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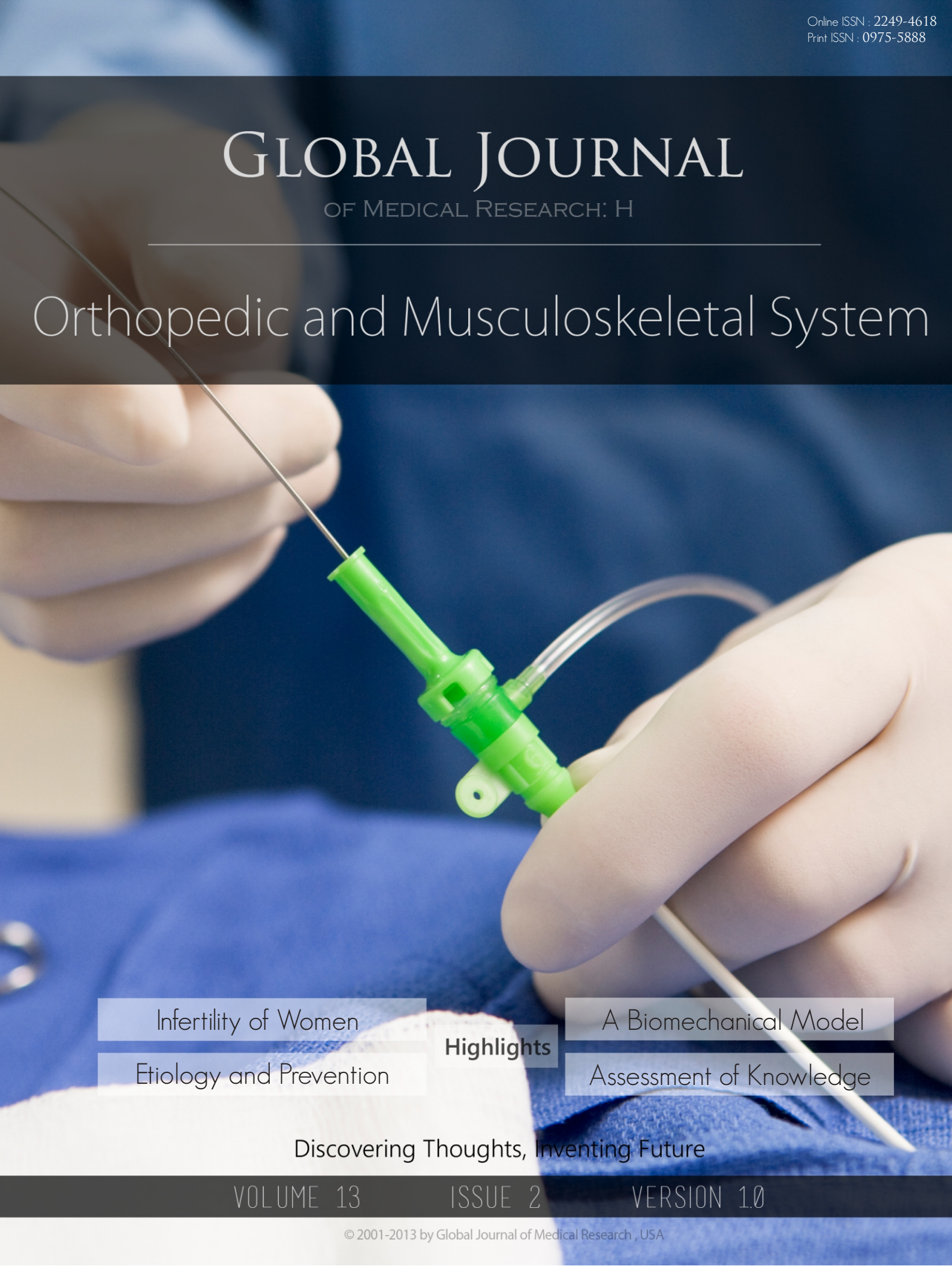

Infertility of Women

Etiology and Prevention

Highlights

A Biomechanical Model

Assessment of Knowledge

Discovering Thoughts, Inventing Future

VOLUME 13 ISSUE 2 VERSION 1.0

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Oxidative Stress in Primary Infertility of Women

By Majid K. Hussain, Hamza J. Mohammed, Basima S. Al- Ghazali & Mazin Thamir Abdul Hasan

University of Kufa College of Medicine

Abstract - The current study was designed to investigate the changes of oxidative stress (OS) in primary infertility of females. To achieve the intended aim, 84 infertile women of ages 28.66 ± 6.29 years (mean ± SD) and 30 healthy fertile women of ages 30.3± 6.45 years (mean±SD) were enrolled. The levels of malondialdehyde (MDA), catalase (CAT) and glutathione-S-transferase (GST) were determined by spectrophotometric methods. Serum follicule stimulating hormone (FSH) and luteinizing hormone (LH) levels were measured by an enzyme linked fluorescent assay (ELFA). The results indicated a significant ($p<0.001$) increase of MDA concentration and significant ($p<0.001$) decreases of CAT and GST activities in the infertile women when compared with those of the control group. The linear regression analysis demonstrated significant ($r = 0.27, p<0.05$) positive correlation for MDA levels and significant negative correlations for CAT ($r = - 0.24$, $p<0.05$) and GST levels ($r = - 0.26, p<0.05$) with the age of infertile women.

Changes of oxidative stress was observed to be dependent on the body mass index (BMI) and the duration of infertility of the enrolled women. The changes of MDA, CAT and GST levels seem to be independent on etiology of infertility and the menstruation pattern. The2linear regression analysis revealed significant ($r = 0.28$, $p<0.05$) positive correlation for MDA levels with the FSH concentration and significant($r = - 0.29$, $p<0.05$) negative correlation with the LH concentration.CAT exhibited significant ($r = 0.30$, $p<0.05$) positive correlation with the FSH concentration, while GST activity demonstrated significant($r = 0.24$, $p<0.05$) positive correlation with the LH concentration.

