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Microbiology & Pathology

Catenin Role and Expression

Intractable Nausea and Vomiting

Highlights

Case of Systemic Amyloidosis

Spectrum of Disorders Diagnosed

Discovering Thoughts, Inventing Future

VOLUME 15 ISSUE 5 VERSION 1.0

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A Diagnostic Challenge in a Patient with Intractable Nausea and Vomiting: A Case of Systemic Amyloidosis

By Naveed Ali, Ali Ghani, Apurva Gandhi, Ritesh Rampure & Herbert E. Auerbach

Abstract- Amyloidosis is a rare disorder caused by deposition of amyloid fibrils in various tissues causing structural and functional defects. Depending upon organs involved, it may be categorized as localized or systemic. Systemic amyloidosis involves multiple organs where some organs are affected more commonly than others. Diagnosis is often challenging as in a 76-years-old female described here who presented with intractable nausea and vomiting. Clinical course was complicated because of simultaneous presence of peptic ulcer disease and hypothyroidism. Involvement of multiple systems including gastrointestinal tract, thyroid, liver, heart and kidneys was seen, and diagnosis was achieved after renal biopsy showing Congo red staining and apple green birefringence. Gastric and thyroid infiltration by amyloidosis are extremely rare occurrences described very infrequently in the literature. However, to our knowledge, involvement of both organs in a single patient has not been reported in the literature.

GJMR-C Classification : NLMC Code: WI 146

ADIAGNOSTICCHALLENGEINAPATIENTWITHINTRACTABLENAUSEAANDVOMITINGACASEOFSYSTEMICAMYLOIDOSIS

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A Diagnostic Challenge in a Patient with Intractable Nausea and Vomiting: A Case of Systemic Amyloidosis

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I. Introduction

Nausea and vomiting are universal symptoms encountered in daily clinical practice, mostly as a part of medical illnesses involving the gastrointestinal tract with causes ranging from relatively benign to at times serious pathology. In either case, these symptoms are very distressing to patients. Therefore, a systematic approach is warranted to determine the cause particularly in cases of intractable nausea and vomiting. We report a 76-years-old female with intractable nausea and vomiting where diagnosis of systemic amyloidosis was made after an extensive workup. Being a systemic disease, amyloidosis affected multiple systems including extremely rarely involved organs.

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II. Case Presentation

A76 years old non-alcoholic female with history of coronary artery disease (CAD) developed intractable nausea and vomiting lasting two months with repeated admissions to various hospitals. An upper endoscopy (EGD) was done which showed duodenal ulcer and Helicobacter pylori was identified on biopsy. She was subsequently treated with triple therapy. At the same time, she was diagnosed with severe primary hypothyroidism and was started on levothyroxine supplementation. Despite completing triple therapy for Helicobacter pylori infection, she had persistent nausea and vomiting, and presented to our hospital. Furthermore, she had developed generalized body swelling and a skin rash.

On examination, she was noted to have bilateral feet and leg swelling, epigastric tenderness and a faint maculopapular rash was evident on the abdomen. Laboratory investigations were noteworthy of the following: BUN 26 mg/dl, Cr. 1.30 mg/dl, Na 129 mEq/l, K 5.2 mEq/l, HCO^3 16 mEq/l, AST 169 U/l, ALT 86 U/l, ALP 2390 U/l, total bilirubin 0.6 mg/dl, albumin 1.2 gm/dl and γ-glutamyl transpeptidase (GGTP) 849 U/l. Hemogram showed a WBC count of 10.2 x 10^3 per μl, hemoglobin level of 18.7 gm/dl and platelet count of 238 x 10^3 per μl. Thyroid function tests showed elevated TSH at 51 IU/ml (which was markedly elevated at > 200 per μIU/ml on previous admission to another hospital), decreased free T4 at 0.59 ng/dl and decreased free T3 at 1.13 pg/dl. Her troponin level was also found to be elevated at 0.47 ng/ml.

Renal function abnormalities were presumed to be secondary to pre-renal etiology from dehydration consequent to vomiting. Electrolyte derangements were corrected and therapy was instituted for severe hypothyroidism as intravenous levothyroxine. Deranged hepatic enzymes were evaluated for hepatobiliary pathology with a computerized tomography (CT) scan of the abdomen which showed bilateral pleural effusions and findings compatible with hepatic cirrhosis and ascites (*Figure 1*). Further evaluation of hepatic cirrhosis was negative for infectious or autoimmune causes. The elevation in liver and biliary tract enzymes in particular

markedly elevated alkaline phosphatase was presumed to be due to severe hypothyroidism.

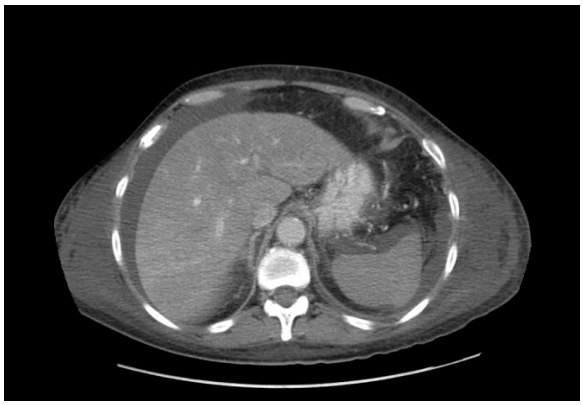

Figure 1 : CT scan showing mildly nodular liver contour, hepatomegaly, ascities

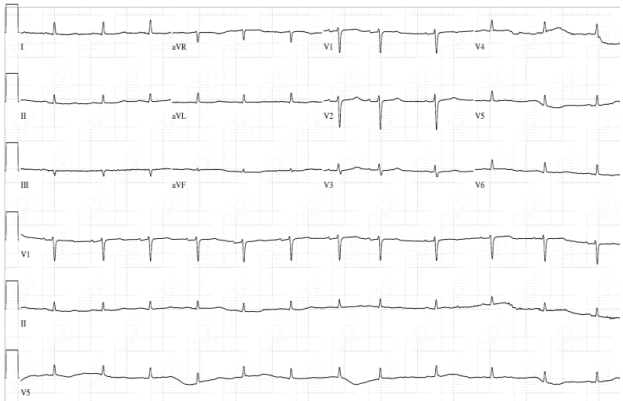

Figure 2 : EKG showing low voltages QRS complexes

Elevated troponin level in the setting of CAD history was evaluated by an echocardiogram which showed moderate asymmetrical left ventricular hypertrophy (*Figure 3a*) without left ventricular outflow tract obstruction (*Figure 3b*), which along with low voltage EKG QRS complexes (*Figure 2*) suggested an underlying systemic infiltrative disease such as hemochromatosis and amyloidosis. Hence, iron studies were done which showed a ferritin level of 581 ng/dl, iron (Fe) of 86 μg/dl, transferrin (TIBC) of 109 μg/dl and iron saturation of 79%, findings not compatible with hemochromatosis.

