool such as Reference Manager for reference management and formatting.

Tables, Figures and Figure Legends

Tables: Tables should be few in number, cautiously designed, uncrowned, and include only essential data. Each must have an Arabic number, e.g. Table 4, a self-explanatory caption and be on a separate sheet. Vertical lines should not be used.

Figures: Figures are supposed to be submitted as separate files. Always take in a citation in the text for each figure using Arabic numbers, e.g. Fig. 4. Artwork must be submitted online in electronic form by e-mailing them.

Preparation of Electronic Figures for Publication

Even though low quality images are sufficient for review purposes, print publication requires high quality images to prevent the final product being blurred or fuzzy. Submit (or e-mail) EPS (line art) or TIFF (halftone/photographs) files only. MS PowerPoint and Word Graphics are unsuitable for printed pictures. Do not use pixel-oriented software. Scans (TIFF only) should have a resolution of at least 350 dpi (halftone) or 700 to 1100 dpi (line drawings) in relation to the imitation size. Please give the data for figures in black and white or submit a Color Work Agreement Form. EPS files must be saved with fonts embedded (and with a TIFF preview, if possible).

For scanned images, the scanning resolution (at final image size) ought to be as follows to ensure good reproduction: line art: >650 dpi; halftones (including gel photographs) : >350 dpi; figures containing both halftone and line images: >650 dpi.



Color Charges: It is the rule of the Global Journals Inc. (US) for authors to pay the full cost for the reproduction of their color artwork. Hence, please note that, if there is color artwork in your manuscript when it is accepted for publication, we would require you to complete and return a color work agreement form before your paper can be published.

Figure Legends: Self-explanatory legends of all figures should be incorporated separately under the heading 'Legends to Figures'. In the full-text online edition of the journal, figure legends may possibly be truncated in abbreviated links to the full screen version. Therefore, the first 100 characters of any legend should notify the reader, about the key aspects of the figure.

6. AFTER ACCEPTANCE

Upon approval of a paper for publication, the manuscript will be forwarded to the dean, who is responsible for the publication of the Global Journals Inc. (US).

6.1 Proof Corrections

The corresponding author will receive an e-mail alert containing a link to a website or will be attached. A working e-mail address must therefore be provided for the related author.

Acrobat Reader will be required in order to read this file. This software can be downloaded

(Free of charge) from the following website:

www.adobe.com/products/acrobat/readstep2.html. This will facilitate the file to be opened, read on screen, and printed out in order for any corrections to be added. Further instructions will be sent with the proof.

Proofs must be returned to the dean at dean@globaljournals.org within three days of receipt.

As changes to proofs are costly, we inquire that you only correct typesetting errors. All illustrations are retained by the publisher. Please note that the authors are responsible for all statements made in their work, including changes made by the copy editor.

6.2 Early View of Global Journals Inc. (US) (Publication Prior to Print)

The Global Journals Inc. (US) are enclosed by our publishing's Early View service. Early View articles are complete full-text articles sent in advance of their publication. Early View articles are absolute and final. They have been completely reviewed, revised and edited for publication, and the authors' final corrections have been incorporated. Because they are in final form, no changes can be made after sending them. The nature of Early View articles means that they do not yet have volume, issue or page numbers, so Early View articles cannot be cited in the conventional way.

6.3 Author Services

Online production tracking is available for your article through Author Services. Author Services enables authors to track their article - once it has been accepted - through the production process to publication online and in print. Authors can check the status of their articles online and choose to receive automated e-mails at key stages of production. The authors will receive an e-mail with a unique link that enables them to register and have their article automatically added to the system. Please ensure that a complete e-mail address is provided when submitting the manuscript.

6.4 Author Material Archive Policy

Please note that if not specifically requested, publisher will dispose off hardcopy & electronic information submitted, after the two months of publication. If you require the return of any information submitted, please inform the Editorial Board or dean as soon as possible.