These results suggest that oxidative stress is involved in the path ophysiology of primary infertility in females, in particular through the directing of gonadotrophin changes in these patients.

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Oxidative Stress in Primary Infertility of Women

Majid K. Hussain [α], Hamza J. Mohammed [σ], Basima S. Al- Ghazali [ρ] & Mazin Thamir Abdul Hasan[ω]

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I. Introduction

Oxidative stress (OS) is a common condition caused by biological systems in aerobic conditions such that antioxidants cannot scavenge the reactive oxygen species (ROS). This causes an excessive generation of ROS, which damages cells, tissues, and organs (1). Evidence suggests that OS induced by ROS such as superoxide anion ($O2^{\bullet-}$), hydroxyl radicals ($OH^{\bullet}$) and a range of lipid peroxyl radicals produced in vascular cells is involved in the pathogenesis of a wide range of diseases of there productive system such as endometriosis and infection (2).

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OS impacts fertilization and can further induce apoptosis, resulting in embryo fragmentation, implantation failure, or abortion. In the fallopian tubes, OS may induce damaging effects in an embryo. The endometrium, which facilitates embryo implantation and development, can become defective when the female reproductive tract experiences an ROS–antioxidant imbalance (3). OS may hinder the support required for the continuation of a pregnancy by causing luteal regression and insufficient luteal hormone levels (4). Several other known causes of infertility, such as endometriosis, hydrosalpinx, polycystic ovarian disease, unexplained infertility, and recurrent pregnancy loss (RPL) may be attributed to O in the environment (5).3

OS induces infertility in women through a varietyof mechanisms. Ovarian follicles experiencing OS can lead to direct damage to oocytes. Oocytes and spermatozoa can also experience direct damage, which can lead to impaired fertilization due to an environment of OS in the peritoneal cavity. Even when fertilization occurs, apoptosis leading to embryo fragmentation, implantation failure, abortion, or congenital abnormalities in offspring can occur. OS in the fallopian tubes can cause direct adverse effects on the embryo defects in the endometrium, which normally supports the embryo and its development, can arise when there is an ROS antioxidant imbalance in the female reproductive tract (3).ROS-antioxidant imbalance is also implicated in luteal regression and insufficient luteal hormonal support for the continuation of a pregnancy(4). OS has been implicated in many other causes of infertility, such asendo metriosis, hydrosalpinx, polycystic ovarian disease, unexplained infertility, and recurrent pregnancy loss (6).

II. Patients And The Control Groups

A total of eighty four women with primary infertility of age's 18-41years with a mean ± SD 28.66 ±6.29 years attending the fertility centerin the AL-Sadder Teaching Hospital in Najaf city fromOctober2008 to May 2009 were included in the study. To compare the results, thirty healthy age matched (mean ± SD 30.3±6.45 years) females with history of at least one child birth were also enrolled. Subjects suffered from diseases (hypertension, asthma and diabetes mellitus) interfere with the data obtained were excluded.

Disposable syringes and needles were used for blood collection. Venous blood samples, about 10 ml were collected from patients and healthy volunte erson day-2 of their menstrual cycle in tubes. After4allowing

the blood to clot at room temperature for 15 min, blood samples were centrifuged at 3000 xg for 15 min. Sera were separated and divided into five aliquot samples stored at _17C°, two for determination of the hormonal profile, the three others were used for estimation of oxidatives tress parameters.

III. Determination of Malondialdehyde, Catalase and Glutathione – S – Transferase Levels

The level of malondialdehyde was determined by modified procedure described by Guidet B. and Shah S.V. (7).

Catalase (CAT) activity was determined by the measurement of the decrease in the absorbance due to hydrogen peroxide (H2O2) consumption as described by Aebi H. (8).

GST activity was analyzed by measuring the conjugation of glutathione (GSH) and 1-chloro2, 4dinitrobenzene (CDNB) as asubstrate, as described by Habig WH.et al (9)

IV. Determination of Serum FSH and LH Concentration

VIDAS® FSH and LH are an automated quantitative test for use on the VIDAS instruments for the determination of human folliculestimulating hormone (FSH) and human luteinizing hormone (LH), inhuman serum or plasma using the Enzyme Linked Fluorescent Assay(ELFA) technique.(10)

V. Results

a) Level of Malondialdehyde, Catalase and Glutathione -STransferasein Infertile Women and the Control Group

Malondialdehyde (MDA), catalase (CAT) and glutathione-Stransferasefemales with primary infertility and thirty healthy women. The results were analyzed using student's-test. There were significant ($p<0.001$) decreases in CAT and GST activity level sins era of females with primary infertility when compared with those of the control group. In contrast, MDA levels were found to increase significantly ($p<0.001$) in females with primary infertility when compared with those of the control group (Table 3.1).

Table 3.1 : Levels of Malondialdehyde (MDA), Catalase (CAT) and Glutathione -S -Transferase (GST) in Infertile Women and Control Group

Parameters	Subjects	NO.	Mean ± SD	Range	P-value
MDA (µM)	Control	30	1.74 ± 0.75	0.54 –3.10	
	Patients	84	4.12 ± 1.24	2.29 –8.08	<0.001
CAT (U/ml)	Control	30	6.82 ± 4.72	1.74 –22.42	
	Patients	84	4.5 ± 2.21	0.78 –9.68	<0.001
GST (U/L)	Control	30	1628.42 ± 284.86	1104.69 –2335.63	
	Patients	84	731.57 ± 190.90	284.06 –1136.25	<0.001

b) Relevance of Ages of Infertile Women with Malondialdehyde, Catalase and Glutathione –S-Transferase Levels

To verify the impact of age on MDA, CAT and GST values in infertile women, patients were categorized into 3 groups. Group A consisted of 29 patients of ages (18–25 years), group B consist of 34patients of ages (26– 33 years) and group C consist of 21 patients of ages (34–41 years).