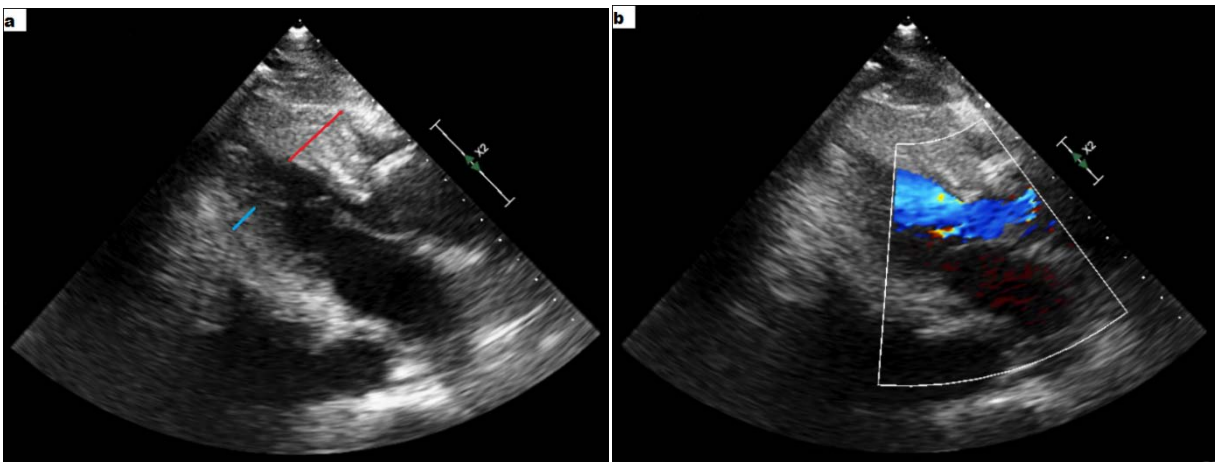

Figure 3 : a) parasternal long axis view showing asymmetrical septal hypertrophy (red line – septum, blue line – left ventricular free wall) b) parasternal long axis view with color doppler showing laminar flow (blue) across left ventricular outflow tract

During the course of her treatment, she developed worsening anasarca and severe hypoalbuminemia raising suspicion of nephrotic syndrome. Therefore, a 24 hour urinary protein quantification demonstrated proteinuria of 4 grams. As part of nephrotic syndrome workup, she was noted to have IgA lambda monoclonal gammopathy on serum protein immunofixation, however, serum protein electrophoresis did not show any abnormal monocloncal spike. Serum immunoglobulin analysis revealed elevated immunoglobulin A level at 544 mg/dl and decreased IgG level at 442 mg/dl. Serum kappa free light chains were 30 mg/l, lambda free light chains were 148 mg/l and kappa/lambda ratio was decreased to < 0.2. Ultimately, a kidney biopsy was done to find out the exact cause of nephrotic syndrome which stained positive for Congo red and birefringence (*Figure 4a & 4b*). PAS, Jones and trichrome stain were compatible with amyloidosis. She was diagnosed with type AL systemic amyloidosis with gastric, cardiac, thyroid, liver and kidney involvement. The morbiliform skin rash was thought to be secondary to amoxicillin which she received as part of H. pylori treatment and it improved over the course of her hospital stay. She was given diuretics, albumin infusions and steroids. After stabilization in the hospitalization, she was discharged. Unfortunately, bone marrow biopsy could not be performed as patient was readmitted to another hospital and passed away.

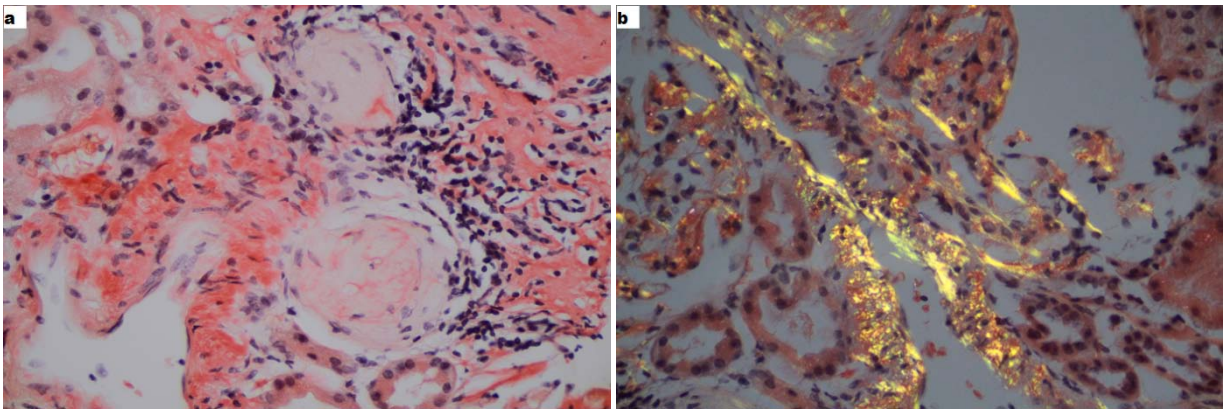

Figure 4 : a) renal biopsy staining with Congo red stain b) apple green birefringence under polarized light

III. Discussion

Amyloidosis is characterized by deposition of misfolded filbrillar proteins in the extracellular space, leading to multiple organ and tissue derangements [1]. The primary pathogenetic mechanism involves antiparallel beta-pleated sheet conformation of polypeptide molecules resulting in insoluble protein aggregates that get deposited in tissues as amyloid. This abnormal folding of native proteins occurs due to various factors including intrinsic amyloidogenic propensity, increased serum concentrations, aging, genetics and proteolytic remodeling [2]. Amyloidosis is classified according to the precursor protein. Primary or AL amyloidosis is caused by deposition of monoclonal immunoglobulin light chains and occurs in association with plasma cell dyscrasias. Secondary or AA amyloidosis is derived from serum amyloid A protein and occurs in association with chronic underlying inflammatory disorders. Several familial forms of amyloidosis have been identified such as transthyretin, apolipoprotein A-1 and fibrinogen A. Long term dialysis also results in amyloidosis derived from β-2 microglobulin [1, 3, 4].