6.5 Offprint and Extra Copies

A PDF offprint of the online-published article will be provided free of charge to the related author, and may be distributed according to the Publisher's terms and conditions. Additional paper offprint may be ordered by emailing us at: editor@globaljournals.org .



Before start writing a good quality Computer Science Research Paper, let us first understand what is Computer Science Research Paper? So, Computer Science Research Paper is the paper which is written by professionals or scientists who are associated to Computer Science and Information Technology, or doing research study in these areas. If you are novel to this field then you can consult about this field from your supervisor or guide.

TECHNIQUES FOR WRITING A GOOD QUALITY RESEARCH PAPER:

1. Choosing the topic: In most cases, the topic is searched by the interest of author but it can be also suggested by the guides. You can have several topics and then you can judge that in which topic or subject you are finding yourself most comfortable. This can be done by asking several questions to yourself, like Will I be able to carry our search in this area? Will I find all necessary recourses to accomplish the search? Will I be able to find all information in this field area? If the answer of these types of questions will be "Yes" then you can choose that topic. In most of the cases, you may have to conduct the surveys and have to visit several places because this field is related to Computer Science and Information Technology. Also, you may have to do a lot of work to find all rise and falls regarding the various data of that subject. Sometimes, detailed information plays a vital role, instead of short information.

2. Evaluators are human: First thing to remember that evaluators are also human being. They are not only meant for rejecting a paper. They are here to evaluate your paper. So, present your Best.

3. Think Like Evaluators: If you are in a confusion or getting demotivated that your paper will be accepted by evaluators or not, then think and try to evaluate your paper like an Evaluator. Try to understand that what an evaluator wants in your research paper and automatically you will have your answer.

4. Make blueprints of paper: The outline is the plan or framework that will help you to arrange your thoughts. It will make your paper logical. But remember that all points of your outline must be related to the topic you have chosen.

5. Ask your Guides: If you are having any difficulty in your research, then do not hesitate to share your difficulty to your guide (if you have any). They will surely help you out and resolve your doubts. If you can't clarify what exactly you require for your work then ask the supervisor to help you with the alternative. He might also provide you the list of essential readings.

6. Use of computer is recommended: As you are doing research in the field of Computer Science, then this point is quite obvious.

7. Use right software: Always use good quality software packages. If you are not capable to judge good software then you can lose quality of your paper unknowingly. There are various software programs available to help you, which you can get through Internet.

8. Use the Internet for help: An excellent start for your paper can be by using the Google. It is an excellent search engine, where you can have your doubts resolved. You may also read some answers for the frequent question how to write my research paper or find model research paper. From the internet library you can download books. If you have all required books make important reading selecting and analyzing the specified information. Then put together research paper sketch out.

9. Use and get big pictures: Always use encyclopedias, Wikipedia to get pictures so that you can go into the depth.

10. Bookmarks are useful: When you read any book or magazine, you generally use bookmarks, right! It is a good habit, which helps to not to lose your continuity. You should always use bookmarks while searching on Internet also, which will make your search easier.

11. Revise what you wrote: When you write anything, always read it, summarize it and then finalize it.



12. Make all efforts: Make all efforts to mention what you are going to write in your paper. That means always have a good start. Try to mention everything in introduction, that what is the need of a particular research paper. Polish your work by good skill of writing and always give an evaluator, what he wants.

13. Have backups: When you are going to do any important thing like making research paper, you should always have backup copies of it either in your computer or in paper. This will help you to not to lose any of your important.

14. Produce good diagrams of your own: Always try to include good charts or diagrams in your paper to improve quality. Using several and unnecessary diagrams will degrade the quality of your paper by creating "hotchpotch." So always, try to make and include those diagrams, which are made by your own to improve readability and understandability of your paper.

15. Use of direct quotes: When you do research relevant to literature, history or current affairs then use of quotes become essential but if study is relevant to science then use of quotes is not preferable.