The results indicated significant ($p<0.001$) elevation of MDA levels in the three groups of patients when compared with those of the control group. On the other hand, CAT and GST activities exhibited significant ($p<0.01$ and <0.001 respectively) decreases in the three groups of patients with respect to those of the control groups. The linear regression analysis demon strated significant ($r = 0.27$, $p<0.05$) positive correlation for MDA levels and significant negative correlations for CAT ($r = - 0.24$, $p<0.05$) and GST levels ($r = - 0.26$, $p<0.05$) with the age of in far tile women (Table 3.2, 3.3).

Table 3.2 : Levels of Malondialdehyde (MDA) , Catalase (CAT) and Glutathione -S- Transferase (GST) in Various age Related Groups of Infertile Women

Parameters	Group	NO.	Mean ± SD	Range	P-value
MDA (µM)	Control	30	1.74 ± 0.75	0.54 –3.10	
	18-25 y	29	3.85 ± 1.33	2.42 –8.08	<0.001
	26-33 y	34	4.0 ± 0.78	2.29 –6.06	<0.001
	34-41 y	21	4.74 ± 1.42	2.69 –7.81	<0.001
CAT (U/ml)	Control	30	6.82 ± 4.72	1.74 –22.42	
	18-25 y	29	4.54 ± 2.52	1.57 –9.68	<0.01
	26-33 y	34	4.97 ± 2.12	0.92 –8.59	<0.01
	34-41 y	21	3.64 ± 1.62	0.78 –6.48	<0.01
GST (U/L)	Control	30	1628.42 ± 284.86	1104.69 –2335.63	
	18-25 y	29	733.56 ± 222.33	284.06 –1136.25	<0.001
	26-33 y	34	746.89 ± 166.82	441.88 –1073.13	<0.001
	34-41 y	21	650.79 ± 167.75	347.19 –883.75	<0.001

Table 3.3 : Correlation Factors of Serum Malondialdehyde (MDA), Catalase(CAT) and Glutathione-S-Transferase (GST) Levels with Age in Infertile Women

Parameters	**r**	**P-value**
MDA	**0.27**	**<0.05**
CAT	**– 0.24**	**<0.05**
GST	**– 0.26**	**<0.05**

c) Influence of Body Mass Index on Malondialdehyde, Catalase and Glutathione – S Transferase Levels in Infertile Women

To understand the effect of body mass index (BMI) on the levels of serum MDA, CAT and GST in female infertility, patients were categorized into three groups. Group 1 consisted of 26 patients who had BMI values ≤ 25 Kg/m2 (normal females). Group 2 comprised 28patients who had BMI > 25–30 Kg/m2 (overweight) and Group 3comprised 30 patients who had BMI >30 Kg/m2 (obese).

The results pointed out a significant ($p<0.001$) increase of MDA and significant decreases of CAT ($p<0.01$) and GST ($p<0.001$) levels in the three groups of infertile women when compared with the control group (Table 3.4). The linear regression analysis stated significant ($r = 0.23$, $p<0.05$) positive correlation for MDA and significant ($r = – 0.26$, $p<0.05$) negative correlation for CAT levels with BMI values in the infertile women (Table 3.5).

Table 3.4 : Influenc of Body Mass Index (BMI) on Malondialdehyde (MDA), Catalase(CAT) and Glutathione -S- Transferase (GST) Levels in Infertile Women

Parameters	Group	NO.	Mean ± SD	Range	P-value
MDA (µM)	Control	30	1.74 ± 0.75	0.54 –3.10	
	≤25	26	3.77 ± 1.04	2.29 –6.59	<0.001
	>25-30	28	4.17 ± 1.33	2.56 –8.08	<0.001
	>30	30	4.42 ± 1.29	2.42 –7.81	<0.001
CAT (U/ml)	Control	30	6.82 ± 4.72	1.74 –22.42	
	≤25	26	5.34 ± 2.32	0.92 –9.68	<0.01
	>25-30	28	4.41 ± 2.09	0.78 –8.59	<0.01
	>30	30	3.86 ± 2.06	1.26 –8.59	<0.01
GST (U/L)	Control	30	1628.42 ± 284.86	1104.69 –2335.63	
	≤25	26	768.43 ± 208.21	441.88 –1136.25	<0.001
	>25-30	28	729.32 ± 185.9	441.88 –1073.13	<0.001
	>30	30	697.53 ± 183.73	284.06 –1010.00	<0.001

Table 3.5 : Correlation Factors of Serum Malondialdehyde (MDA) , Catalase (CAT) and Glutathione-S-Transferase (GST) Levels with Body Mass Index (BMI) in Infertile women

Parameters	r	P-value
MDA	**0.23**	**<0.05**
CAT	**– 0.26**	**<0.05**
GST	**– 0.12**	**NS**

d) Relevance of Etiology of Infertility to Malondialdehyde, Catalase and Glutathione -S Transferase Levels in Infertile Women

To verify the impact of infertility causes on MDA,CAT and GSTvalues in infertile women, patients were categorized into 3 groups. Group A consisted of 37 females of ovulatory factor, group B consist of 14females of tubal and uterine factors and group C consist of 33 females of unexplained factor. As shown in table 3.6, the three groups of infertile women showed a significant ($p<0.001$) elevation of MDA and significant decreases of CAT ($p<0.05$) and GST ($p<0.001$) levels when compared with those of the control group.