Gastrointestinal disease is present in as many as 60 percent of patients with amyloidosis which can occur as an isolated entity or as part of multiorgan involvement [5, 6]. GI involvement is more common in AL type rather than AA type amyloidosis [7, 8]. Gastrointestinal disease in amyloidosis results from either mucosal or neuromuscular infiltration. In addition, an extrinsic autonomic neuropathy may also affect gut function [5]. Infiltration may occur anywhere along the GI tract presenting as GI bleeding, malabsorption, protein losing enteropathy and chronic GI dysmotility. GI dysmotility presenting as nausea, vomiting and pseudo obstruction is a rare presentation that occurs in 1% of patients with GI amyloidosis [5, 6, 7, 9]. There have been rare cases reported with systemic amyloidosis presenting solely as a gastrointestinal obstruction or pseudo obstruction [10, 11, 12, 13]. Even though there were multiple systems involved in this patient, but amyloid gastropathy presenting as nausea and vomiting was most predominant.

Being a systemic disease, amyloid can infiltrate the thyroid gland. Thyroid infiltration can present as progressively enlarging goiter and can be confused with rapidly enlarging thyroid cancer. The majority of amyloidosis affected patients develop infiltration of the thyroid gland; yet thyroid dysfunction in the form of hypothyroidism rarely occurs [14]. Literature search reveals only a few case reports of severe hypothyroidism as manifestation of systemic amyloidosis and most of these cases were diagnosed at

autopsy [15, 16]. Severe hypothyroidism in this case was presumed to be due to amyloidosis involving thyroid gland. Interestingly, we did not see goiter in our patient which is a more common manifestation of thyroid infiltration.

Because amyloidosis is a systemic disease, we find involvement of multiple systems in our case besides GI tract and thyroid gland. Firstly, involvement of liver was noted when CT scan of the abdomen was done. Although hepatic involvement is very common in patients with amyloidosis, the clinical manifestations of hepatic involvement are usually mild [17, 18]. Liver infiltration is more common in AL amyloidosis than AA amyloidosis [6]. Hepatomegaly is present in up to 81-92% of patients in amyloidosis [6, 20]. Contrast-enhanced CT scan, although not diagnostic, may show an enlarged liver with heterogeneous decreased attenuation or rarely a mass [18, 19]. The patients are often misdiagnosed with hepatic cirrhosis based on imaging features. In this patient, cirrhosis was thought to be secondary to amyloidosis because all causes of hepatic cirrhosis (HBV, HCV, autoimmune, alcohol, hemochromatosis) were excluded. Elevated alkaline phosphatase, usually along with elevated GGTP, is the most common laboratory abnormality in systemic amyloidosis [17, 20]. In our patient, markedly elevated alkaline phosphatase and CT scan findings strongly suggested amyloid infiltration of liver.

Secondly, cardiac involvement occurs in up to 50 percent of patients with AL amyloidosis compared to less than 5 percent with AA amyloidosis [21, 22]. The heart is considered involved if either an endomyocardial biopsy demonstrates amyloidosis in the presence of clinical or laboratory evidence of involvement or echocardiographic evidence of amyloidosis is found in a patient with a positive result of noncardiac biopsy [23]. Besides EKG which shows low voltage QRS complexes, echocardiography is particular useful in diagnosis especially if there are not significant cardiac symptoms [22]. In our patient, asymmetrical septal hypertrophy and lack of outflow tract obstruction favored an infiltrative disease. It is of great importance to pay particular attention to details such as low voltage QRS complexes, as it may be a clue towards a rare yet significant disease.

Thirdly, severe hypoalbuminemia and nephrotic range proteinuria were secondary to renal involvement of amyloidosis, which was confirmed by renal biopsy. The kidney is affected in 50% to 80% of patients with AL amyloidosis and is the most common cause of mortality in these patients along with cardiac manifestations [24]. Diagnosis is made by renal biopsy demonstrating Congo red staining and apple-green birefringence upon polarization [24, 25]. Renal manifestations in amyloidosis are characterized by nephrotic syndrome with heavy proteinuria and impaired renal functions [26]. Our patient exhibited both nephrotic syndrome and impairment of renal functions.

The present case is very unique in presentation as there were two exceedingly rare manifestations of systemic amyloidosis: amyloid gastropathy and severe hypothyroidism. The diagnosis in the patient was confounded by recent diagnosis of H. pylori related duodenal ulcer. However, the symptoms persisted even after undergoing therapy leading to repeated admissions in various hospitals. Moreover, the diagnosis was challenging in the presence of another systemic disease, hypothyroidism. Although recurrent nausea and vomiting is relatively uncommon in hypothyroidism, its concomitant presence in this case complicated the diagnosis. After extensive investigations, the clue towards a systemic infiltrating disease (amyloidosis) was provided by EKG which showed low voltage complexes, underscoring the importance of even basic investigations. Ultimately, diagnosis of systemic amyloidosis was reached after renal biopsy.

Amyloidosis, being a great masquerader, is one of the unusual diseases that physicians encounter and often presents a diagnostic challenge as in our patient. Suspicion of GI involvement may be very low if other organs are unaffected. However, unexplained nausea and vomiting and lack of resolution of these symptoms should raise possibility of such rare yet significant disease as amyloidosis. It becomes more crucial to consider amyloidosis in the differential if there is multiorgan involvement. Lastly, early diagnosis is important to initiate timely therapy as the response to treatment could be very different, and ultimately affects patient morbidity and mortality.

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α-Catenin Role and Expression in Oral Squamous Cell Carcinoma

By khaled Zaid, Mansour Chantiri, Mhd Thabit Murad & Mostafa Almoustafa Alhosni

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Abstract- This study aimed to reveal the role and altered immunohistochemical expression of α-catenin in oral squamous cell carcinoma progression in its three histopathological differentiations. Immunohistochemical method was used to stain 81 biopsy taken from 81 patients and 15 control sample from normal oral mucosa. α-catenin was detected with homogenous strong staining in 56.6%, 40%, 15% of well, moderately, poorly differentiated squamous cell carcinomas, respectively with $p<0.05$. the heterogenous slight staining appeared in 40%, 52%, 61.5% respectively with $p<0.05$. the loss of α-catenin is observed in oral squamous cell carcinoma progression. The appearance of α-catenin oral SCC and invasive carcinomas might suggest its role in tumor progression by influencing on APC to control β-catenin dissolution and transcriptional suppression of Wnt pathway in this type of carcinogenesis.

Keywords: oral squamous cell carcinoma, α-catenin, immunohistochemical expression.