16. Use proper verb tense: Use proper verb tenses in your paper. Use past tense, to present those events that happened. Use present tense to indicate events that are going on. Use future tense to indicate future happening events. Use of improper and wrong tenses will confuse the evaluator. Avoid the sentences that are incomplete.

17. Never use online paper: If you are getting any paper on Internet, then never use it as your research paper because it might be possible that evaluator has already seen it or maybe it is outdated version.

18. Pick a good study spot: To do your research studies always try to pick a spot, which is quiet. Every spot is not for studies. Spot that suits you choose it and proceed further.

19. Know what you know: Always try to know, what you know by making objectives. Else, you will be confused and cannot achieve your target.

20. Use good quality grammar: Always use a good quality grammar and use words that will throw positive impact on evaluator. Use of good quality grammar does not mean to use tough words, that for each word the evaluator has to go through dictionary. Do not start sentence with a conjunction. Do not fragment sentences. Eliminate one-word sentences. Ignore passive voice. Do not ever use a big word when a diminutive one would suffice. Verbs have to be in agreement with their subjects. Prepositions are not expressions to finish sentences with. It is incorrect to ever divide an infinitive. Avoid clichés like the disease. Also, always shun irritating alliteration. Use language that is simple and straight forward. put together a neat summary.

21. Arrangement of information: Each section of the main body should start with an opening sentence and there should be a changeover at the end of the section. Give only valid and powerful arguments to your topic. You may also maintain your arguments with records.

22. Never start in last minute: Always start at right time and give enough time to research work. Leaving everything to the last minute will degrade your paper and spoil your work.

23. Multitasking in research is not good: Doing several things at the same time proves bad habit in case of research activity. Research is an area, where everything has a particular time slot. Divide your research work in parts and do particular part in particular time slot.

24. Never copy others' work: Never copy others' work and give it your name because if evaluator has seen it anywhere you will be in trouble.

25. Take proper rest and food: No matter how many hours you spend for your research activity, if you are not taking care of your health then all your efforts will be in vain. For a quality research, study is must, and this can be done by taking proper rest and food.

26. Go for seminars: Attend seminars if the topic is relevant to your research area. Utilize all your resources.



27. Refresh your mind after intervals: Try to give rest to your mind by listening to soft music or by sleeping in intervals. This will also improve your memory.

28. Make colleagues: Always try to make colleagues. No matter how sharper or intelligent you are, if you make colleagues you can have several ideas, which will be helpful for your research.

29. Think technically: Always think technically. If anything happens, then search its reasons, its benefits, and demerits.

30. Think and then print: When you will go to print your paper, notice that tables are not be split, headings are not detached from their descriptions, and page sequence is maintained.

31. Adding unnecessary information: Do not add unnecessary information, like, I have used MS Excel to draw graph. Do not add irrelevant and inappropriate material. These all will create superfluous. Foreign terminology and phrases are not apropos. One should NEVER take a broad view. Analogy in script is like feathers on a snake. Not at all use a large word when a very small one would be sufficient. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Amplification is a billion times of inferior quality than sarcasm.

32. Never oversimplify everything: To add material in your research paper, never go for oversimplification. This will definitely irritate the evaluator. Be more or less specific. Also too, by no means, ever use rhythmic redundancies. Contractions aren't essential and shouldn't be there used. Comparisons are as terrible as clichés. Give up ampersands and abbreviations, and so on. Remove commas, that are, not necessary. Parenthetical words however should be together with this in commas. Understatement is all the time the complete best way to put onward earth-shaking thoughts. Give a detailed literary review.

33. Report concluded results: Use concluded results. From raw data, filter the results and then conclude your studies based on measurements and observations taken. Significant figures and appropriate number of decimal places should be used. Parenthetical remarks are prohibitive. Proofread carefully at final stage. In the end give outline to your arguments. Spot out perspectives of further study of this subject. Justify your conclusion by at the bottom of them with sufficient justifications and examples.

34. After conclusion: Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium through which your research is going to be in print to the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects in your research.