Table 3.6 : Levels of Malondialdehyde(MDA), Catalase (CAT) and Glutathione-S- Transferase (GST) in Infertile Women of Various Etiologies

Parameters	Group	NO.	Mean ± SD	Range	P-value
MDA (µM)	Control	30	1.74 ± 0.75	0.54 –3.10	
	OF	37	4.23 ± 1.16	2.42 –7.81	<0.001
	TUF	14	4.20 ± 1.41	2.56 –7.54	<0.001
	UF	33	3.93 ± 1.28	2.29 –8.08	<0.001
CAT (U/ml)	Control	30	6.82 ± 4.72	1.74 –22.42	
	OF	37	4.79 ± 2.35	0.78 –9.68	<0.05
	TUF	14	4.41 ± 2.09	1.59 –8.59	<0.05
GST (U/L)	UF	33	4.43 ± 2.14	0.92 –8.59	<0.05
	Control	30	1628.42 ± 284.86	1104.69 –2335.63	
	OF	37	751.53 ± 191.96	441.88 –1136.25	<0.001
	TUF	14	678.59 ± 215.41	284.06 –1136.25	<0.001
	UF	33	737.41 ± 201.30	284.06 –1041.56	<0.001

O F: Ovulatory Factor
TUF: Tubal and Uterine Factor
U F: Unexplained Factor

e) The Dependency of Malondialdehyde, Catalase and Glutathione –S-Transferase Levels on the Duration of Infertility in Infertile Women

To demonstrate the influence of duration of infertility on MDA, CAT and GST values in infertile women, the linear regression analysis was used to evaluate the data. Significant negative correlations were obtained for CAT ($r = – 0.23$, $p<0.05$) and GST ($r = – 0.27$, $p<0.05$) levels with the duration of infertility. MDA levels stated significant($r = 0.30$, $p<0.01$) positive correlation with duration of infertility (Table3.7).

Table 3.7 : Correlation Factors of Serum Malondialdehyde (MDA), Catalase (CAT), Glutathione-S-Transferase (GST) Levels with the Duration of Infertility in Infertile Women

Parameters	r	P-value
MDA	**0.30**	**<0.01**
CAT	**– 0.23**	**<0.05**
GST	**– 0.27**	**<0.05**

f) The Impact of Menstruation Pattern on the Levels of Malondialdehyde, Catalase and Glutathione -S - Transferase in Infertile Women

To perceive the impact of menstruation pattern on thelevels of MDA, CAT and GST in infertile women, patients were categorized into 2groups. Those of regular cycle were 45 patients and those of irregularcycle were 39 patients. Their data were compared with the values of the control group by using the ANOVA analysis. A significant($p<0,001$)increase of MDA levels andsignificant decreases for CAT ($p<0.01$) andGST ($p<0.001$) activities were observed in the two groupsofpatientswhen compared with those of control group (Table 3.8).

Levels of Malondialdehyde(MDA), Catalase (CAT Table) and Glutathione –S-Transferase (GST) in Infertile Women with Regular and Irregular Cycle

Parameters	Group	NO.	Mean ± SD	Range	P-value
MDA (µM)	Control	30	1.74 ± 0.75	0.54 –3.10	
	RC	45	4.29 ± 1.31	2.29 –8.08	<0.001
	IRC	39	3.93 ±1.14	2.42 –6.99	<0.001
CAT (U/ml)	Control	30	6.82 ± 4.72	1.74 –22.42	
	RC	45	4.32 ± 2.12	0.78 –8.59	<0.01
	IRC	39	4.73 ± 2.24	1.26 –9.68	<0.01
GST (U/L)	Control	30	1628.42 ± 284.86	1104.69 –2335.63	
	RC	45	740.67 ± 177.99	347.19 –1073.13	<0.001
	IRC	39	713.80 ± 207.93	284.06 –1136.25	<0.001

RC: Regular Cycle
IRC: Irregular Cycle

g) Correlations of FSH and LH Concentrations with Malondialdehyde, Catalase and Glutathion STransferase Levels in Infertile Women

To verify the relevance of FSH and LH concentrations to the MDA, CAT and GST levels in infertile women, the linear regression analysis was used to evaluate the data. The results indicated significant ($r = 0.28$, $p<0.05$) positive correlation for MDA levels with the FSH concentrations and significant ($r = -0.29$, $p<0.05$) negative correlation with LH concentrations. CAT showed significant ($r = 0.30$, $p<0.05$) positive correlation with FSH concentrations. GST activity exhibited significant ($r = 0.24$, $p<0.05$) positive correlation with LH levels in infertile women (Table 3.9).

Table 3.9 : Correlations of Serum Malondialdehyde (MDA),Catalase (CAT) and Glutathione-S-Transferase (GST) with FSH and LH Levels in Infertile Women

Parameters		**r**	**p-value**
MDA	**FSH**	**0.28**	**<0.05**
	LH	**– 0.29**	**<0.05**
CAT	**FSH**	**0.30**	**<0.01**
	LH	**0.02**	**NS**
GST	**FSH**	**– 0.07**	**NS**
	LH	**0.24**	**<0.05**

VI. Discussion

Successful pregnancy results from an interaction between myriad physiological processes in both men and women. Any disruption to this interactive system, whether in a man or woman, can result in an inability to have a biological child called infertility (4). ROS exert their cytotoxic effects by causing per oxidation of membrane phospholipids, which results in an increase in membrane permeability, loss of membrane integrity, enzyme inactivation, structural damage to DNA and cell death (11). Oxidative stress can have detrimental effects on female fertility by affecting ovulation, fertilization, embryo development, and implantation (4,12). Thus, OS is considered a cause of female infertility. This is particularly clear in cases of

endometriosis (13). It is suggested that OS is caused by ROS overproduction rather than antioxidant depletion (14).

The results indicate that infertile women have increased serum level of MDA and decreased serum levels of GST and CAT as compared to fertile women. They are in agreement with previous reports.