GJMR-C Classification : NLMC Code: WP 460

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I. Introduction

Catenin present as α-catenin (102 kDa), β-catenin (88 kDa), and γ-catenin (80 kDa) are anchoring proteins present in cytoplasm and verry essential in maintaining the normal functions of E-cadherin protein in the cross-linkage action between actin filament and the intracellular membranous proteins, Na+/K+ adenosine triphosphatase and E-cadherin [1].

α-catenin or alpha-1-catenin (also called alpha-E-catenin) binding protein, is effectively coordinating the cortical actin networks of adjacent cells [2], Roles for α-cat are best understood at cell junctions, where itis essential for cell cohesion and tissue organization[3-5]. Asa homodimer, α-cat directly interacts with filamentous (F) actin [6] but α-cat can also indirectly associate with the cytoskeleton through other actin-binding proteins, such as epithelial protein lostin neoplasm (EPLIN) (figure 1)[7][8], vinculin [9], afadin [10], α-actinin [11], and zonula occludens-1 (ZO-1) [12]. In addition, α-cat can impact F-actin remodeling by directly inhibiting Arp2/3-mediated actin polymerization in vitro [13], lamellipodial dynamics in cells [14],and by promoting F-actin bundling in vitro [15].

α-Catenin might serve as an invasion suppressor molecule, and reduced expression of α -catenin has been related to poor differentiation of tumours, infiltrative growth, and lymph node metastasis [16-18]. Furthermore, the disappearance of membranous α-catenin is predictive of an unfavourable outcome in prostate, ovarian, and colorectal cancer [19-21]. many studies have shown that α-catenin represses the transcriptional activities by segregating the YAP1/TAZ transcriptional coactivator in inactive complexes within the cytoplasm[22]

According to World Health Organization, carcinoma of oral cavity in males in developing countries, is the sixth commonest cancer after lung, prostrate, colorectal, stomach and bladder cancer, while in females, it is the tenth commonest site of cancer after breast, colorectal, lung, stomach, uterus, cervix, ovary, bladder and liver[23]. More than 90% of all oral cancers are squamous cell carcinomas (SCC) [1]and this type of cancers composes About 95% of oral cancers in India [24].This malignancy constitute a major health problem in developing countries, representing a leading cause of death. The survival index continues to be small (50%), as compared to the progress in diagnosis and treatment of other malignant tumors[25].

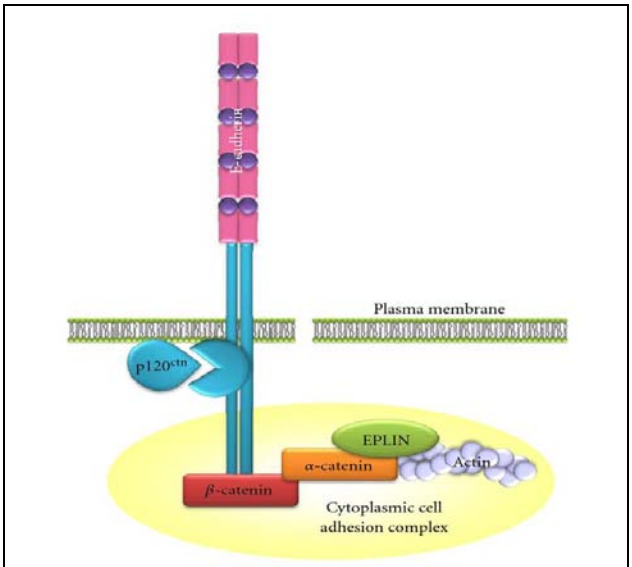

Figure 1 : Cell adhesion Complex. E-cadherin is stabilised at the cell surface by its link to the actin cytoskeleton via β-catenin, α-catenin, and, possibly, Epithelial Protein Lost in Neoplasm (EPLIN). [7]

This study aimed to show the relation between altered expression of α-catenin and the histopathological differentiations of oral squamous cell carcinoma.

II. Materials and Methods

81 Formalin-fixed, paraffin embedded representative tissue sections 3μm in thickness of 30 well

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differentiated oral scc (WDOSCC), 25 moderately differentiated oral scc (MDOSCC), 26 poorly differentiated oral scc, sections were retrieved from the archive of Pathology an Histology Department, faculty of dentistry, Damascus University, in addition to 15 normal oral tissues as a control group were harvested during surgical extraction of third impacted molars.

Sections were dewaxed, rehydrated in graded alcohols, and immunostained using a standard streptavidin-biotin immuno-peroxidase method. Monoclonal antibodies against α-Catenin (RB-089-P, 1:5 dilution, Neomarkers, USA) were used.

Normal oral epithelium was used as a positive control and sections incubated with a negative control serum (Dako, Denmark) were used as negative controls. Immunostaining was evaluated according to the intensity (slight/ strong) and the distribution of staining pattern (homogenous-membranous; heterogenouscyto-plasmic and/or membranous).

Immunostaining pattern was scored as follows: 0= nostaining, +1= heterogenous slight staining, +2= homogenous strong staining with respect to the control positive tissue. The intensity and the staining pattern in normal oral squamous epithelium were regarded as +2 homogenous strong staining.

a) Statistical analysis

The chi-square test was used to assess the statistical significance of α -Catenin expression in relation to histopathological grade.

III. Results

a) Normal epethelium

α-catenin staining was cytoplasmic with a clearly strong intensity and showed homogenous strong membranous staining in basal, parabasal and intermediate layers of squamous epithelium of the normal tissues (figure 2).

b) study sample

homogenous strong positivity appeared in 56.6% of the WDOSCC sections in the epithelium and the tumoral islands, 40% revealed +1 and in one section we noticed that there was no staining (figure 3). MDOSCCC revealed 40%(+2) immunostaining, 52% (+1) and two showed no staining (figure 4). PDOSCC had only 4 (15%) strong immunostaining (figure 5) (p=0.0001). Aberrant nuclear staining of α-catenin was observed in a few cells of PDOSCC. (table 1) (figure 6)