INFORMAL GUIDELINES OF RESEARCH PAPER WRITING

Key points to remember:

- Submit all work in its final form.
- Write your paper in the form, which is presented in the guidelines using the template.
- Please note the criterion for grading the final paper by peer-reviewers.

Final Points:

A purpose of organizing a research paper is to let people to interpret your effort selectively. The journal requires the following sections, submitted in the order listed, each section to start on a new page.

The introduction will be compiled from reference matter and will reflect the design processes or outline of basis that direct you to make study. As you will carry out the process of study, the method and process section will be constructed as like that. The result segment will show related statistics in nearly sequential order and will direct the reviewers next to the similar intellectual paths throughout the data that you took to carry out your study. The discussion section will provide understanding of the data and projections as to the implication of the results. The use of good quality references all through the paper will give the effort trustworthiness by representing an alertness of prior workings.



Writing a research paper is not an easy job no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record keeping are the only means to make straightforward the progression.

General style:

Specific editorial column necessities for compliance of a manuscript will always take over from directions in these general guidelines.

To make a paper clear

- Adhere to recommended page limits

Mistakes to evade

- Insertion a title at the foot of a page with the subsequent text on the next page
- Separating a table/chart or figure - impound each figure/table to a single page
- Submitting a manuscript with pages out of sequence

In every sections of your document

- Use standard writing style including articles ("a", "the," etc.)
- Keep on paying attention on the research topic of the paper
- Use paragraphs to split each significant point (excluding for the abstract)
- Align the primary line of each section
- Present your points in sound order
- Use present tense to report well accepted
- Use past tense to describe specific results
- Shun familiar wording, don't address the reviewer directly, and don't use slang, slang language, or superlatives
- Shun use of extra pictures - include only those figures essential to presenting results

Title Page:

Choose a revealing title. It should be short. It should not have non-standard acronyms or abbreviations. It should not exceed two printed lines. It should include the name(s) and address (es) of all authors.



Abstract:

The summary should be two hundred words or less. It should briefly and clearly explain the key findings reported in the manuscript-- must have precise statistics. It should not have abnormal acronyms or abbreviations. It should be logical in itself. Shun citing references at this point.

An abstract is a brief distinct paragraph summary of finished work or work in development. In a minute or less a reviewer can be taught the foundation behind the study, common approach to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Yet, use comprehensive sentences and do not let go readability for brevity. You can maintain it succinct by phrasing sentences so that they provide more than lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study, with the subsequent elements in any summary. Try to maintain the initial two items to no more than one ruling each.

- Reason of the study - theory, overall issue, purpose
- Fundamental goal
- To the point depiction of the research
- Consequences, including definite statistics - if the consequences are quantitative in nature, account quantitative data; results of any numerical analysis should be reported
- Significant conclusions or questions that track from the research(es)

Approach:

- Single section, and succinct
- As an outline of job done, it is always written in past tense
- A conceptual should situate on its own, and not submit to any other part of the paper such as a form or table
- Center on shortening results - bound background information to a verdict or two, if completely necessary
- What you account in an abstract must be regular with what you reported in the manuscript
- Exact spelling, clearness of sentences and phrases, and appropriate reporting of quantities (proper units, important statistics) are just as significant in an abstract as they are anywhere else

Introduction:

The **Introduction** should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable to comprehend and calculate the purpose of your study without having to submit to other works. The basis for the study should be offered. Give most important references but shun difficult to make a comprehensive appraisal of the topic. In the introduction, describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will have no attention in your result. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here. Following approach can create a valuable beginning:

- Explain the value (significance) of the study
- Shield the model - why did you employ this particular system or method? What is its compensation? You strength remark on its appropriateness from a abstract point of vision as well as point out sensible reasons for using it.
- Present a justification. Status your particular theory (es) or aim(s), and describe the logic that led you to choose them.
- Very for a short time explain the tentative propose and how it skilled the declared objectives.