Veena Bhaskar S et al have found significantly higher concentration of MDA in serum of infertile women than in fertile women (15). Savita Setal have shown significantly high plasma levels of MDA in infertile women when compared to parous women and this is noticed from there ductions of levels of eicosapentaenoic acid (EPA), and more so indocosahexaenoic acid (DHA), they suggested that these changes are consequence of increased oxidative stress that mediate lipid per oxidation Product , i.e. MDA (16).

In the present study, MDA levels were found to be elevated with advancing age in infertile women suggesting raised lipid per oxidation in these patients. The rise seems to be developed as a consequence of 15declined production of antioxidant enzymes. Such decline was apparent for the activities of CAT and GST in association with the elevation of MDA levels as ages of the patients were advanced. Thus, aging could be considered as a risk factor for elevation of oxidative stress, and impaired fertility in aged females involves the imbalance in there do x potentials of these patients.

The present results were in a agreement with previous works in which follicular fluid aspirates from twelve young women aged 27–32years and twelve older women aged 39–45 years undergoing IVF treatment were analysed for the activity and protein expression of catalase, SOD, G-PX, GST and G-Red. The specificactivity of catalasewas _60% lower in the older women when compared with the youngerwomen. GST was also lower in the older women with respect to the younger patients (17). It is well known that germ cell membranes are particularly vulnerable to be attacked by ROS, being very rich in polyunsaturated fatty acids (18).

The current results illustrated elevated lipid peroxidation in association with depleted cytoprotective enzyme activity, i.e., CAT and GST, as weight of infertile women was raised. The reason of the dysregulation of the redoxe system may due to increased levels of adipose NADPH oxidase activity which raise the production of ROS in accumulated fat (19). This hypothesis was proved by experimental obeserats, in which rised lipid peroxidation has been observed (20).

The link between obesity and oxidative stress has been suggested in some studies. A good correlation between BMI and oxidative stress has been reported, indicating obesity as an independent risk factor for plasma lipid peroxidation (21,22). Obesity may induce systemic oxidative stress, which is, in turn, the underlying cause of selective increase in ROS, 16 dysregulation of adipocytokines and development of metabolic syndrome (23).

In the present investigation, the elevation of lipid peroxidation and the depletion of antioxidant enzymes seems to vary similarly in the infertile women regardless to the etiology of infertility. The consequences appear to be equal precipitation in the pathophysiology of there productive systems in infertile patients. These evidences suggest that oxidative stress is an independent etiologic factor in female infertility. Such independency may relate to the activation of macrophages which are a source of generation of ROS (24).

In the present study, raised lipid peroxidation and decreased antioxidant enzyme activities are evident as the duration of infertility was prolonged in the enrolled infertile women. The results suggest that prolonging of the duration of infertility exaggerate the implication of oxidative stress in the impairment of female infertility.

OS is involved in the modulation of cyclical changes in the endometrium. Altered SOD and ROS levels have been demonstrated in the endometrium during the late-secretory phase, just before menstruation. An elevated lipid peroxide concentration and decreased SOD concentrations have been reported in human endometrium in the latesecretory phase, and these changes may be responsible for the breakdown of the endometrium, implicating the involvement of OSin the process of menstruation (25). The expression of endothelial nitric oxide synthase(NOS) and inducible NOS have been demonstrated in the humanendometrium and the endometrial vessels (26,27). Endothelial NOS is also thought to bring about changes that prepare the ndometrium for im plantation (25).

FSH was found to be positively correlated with MDA and CAT levels, suggesting oxidative effect in there productive system of the infertile women. In contrast, LH was ascertained to be correlated negatively with MDA level and positively with GST activity, suggesting antioxidative, i.e. protective role in the reproductive system of these patients. The oxidative effect of FSH may be induced through the action of progesterone, since this hormone has been documented to elicit oxidative stress in rats (28). Unfortunately progesterone and estradiolconcentrations could not be measured in the studied patients due to technical limitations. The protective role of LH may be produced through the action of estradiol, the beneficial function of estradiol has been elucidated in rats (28).

Elevated endogenous LH concentration seems to be a powerful protective enzyme against oxidative stress, since it is correlated negatively with MDA level and positively with GST activity. These observations are essentially related to vitamin E. It was demonstrated that LH administration is associated with accumulation of ovarian vitamin E (29). The mechanism of LH stimulation of vitamin E accumulation is not clear, but may be due

to increased lipoprotein accumulation by the corpusluteum. Vitamin E is transported by lipoproteins inplasma (30). LH isknown to stimulate the accumulation of lipoproteins by the rat corpusluteum (31,32). Hence, the accumulation of lipoproteins, may be the reason of elevated vitamin E and consequently the antioxidative function of LH in the reproductive tract.

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Continuous Movement of Stems and Cement in both Polished and Rough Tapered Femoral Stems in a Biomechanical Model

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Abstract - Polished tapered stems used in hip replacement subside into bone cement without loosening. However, subsidence of rough stems leads to loosening of the prosthesis. There have been no reports on continuous movement of cement and stem. We believed that the relation of stem subsidence to cement differed by stem surface finish. To determine whether this was the case, we compared the pattern of movement of stem and cement in both polished and rough stems in a biomechanical model. Methods Two sizes of polished stems and of roughprocessed stems (rough stems) were fixed into composite femurs with different cement thickness, and a 1-Hz dynamic load was applied for a total of 2 million cycles. An 8-hour no load period was set after every 16 hours of load. Continuous stem motion was measured by a digital displacement gauge, and continuous cement motion was recorded by a strain gauge on an aluminum plate inserted in the cement.