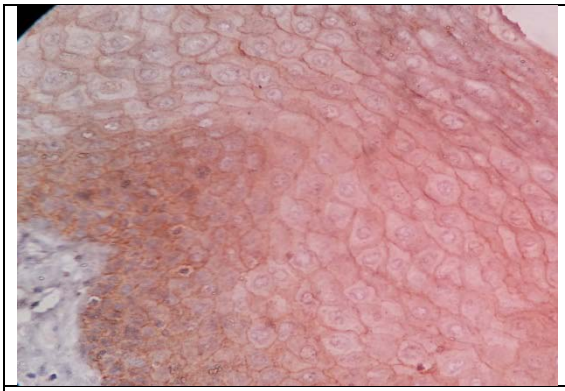

Figure 2 : Expression of α-catenin in normal oral epethelium .40X

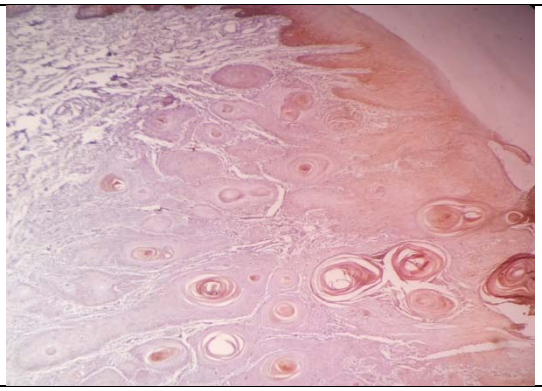

Figure 3 : Expression of α-catenin in well differentiated OSCC .40X

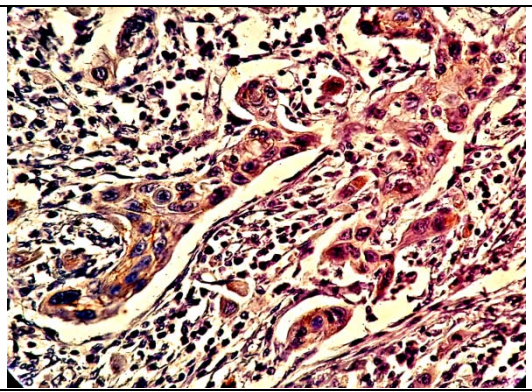

Figure 4 : Expression of α-catenin in moderately differentiated OSCC .40X

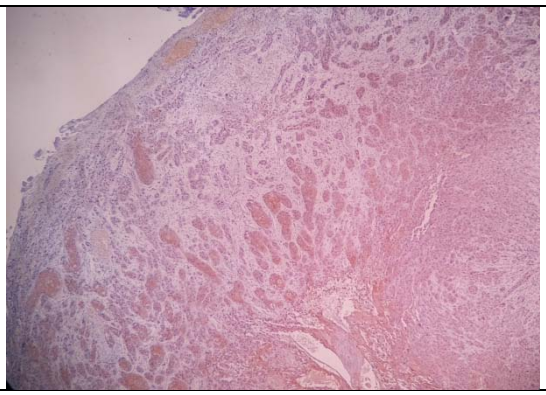

Figure 5 : Expression of α-catenin in moderately differentiated OSCC .10X

Table (1)

Distribution of immunopositivity of α-Catenin

	+2	+1	0
	positivity% (n)	positivity% (n)	% (n)
WDOSCC	56.6% (17)	40% (12)	3.3% (1)
MDOSCC	40% (10)	52% (13)	8% (2)
PDOSCC	15% (4)	61.5% (16)	23% (6)

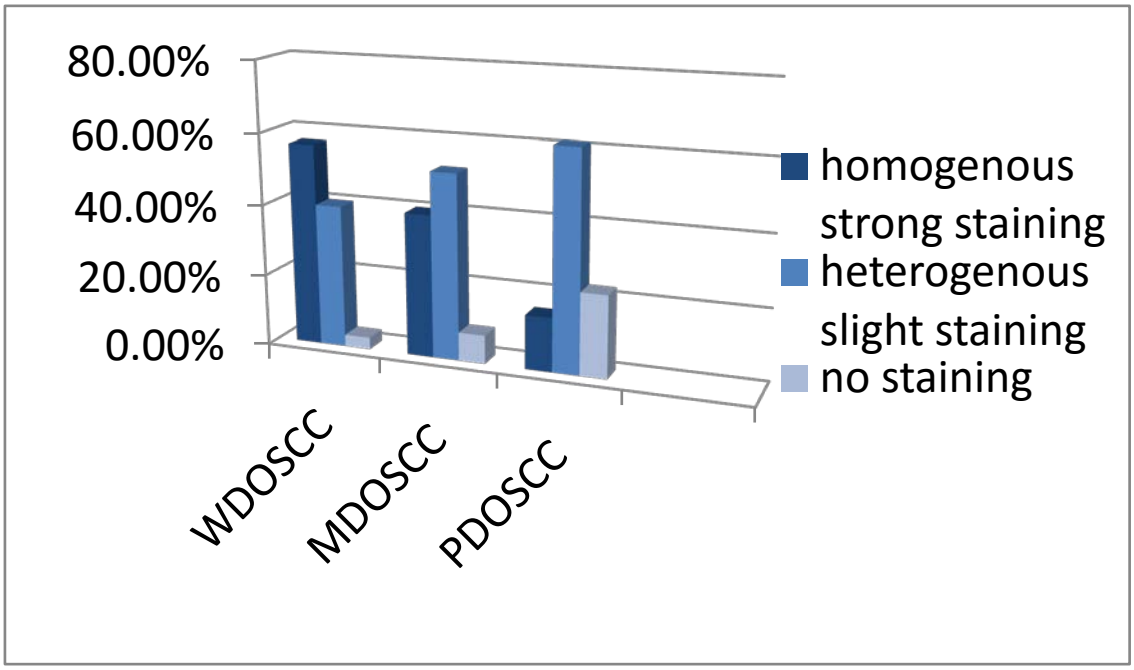

Figure 6 : Distribution of immunopositivity of α-Catenin in the study sample

IV. Discussion

Loss of cell adhesion molecules or altered expression of these molecules plays an essential role in tumor progression in epithelial tissues [26]. E-cadherin and its associated cytoplasmic protein α-catenin are of the main parts of cell adhesion complex in squamous epithelial tissues [27].

We investigated the expression α-catenin in oral squamous cell carcinoma progression from the well differentiated stage to the poorly differentiated.