Approach:

- Use past tense except for when referring to recognized facts. After all, the manuscript will be submitted after the entire job is done.
- Sort out your thoughts; manufacture one key point with every section. If you make the four points listed above, you will need a least of four paragraphs.



- Present surroundings information only as desirable in order hold up a situation. The reviewer does not desire to read the whole thing you know about a topic.
- Shape the theory/purpose specifically - do not take a broad view.
- As always, give awareness to spelling, simplicity and correctness of sentences and phrases.

Procedures (Methods and Materials):

This part is supposed to be the easiest to carve if you have good skills. A sound written Procedures segment allows a capable scientist to replacement your results. Present precise information about your supplies. The suppliers and clarity of reagents can be helpful bits of information. Present methods in sequential order but linked methodologies can be grouped as a segment. Be concise when relating the protocols. Attempt for the least amount of information that would permit another capable scientist to spare your outcome but be cautious that vital information is integrated. The use of subheadings is suggested and ought to be synchronized with the results section. When a technique is used that has been well described in another object, mention the specific item describing a way but draw the basic principle while stating the situation. The purpose is to text all particular resources and broad procedures, so that another person may use some or all of the methods in one more study or referee the scientific value of your work. It is not to be a step by step report of the whole thing you did, nor is a methods section a set of orders.

Materials:

- Explain materials individually only if the study is so complex that it saves liberty this way.
- Embrace particular materials, and any tools or provisions that are not frequently found in laboratories.
- Do not take in frequently found.
- If use of a definite type of tools.
- Materials may be reported in a part section or else they may be recognized along with your measures.

Methods:

- Report the method (not particulars of each process that engaged the same methodology)
- Describe the method entirely
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures
- Simplify - details how procedures were completed not how they were exclusively performed on a particular day.
- If well known procedures were used, account the procedure by name, possibly with reference, and that's all.

Approach:

- It is embarrassed or not possible to use vigorous voice when documenting methods with no using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result when script up the methods most authors use third person passive voice.
- Use standard style in this and in every other part of the paper - avoid familiar lists, and use full sentences.

What to keep away from

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings - save it for the argument.
- Leave out information that is immaterial to a third party.

Results:

The principle of a results segment is to present and demonstrate your conclusion. Create this part a entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Carry on to be to the point, by means of statistics and tables, if suitable, to present consequences most efficiently. You must obviously differentiate material that would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matter should not be submitted at all except requested by the instructor.



Content

- Sum up your conclusion in text and demonstrate them, if suitable, with figures and tables.
- In manuscript, explain each of your consequences, point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation an exacting study.
- Explain results of control experiments and comprise remarks that are not accessible in a prescribed figure or table, if appropriate.
- Examine your data, then prepare the analyzed (transformed) data in the form of a figure (graph), table, or in manuscript form.

What to stay away from

- Do not discuss or infer your outcome, report surroundings information, or try to explain anything.
- Not at all, take in raw data or intermediate calculations in a research manuscript.
- Do not present the similar data more than once.
- Manuscript should complement any figures or tables, not duplicate the identical information.
- Never confuse figures with tables - there is a difference.

Approach

- As forever, use past tense when you submit to your results, and put the whole thing in a reasonable order.
- Put figures and tables, appropriately numbered, in order at the end of the report
- If you desire, you may place your figures and tables properly within the text of your results part.

Figures and tables

- If you put figures and tables at the end of the details, make certain that they are visibly distinguished from any attach appendix materials, such as raw facts
- Despite of position, each figure must be numbered one after the other and complete with subtitle
- In spite of position, each table must be titled, numbered one after the other and complete with heading
- All figure and table must be adequately complete that it could situate on its own, divide from text

Discussion:

The Discussion is expected the trickiest segment to write and describe. A lot of papers submitted for journal are discarded based on problems with the Discussion. There is no head of state for how long a argument should be. Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implication of the study. The purpose here is to offer an understanding of your results and hold up for all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of result should be visibly described. Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved with prospect, and let it drop at that.