All stems subsided downward during the load periods but rose during the no load periods in a 1-day cycle, and a great deal of subsidence were seen by 200,000 cycles– after loading. For polished stems, more than 85% of the total subsidence occurred by 1 million loading cycles, and subsidence rates converged after that. Stem subsidence was not accompanied with cement subsidence. For rough stems, however, subsidence progressed linearly and was accompanied by cement subsidence.The convergence of stem subsidence and lack of synchronization with cement subsidence in polished stems indicated taper slip into cement without loosening. Early subsidence in rough stems leads to progressive subsidence.

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Abstract - Polished tapered stems used in hip replacement subside into bone cement without loosening. However, subsidence of rough stems leads to loosening of the prosthesis. There have been no reports on continuous movement of cement and stem. We believed that the relation of stem subsidence to cement differed by stem surface finish. To determine whether this was the case, we compared the pattern of movement of stem and cement in both polished and rough stems in a biomechanical model.

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I. Introduction

According to fixation theory, femoral stems for cemented hip replacements are of two types: loaded tapered stems and composite-beam stems [9, 14]. In composite-beam stems, tight bonding of the stem and cement is necessary to achieve long-term stem stability. Stem surfaces are processed to be either matte or rough, with or without a pre-coating of polymethylmethacrylate. In contrast, loaded tapered stems slip in cement, and the taper operates like a wedge to transfer the weight load to the cement and bone.

Therefore, these stems are polished tapers without collars [9]. Lee et al. [12] noted that a polished tapered stem does not cause shear stress but that compressive force and hoop stress will occur because of taper slip at the stem–cement interface. In the rough stem, micromotion at the stem–cement interface does not occur; instead, the risk of subsidence exists when weak bonding at the cement–bone interface is broken by overload.

Researchers have demonstrated, using radiostereometric analysis, that polished tapered stems slip in vivo in cement [1, 2, 15, 16], and others have detected slight stem subsidence and retroversion even in composite-beam stems [1, 2, 16].

Most subsidence of polished tapered stems has been seen in the early postoperative phase, with some detected later in the clinical setting [15, 16]. However, there have been no reports of continuous observation of stem and cement movement even in experimental studies. Therefore, we conducted a study to observe consecutive subsidence for polished tapered stems, rough stems, and cement around stems in an ex vivo cemented total hip arthroplasty model designed to mimic the conditions of walking throughout the human life cycle.

II. Materials and Methods

a) Cemented Stem Model

For the polished stem, we used a collarless polished tapered stem (CPT stem, Zimmer, Warsaw, IN, USA) with a surface roughness of ≤0.1 μm and tapered in the coronal and sagittal planes. For the rough stem, we used a CPT stem processed to a rough finish with a roughness of 5.291 μm (SD, 1.100 μm) (Fig. 1). A centralizer dedicated to the CPT stem was attached to the stem tip. Two sizes (sizes 2 and 3) were used both for the polished stems and for the rough stems in this experiment. The proximal transverse diameter and offset for size 3 were larger than those for size 2 by 2.5 mm

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and 1 mm, respectively. A size 3 rasp was used for the preparation of implantation in all femurs.

Therefore, the cement mantle for the experiment using size 2 stems was thicker than that using size 3 stems. The experiment was performed four times: once each for the size 2 polished stem and the size 3 polished stem and once each for the size 2 rough stem and the size 3 rough stem.

We used composite femurs (composite femur 3303, Pacific Research Laboratories, Vashon, WA, USA) similar in shape, mechanical characteristics, and material to those of human femurs for this study [5, 8]. For stem insertion, we cut the composite femur neck obliquely at 20 mm distal to the greater trochanter top and cut the distal part of the femur at 230 mm from the greater trochanter top before its attachment to the fixator.

We created 16 holes, 8 on the proximal side and 8 on the distal side of the composite femur, each 6 mm in diameter, for tight fixation of composite bone to the fixator through rods. After the holes were created, the composite femurs were immersed in blended vegetable oil for 24 hours to simulate an environment of bone humidity. It has been reported that cement creep differs by both temperature and humidity [3].

Therefore, we used vegetable oil to allow adequate cement movement in this study [11]. An aluminum plate for observation of cement subsidence was inserted through one of the holes that we had created in the posterior side of the femur at 22 mm distal to the cutting plane of the femoral neck. The other 15 holes were used for fixation of the composite femur by inserting rods from outside a fixator to the cement–bone interface.

We used a fixator for securing the composite femur using machine-structural-use carbon steel and epoxy resin [11]. The exterior of the fixator was made of carbon steel; the interior's epoxy resin was formed to the contours of the composite femur (Fig. 2A). A composite femur was fixed completely with surrounding epoxy resin and 15 rods inserted from the exterior of the fixator to the cement–bone interface through the epoxy resin (Fig. 2B). The bottom of the fixator was also attached to the basal table of the fatigue tester. We injected vacuum-mixed cement (Osteobond; Zimmer, Warsaw, IN, USA) with a cement gun into the composite femur. The medullary canal was plugged distally, and the stem was fixed into pressurized cement using two thumbs. This composite femur had both a cortex and cancellous bone, and a stem was fixed into the cancellous bone with cement after rasping. After we implanted the stem in the composite femur, we kept the temperature of the femur and cement at 37°C by using a heater (G6A92 240V250W, Takigen Mfg., Tokyo, Japan) and attaching a temperature sensor (T-35 thermocouple, Takigen) to the epoxy resin.

b) Load

A dynamic sine-wave load of 3,000 N was applied 2 million times at a frequency of 1 119 Hz to the metal head, which was fixed to the stem at 15° in the coronal plane [4] using a hydraulic controlled fatigue tester (type 1331, Instron Japan, Kanagawa, Japan). In actual practice, the fixator was inclined 15° horizontally in the coronal plane and the load was applied vertically. The 3,000-N load is equivalent to the load applied to the hip joint when a person weighing 70 kg stands on one leg, and 2 million applications of load correspond to 2 years of walking [6, 19].