Though we revealed α-catenin expression loss in the progression of squamous cell carcinoma, this reduced expression was clearly associated with the histopathological differentiation ($p<0.05$). revealed such loss of α-cateninin the cases of oral squamous cell carcinomas [28, 29]

Unlike β-catenin, which has a role as an oncogene [30], α-catenin is considered a potent suppressor in many tumors, and its loss or down-regulation in many aggressive cancers is clearly correlated with metastasis [31, 32]. In addition to its well-known role in cell-cell adhesion, α-catenin represses signaling through the Wnt, Ras, NF-kB, and Hedgehog pathways [33] which controls organs sizes and cell contact inhibition by way of the Yes-associated protein YAP1. YAP1 is a potent coactivator in many signaling pathways and also interacts with β-catenin in TBX5 complexes to regulate anti-apoptotic genes in colon cancer [34]

At high cell density, phosphorylated YAP1 accumulates in the cytoplasm, where it is sequestered by α-catenin and inhibits Wnt signaling [22] . The YAP1 homolog TAZ is degraded by the APC complex and is required for expression of many Wnt target genes [35]

Mechanistic studies of YAP1 function in TGFb/SMAD signaling further reveal that it both stimulates transcription and promotes the exchange of coactivator and corepressor complexes at target genes [36]

Thus, α-catenin links cell adhesion signals to YAP1 inactivation and the inhibition ofcell proliferation.

α-catenin may potentially control TAZ functions directly at Wnt target genes or guide it to the cytoplasm for degredation by the APC complex. Because α-catenin and APC are recruited with β-cateninto target genes, their transcriptional activities must be under control to prevent premature termination of transcription. [37, 38]. One interesting possibility is that Y177 phosphorylation

of α-catenin could prevent docking of APC prior to activation of the RNAPII elongation complex [39]

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Spectrum of Disorders Diagnosed by Bone Marrow Aspiration

By Dr. Aparajita Tomar, Dr. Vibha Trichal & Dr. RPS Chauhan
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Abstract- *Aims and Objectives:* To identify and analyse the most common hematological disorders diagnosed by doing bone marrow aspiration in a particular group of patients.

Material and Method: Bone marrow aspiration was done from Manubrium of the Sternum after injecting 2% xylocaine to the part. Bone marrow smears were prepared and stained with Leishman stain along with the simultaneous staining of the peripheral smears. A complete hemogram including Hb%, PCV, Red cell indices, platelet count, total leucocyte count and differential leucocyte count was also done by Automated cell counter. Finally, the bone marrow and peripheral smears were examined manually under oil immersion.

Conclusion: In this study it was found that the most frequently diagnosed hematological disorders on bone marrow aspiration are Megaloblastic and Dimorphic anemias followed by Acute Myeloid and Acute Lymphoblastic Leukemias. Hematological disorders are more common in early adulthood. commonest leukemia in adults and children is Acute Myeloid Leukemia, AML and Acute Lymphoblastic Leukemia, ALL respectively with overall prevalence of leukemias being more in adults.

Keywords: *bone marrow aspiration, anemia, leukemia.*

GJMR-C Classification : *NLMC Code: WH 380, WH 175*

Strictly as per the compliance and regulations of:

Spectrum of Disorders Diagnosed by Bone Marrow Aspiration

Dr. Aparajita Tomar [α], Dr. Vibha Trichal [σ] & Dr. RPS Chauhan [ρ]

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Keywords: bone marrow aspiration, anemia, leukemia.

I. Material and Method

Study area and design: The present study was done in the Department of pathology, Gandhi Medical College and associated Hamidia hospital, Bhopal M.P. A total of 135 consecutive prospective cases were studied during a span of one year.

Ethical consideration: Bone marrow aspiration was done under all aseptic precautions and samples were processed according to the established laboratory protocol before generating final report to the patient. Informed consent regarding the procedure was taken prior to the aspiration. It was told to the patients that the information shared by them and the results thereafter will be used for medical research.

Patient's Selection criteria: Our study included all the patients admitted in Hamidia hospital with a clinical suspicion of hematological disorder and demonstrating some abnormality in the peripheral blood smears. OPD patients on clinical suspicion of a hematological disorder by the consultant incharge were also included in the study group after obtaining the detailed history, clinical examination and all relevant investigations. Patients with highly increased bleeding time and clotting time were deterred.

II. Procedure

a) Bone Marrow Aspiration

Patient and his attendants were told about the entire procedure and a written consent was taken. Complete patient preparation (xylocaine sensitivity testing, cleaning and draping) was done prior to the bone marrow aspiration. The skin over the sternum was cleaned with 70% ethyl alcohol. The skin, subcutaneous tissue and the periosteum overlying the manubrium was infiltrated with 1-1.5 ml of 2% xylocaine. Two minutes were given to achieve the effect of anaesthesia. In case of small children and uncooperative patients, sedation with diazepam was used. The site of puncture of the manubrium was opposite to the second intercostal space and slightly to one side of the midline.

The guard on the aspiration needle was adjusted and with the boring movement, needle (salah needle) was passed perpendicularly into the cavity. After piercing the skin and the subcutaneous tissue when the needle point reached the periosteum, the needle was pushed with a boring motion into the cavity and the termination point was achieved when there was loss of resistance. Stilette was removed and a 10 ml dispovan syringe was attached to the needle to suck the marrow contents. Not more than 0.3 ml of marrow fluid was sucked in a single aspiration. Immediately, 6-8 good marrow smears were made and dried quickly with the help of a hair drier. Simultaneously, 2-3 peripheral blood smears were also made. The slides were numbered with a diamond pencil. Two marrow smears and one peripheral blood smear were taken for leishman staining while the rest of the unstained smears, after being fixed in methanol were wrapped in an aluminium foil and kept in a dry place for future use.

b) Leishman Staining of Slides

Bone marrow smears and the peripheral blood smear were placed on a staining rack and leishman stain was put drop by drop on the film so as to cover it completely. After 2 minutes, double the volume of

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buffered water was added and the two were mixed together with the help of a dropper. After 20 minutes, slides of peripheral smear were washed under the running tap water and the scum was drained off while bone marrow smears were washed after 30 minutes. Back side of the slides was wiped off with a clean and dry filter paper. The slides were kept in a vertical position to drain and dry. The slides were now ready for the microscopic examination.

c) Reporting of Bone Marrow Smears

Bone marrow as well as peripheral smears were first scanned with scanner (4X lens) followed by the examination under low power(10X), high power(40X) and oil immersion lenses(100X) respectively. The final reports were dispatched in the prescribed format only.