- Make a decision if each premise is supported, discarded, or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."
- Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work
- You may propose future guidelines, such as how the experiment might be personalized to accomplish a new idea.
- Give details all of your remarks as much as possible, focus on mechanisms.
- Make a decision if the tentative design sufficiently addressed the theory, and whether or not it was correctly restricted.
- Try to present substitute explanations if sensible alternatives be present.
- One research will not counter an overall question, so maintain the large picture in mind, where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

- When you refer to information, differentiate data generated by your own studies from available information
- Submit to work done by specific persons (including you) in past tense.
- Submit to generally acknowledged facts and main beliefs in present tense.



THE ADMINISTRATION RULES

Please carefully note down following rules and regulation before submitting your Research Paper to Global Journals Inc. (US):

Segment Draft and Final Research Paper: You have to strictly follow the template of research paper. If it is not done your paper may get rejected.

- The **major constraint** is that you must independently make all content, tables, graphs, and facts that are offered in the paper. You must write each part of the paper wholly on your own. The Peer-reviewers need to identify your own perceptives of the concepts in your own terms. NEVER extract straight from any foundation, and never rephrase someone else's analysis.
- Do not give permission to anyone else to "PROOFREAD" your manuscript.
- **Methods to avoid Plagiarism is applied by us on every paper, if found guilty, you will be blacklisted by all of our collaborated research groups, your institution will be informed for this and strict legal actions will be taken immediately.)**
- To guard yourself and others from possible illegal use please do not permit anyone right to use to your paper and files.



CRITERION FOR GRADING A RESEARCH PAPER (COMPILATION)
BY GLOBAL JOURNALS INC. (US)

Please note that following table is only a Grading of "Paper Compilation" and not on "Performed/Stated Research" whose grading solely depends on Individual Assigned Peer Reviewer and Editorial Board Member. These can be available only on request and after decision of Paper. This report will be the property of Global Journals Inc. (US).

Topics	Grades		
	A-B	C-D	E-F
<i>Abstract</i>	Clear and concise with appropriate content, Correct format. 200 words or below	Unclear summary and no specific data, Incorrect form Above 200 words	No specific data with ambiguous information Above 250 words
<i>Introduction</i>	Containing all background details with clear goal and appropriate details, flow specification, no grammar and spelling mistake, well organized sentence and paragraph, reference cited	Unclear and confusing data, appropriate format, grammar and spelling errors with unorganized matter	Out of place depth and content, hazy format
<i>Methods and Procedures</i>	Clear and to the point with well arranged paragraph, precision and accuracy of facts and figures, well organized subheads	Difficult to comprehend with embarrassed text, too much explanation but completed	Incorrect and unorganized structure with hazy meaning
<i>Result</i>	Well organized, Clear and specific, Correct units with precision, correct data, well structuring of paragraph, no grammar and spelling mistake	Complete and embarrassed text, difficult to comprehend	Irregular format with wrong facts and figures
<i>Discussion</i>	Well organized, meaningful specification, sound conclusion, logical and concise explanation, highly structured paragraph reference cited	Wordy, unclear conclusion, spurious	Conclusion is not cited, unorganized, difficult to comprehend
<i>References</i>	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring



INDEX

A

Adenocarcinoma · 8
Ayder · 1, 2, 3, 4, 5, 2, 1, 2, 1, 2, 3

C

Carcinoembryonic · 2
Cetuximab · 24, 25, 27, 28

E

Ethidium · 14, 15, 16

F

Fuenlabrada · 8, 24

G

Glucocorticoids · 2
Gonadotropin · 1, 2, 3
Granulosa · 1, 2, 3

H

Hemophilia · 12, 16, 22

L

Lyonization · 12

N

Neoplasia · 2

P

Parishek · 5

T

Testolactone · 2



save our planet



Global Journal of Medical Research

Visit us on the Web at www.GlobalJournals.org | www.MedicalResearchJournal.org
or email us at helpdesk@globaljournals.org

ISSN 9755896



© Global Journals