The tester cannot perform complex motions such as walking; therefore, we tested only single-stance equivalent load in this study. Assuming sleep time, we provided a no-load period of 8 hours between 16-hour periods of load application. Therefore, 38 days were required for one composite femur experiment.

c) Data Measurement

We measured stem subsidence and strain on the aluminum plate inserted in cement. CPT stems have a screw hole on the upper lateral portion. For stem subsidence, a digital displacement gauge (5-mm DTH-A-5, Kyowa Electronic Instruments, Tokyo, Japan) was applied to the attachment screwed into the screw hole of the stem, and stem motion was recorded as the digital data of displacement, with a downward direction being expressed as a positive value (Fig. 2C). Because of complete fixation of the composite femur with a fixator, the data from the digital displacement gauge was considered to represent stem subsidence. The displacement gauge was able to measure upward-direction values because the gauge could move up and down smoothly.

We measured stem subsidence over time; the data were automatically entered into a personal computer via software for measurement collection and analysis (sensor interface PCD-300A, Kyowa Electronic Instruments). The load and no-load periods in a day were classified into early, middle, and late phase at each period. In each phase, 10,000 data sets corresponding to approximately 8 minutes were stored as one file per 30 minutes; we collected a total of 912 files. The obtained data were corrected and converted to distance units. Stem subsidence in each period was defined as the mean of the collected values in the two consecutive files (20,000 data sets) after the start of each phase.

Before the cement hardened, we inserted a 1-mm-thick metal plate into the cement through the posterior-side hole in the composite femur. After the cement had hardened, we exchanged the metal plate for an aluminum plate with a strain gauge pasted onto it (Fig. 3). The deformity of the aluminum plate represented the longitudinal displacement of cement. The data from the strain gauge reflected cement

subsidence or force to the cement around the aluminum plate.

Continuous strain data were automatically recorded by a computer. Using lateral radiographs before loading, we confirmed that the aluminum plate was positioned in the cement and was not in contact with the femoral stem. Deformity of the aluminum plate was confirmed by radiographs obtained after the experiment.

III. Results

Subsidence in both sizes of polished stems was rapid by 200,000 loading cycles and then decreased slowly (Table 1, Fig. 4). The final amount of subsidence was 1.229 mm for the size-2 stem and 0.680 mm for the size-3 stem, respectively. By 1 million loading 163 cycles (early loading cycles), 85.8% and 92.5% of total subsidence had occurred for the size-2 stem and the size-3 stem, respectively.

Polished stems subsided during the load periods but rose during the no load periods in a 1-day cycle (Fig. 5). The average ratio of stem subsidence to stem rising in 1 day, determing by the equation

$$\frac{\text{stem rising}}{\text{stem subsidence}} \times 100\ (\%)$$

was 85.1% in the size-2 stem and 91.6% in the size-3 stem by the early loading cycles and was 96.3% in the size-2 stem and 97.2% in the size-3 stem at a point between 1 million and 2 million loading cycles (late loading cycles). The ratio for stem rising was greater in the late loading cycles of the experiment than in the early loading cycles, and significantly, stems returned to close to their original position before any subsidence ($P < 0.001$; unpaired t-test).

In both sizes of the rough stems, there was a great deal of subsidence early on in loading and then it progressed (Table 1, Fig. 4). The amount subsidence after 2 million loading cycles was 2.715 mm for the size-2 rough stem and 1.971 mm for the size-3 rough stem, respectively, and was greater than that for the polished stems. The amount of subsidence was 1.892 mm for the size-2 rough stem and 1.255 mm for the size-3 rough stem by early loading cycles and was 0.823 mm for the size-2 rough stem and 0.761 mm for the size-3 stem after that.

We analyzed the values only in the size-3 polished and rough stems for the strain of the aluminum plate. Because a setting error occurred in the strain gauges in the size-2 polished stems, making the difference between the data in those stems and the data in the size-2 rough stems much larger than the measurable range. The experiment revealed that there was less deformity of the aluminum plates in the size-3 polished stem than in the size-3 rough stem (Fig. 6A). For the polished stem, the strain of the aluminum plate was not synchronized with stem subsidence. but recovered sometimes independently of stem subsidence (Fig. 7A). Neither stem loosening nor cement cracking were seen in radiographs obtained after the experiment. This demonstrated that the polished tapered stems slipped into cement without cement subsidence.

In contrats the aluminum plate in size-3 rough bent stem was distally (Fig. 6B), and the strain of the plate was synchronized with stem subsidence in the stem (Fig. 7B). This stem subsidence was accompanied with cement subsidence. The aluminum plate in size-2 rough stems was also bent distally. However, the extent of debonding and loosening at the stem–cement interface could not be determined after the experiment in rough stems of either size. Therefore, rough stems failed at the cement–bone interface in the early stage of our experiment and were considered to represent models of loosening cemented stems.

IV. Discussion

Researchers have demonstrated, using radiostereometric analysis, that polished tapered stems slip in vivo into cement [1, 2, 15, 16]. However, it is difficult to observe stem slip continuously in vivo.

Continuous stem subsidence and strain on the aluminum plate inserted into cement were observed for this study. Polished tapered stems subsided, yet the aluminum plates in them did not bend distally, and stem subsidence did not synchronize the strain on aluminum plates. This fact demonstrated that stems slipped into the cement without cement subsidence.

In this study, stem subsidence did not progress linearly but converged slowly after the initial subsidence. The slow subsidence after the initial large amount of subsidence in polished tapered stems is similar to the pattern found in clinical studies using roentgen stereo photogrammetric analysis [1, 15, 16]. Our findings of a lack of stem loosening and a lack of cement cracking were also similar to the findings of clinical studies [9, 10, 18].