III. Observation and Discussion

Table no. 1 : Indications for Bone Marrow Examination

INDICATION		CASES
	No.	%
Anemia Under Evaluation	62	46.0
Pancytopenia Under evaluation	28	20.7
Suspected Leukemia	14	10.4
Thrombocytopenia	12	8.9
Hepatosplenomegaly Under evaluation	04	3.0
Pyrexia Under Evaluation	02	1.5
Others	13	10.0
Total	135	100.0

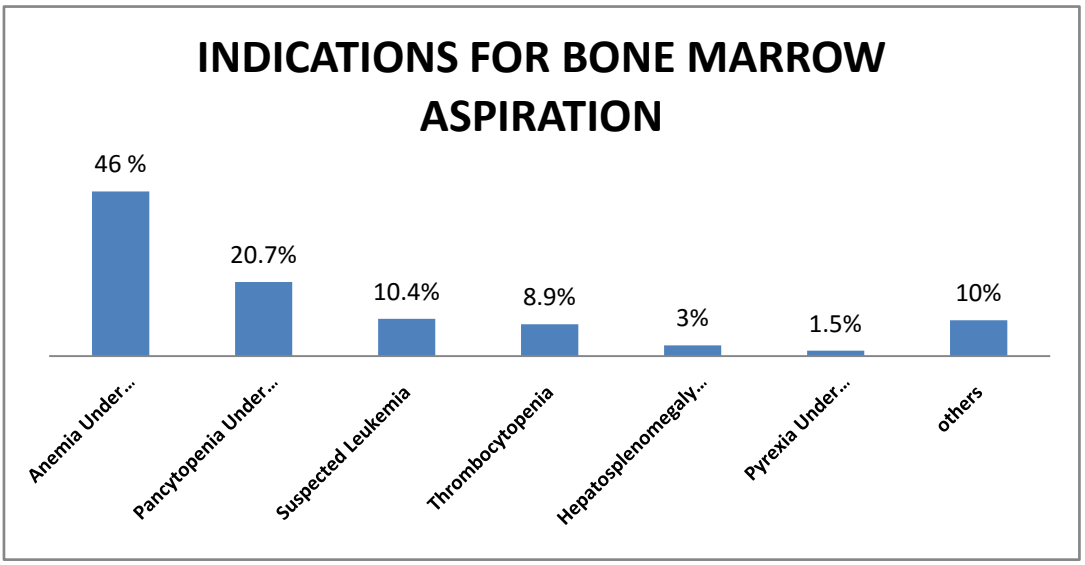


Table no. 2 : Spectrum of Disorders

S.No	Disorder	Total	Percentage (%)
1	Megaloblastic Anemia	59	43.7
2	Dimorphic Anemia	18	13.3
3	Acute Myeloid Leukemia	13	9.6
4	Idiopathic Thrombocytopenic Purpura	13	9.6
5	Hypoplastic Marrow	11	8.1
6	Acute Lymphoblastic Leukemia	09	6.6
7	Plasma Cell Disorder	03	2.2
8	Myeloproliferative Disorder	03	2.2
9	Lymphoproliferative Disorder	02	1.5
10	Chronic Lymphocytic Leukemia	01	0.74
11	Myelodysplastic Syndrome	01	0.74
12	Leishmaniasis	01	0.74
13	Hypersplenism	01	0.74
Total		135	100.0

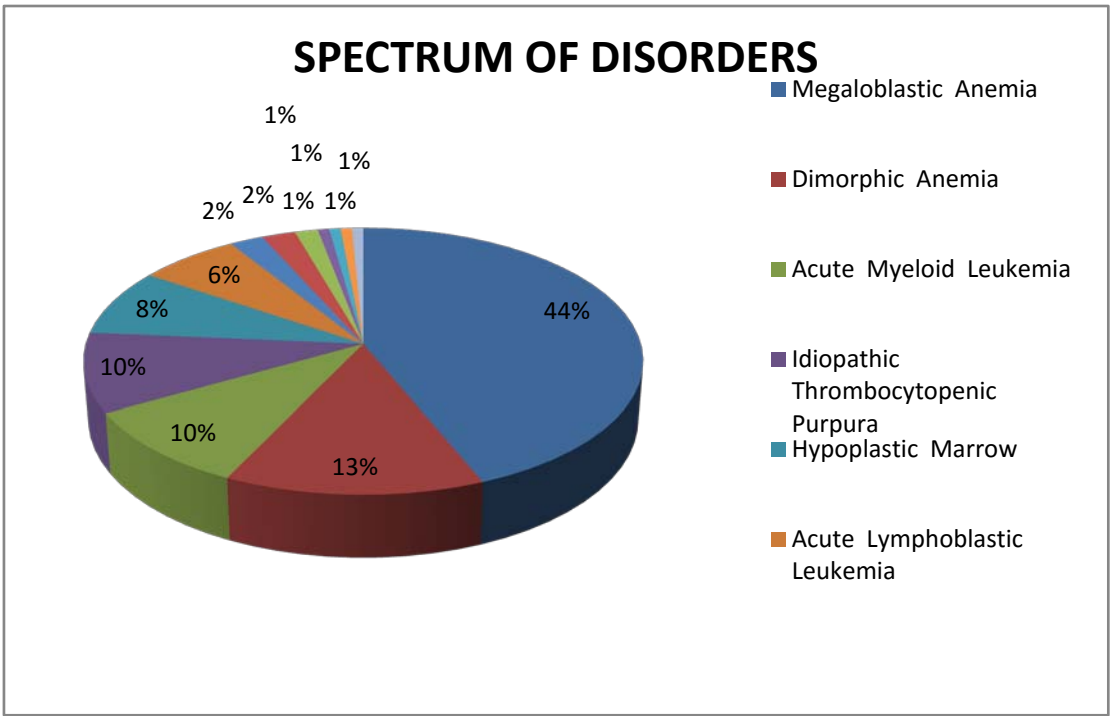


Table no. 3 : Percentage of Cases in Each Age Group

Age (Yrs)	Percentage
0-20	41.5
21-40	33.3
41-60	22.2
>60	3.0

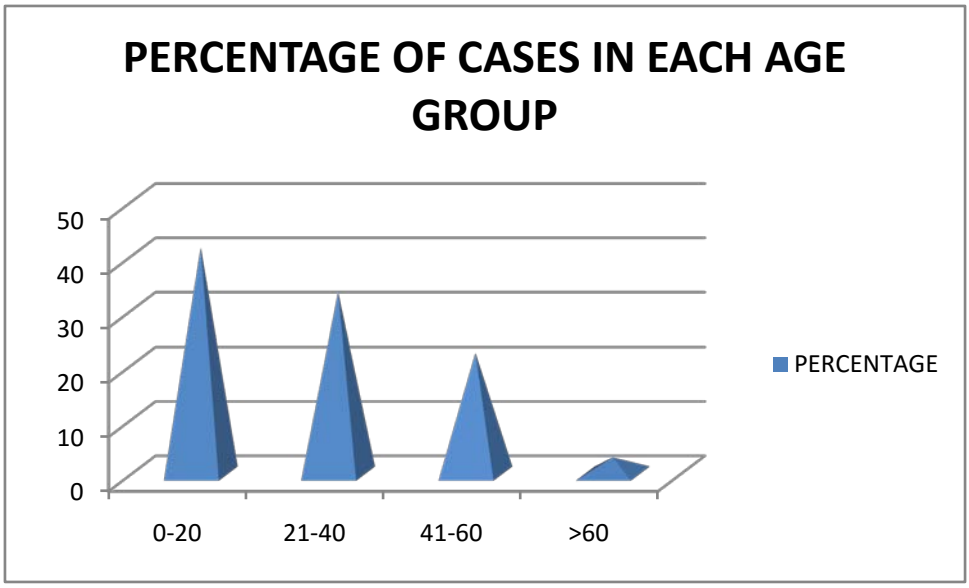
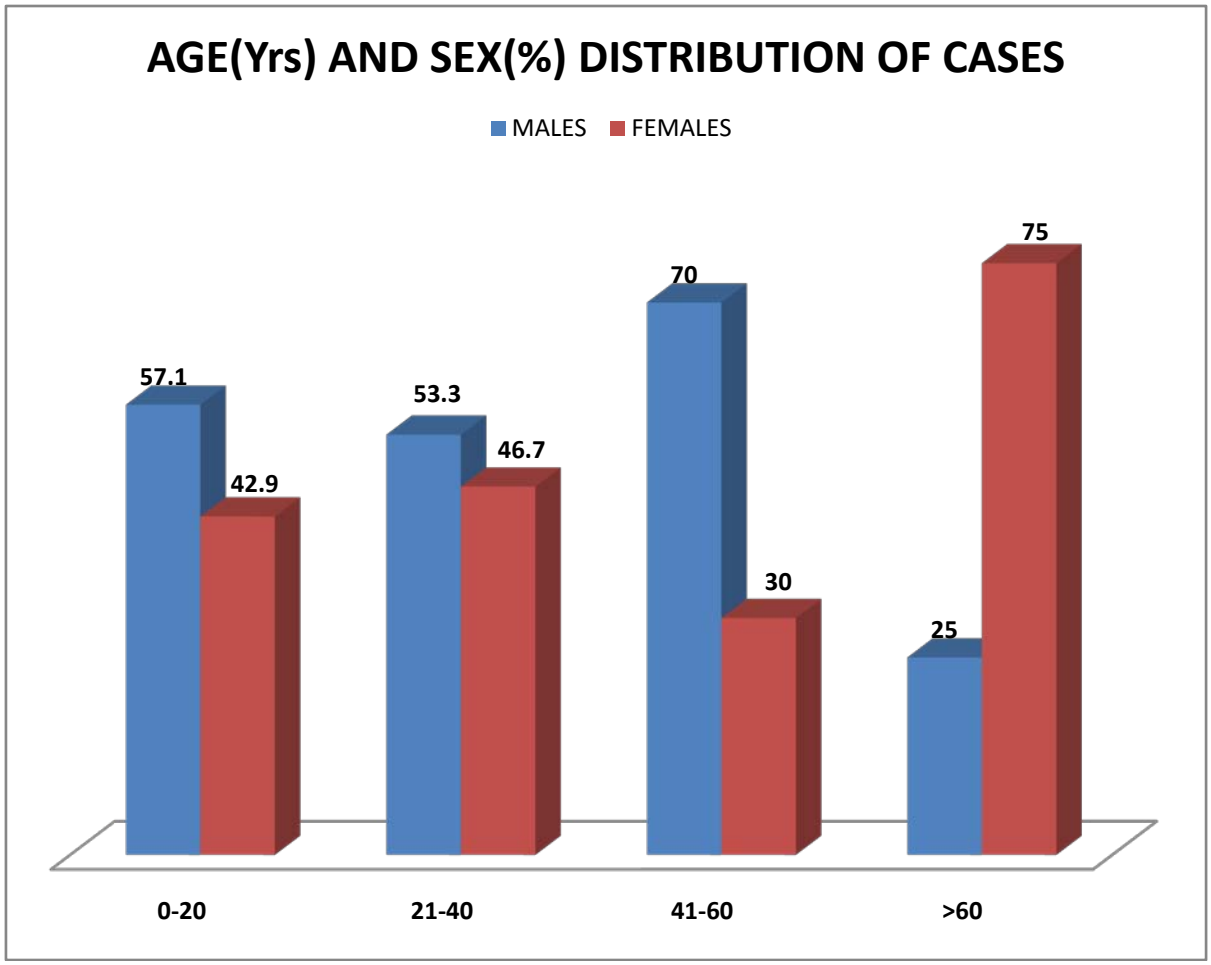


Table no. 4 : Age and Sex Distribution of Cases

Age (Yrs)	Males (%)	Females (%)
0-20	57.1	42.9
21-40	53.3	46.7
41-60	70	30
>60	25	75



IV. Conclusion

In this study, we found that on bone marrow aspiration the most frequently diagnosed haematological disorders[1] are Anemias[9]. Amongst the anemias, the commonest one are the Megaloblastic anemias[4,6,10] and those showing Dimorphic blood picture. Acute Leukemias[2,3,5,7,8] occupy the second position in the list including the Acute Myeloid Leukemias and Acute Lymphoblastic Leukemias with overall prevalence of leukemias being more in adults as compared to children. Hematological disorders are more common during childhood period and in the early adulthood. Commonest Leukemia in adults is Acute Myeloid Leukemia. The most common clinical presentation of Acute Leukemias is Pallor and Fever while Anemias present clinically with Pallor and Fatigue.

V. Acknowledgement

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- 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%.

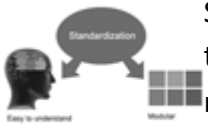
Once FARSM title is accorded, the Fellow is authorized to organize a symposium/seminar/conference on behalf of Global Journal Incorporation (USA). The Fellow can also participate in conference/seminar/symposium organized by another institution as representative of Global Journal. In both the cases, it 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 addres 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 you 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. Afterbecoming 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 benefitscan 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 willbe 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 MARSM 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 MARSM, 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 :

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- 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 conveninet , 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.

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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
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- 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

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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).

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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.

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Please mention proper reference and appropriate acknowledgements wherever expected.

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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 briefness.

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 × 10-3 m3, or 4 mm somewhat than 4 × 10-3 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.

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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 though 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 briefness. 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 a 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 conceptual 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.

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 perceptive 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.

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Topics	Grades		
	A-B	**C-D**	**E-F**
Abstract	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
Introduction	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
Methods and Procedures	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
Result	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
Discussion	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
References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

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