Stem subsidence occurred in the loading periods, but stems rose slightly in the no load periods in both types of stems. We think that the rising of the stem was caused by stress relaxation in the cement. Stress relaxation is a characteristic of cement in which stress stored in the cement during loading is released in the no load periods. The role of stress relaxation has been shown to be self-protection from cement breakage [7, 12]. In our study, stress relaxation tended to occur in the polished tapered stems. The strain gauge, which indicated cement movement or force to the cement, produced higher and lower values also in the polished tapered stem. It also might indicate stress relaxation of cement against a stick-slip phenomenon. Verdonschot

et al. [17] noted that the subsidence pattern was stepwise and that cement creep was related to this phenomenon. The change in strain on the aluminum plate was thought to reveal the change in force in the cement. Therefore, decreasing force, instead of subsidence, might have been caused by stress relaxation.

In the rough stems in our study, most subsidence occurred on the first day of the experiment, and then it decreased linearly. Stem subsidence was accompanied by cement subsidence, which was confirmed by strain gauges. The rough stems became models of loosening in our study.

It was unclear why the bone–cement interface of rough stems broke so quickly in our study. We surmised that the stems could not slip in the cement because of their roughness and because the bonding composite of stem and cement caused shear stress at the bone–cement interface. The artificially processed tapered stems with no collar that were made for this study did not work as a composite beam, and thus they might have led to early deboning at the cement–bone interface.

Subsidence of the size-2 polished tapered stem with a thick cement mantle was greater than that of the size-3 stem with a relatively thin cement mantle. It has been hypothesized that a thin cement mantle can more easily be restricted by bone because the volume of cement is smaller than in thicker mantles [13].

Results were very different by surface roughness in our study. Though stem subsidence occurred in both stem types, subsidence rates converged for polished stems and the use of rough stems led to stem loosening. The early subsidence of rough stems of the composite-beam type must be carefully observed to detect loosening.

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Table 1 : The amount and rate of stem subsidence

	Polished size 2		Polished size 3		Rough size 2		Rough size 3	
Day	Subsidence in mm (SD)	Rate	Subsidence in mm (SD)	Rate	Subsidence in mm (SD)	Rate	Subsidence in mm (SD)	Rate
1–5	0.773 (0.004)	62.9	0.518 (0.008)	76.2	1.094 (0.009)	38.6	0.887 (0.019)	45.0
6–10	0.17 (0.007)	13.8	0.062 (0.004)	9.1	0.355 (0.011)	13.1	0.156 (0.013)	7.9
11–15	0.071 (0.008)	5.8	0.028 (0.006)	4.2	0.302 (0.013)	11.1	0.109 (0.013)	5.5
16–20	0.057 (0.006)	4.6	0.028 (0.008)	4.2	0.279 (0.012)	10.3	0.202 (0.013)	10.2
21–25	0.046 (0.008)	3.7	0.016 (0.007)	2.4	0.247 (0.007)	9.1	0.182 (0.018)	9.2
26–30	0.046 (0.008)	3.7	0.011 (0.005)	1.7	0.200 (0.007)	7.4	0.174 (0.009)	8.8
31–35	0.040 (0.006)	3.2	0.014 (0.006)	2.1	0.172 (0.006)	6.3	0.182 (0.052)	9.2
36–38	0.027 (0.004)	2.2	0.002 (0.006)	0.3	0.110 (0.007)	4.1	0.079 (0.027)	4.0
Totals	**1.229 (0.004)**	**100.0**	**0.680 (0.006)**	**100.0**	**2.715 (0.007)**	**100.0**	**1.971 (0.027)**	**100.0**

Subsidence values are shown as average millimeters (standard deviation) during each period; rates are the percentages for each stem group, obtained by dividing each group's subsidence by the total subsidence for type of stem.

Figure 1A–B : Collarless double-taper stems: (A) a rough surface stem; (B) a polished stem

A **B**

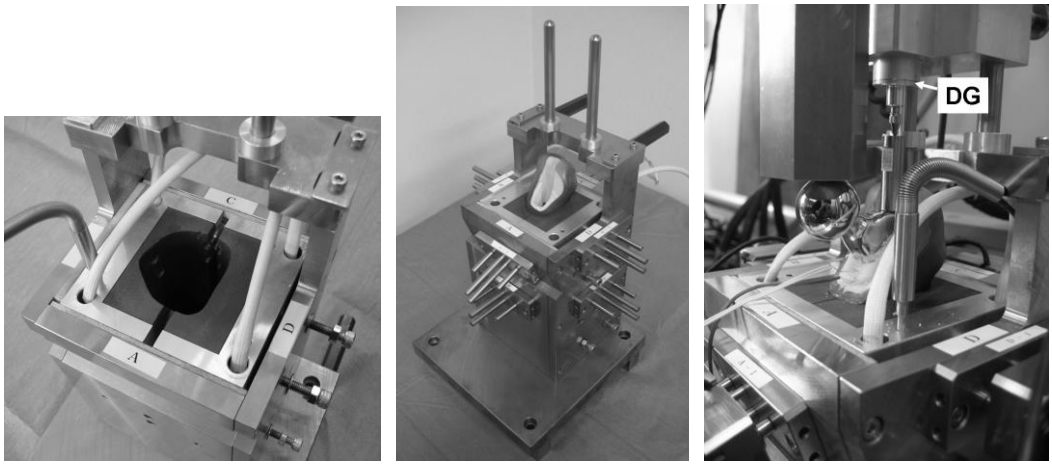


Fig. 2A–C (A) The fixator. The exterior of the fixator was made of carbon steel; the interior's epoxy resin was formed to the contours of the composite femur. (B) A composite femur was fixed completely with surrounding epoxy resin and rods inserted from the exterior of the metal fixator through the epoxy resin. (C) Measurement of stem subsidence. A digital displacement gauge (DG) was applied to the attachment screwed into the proximal lateral side of the stem to measure the amount of displacement.

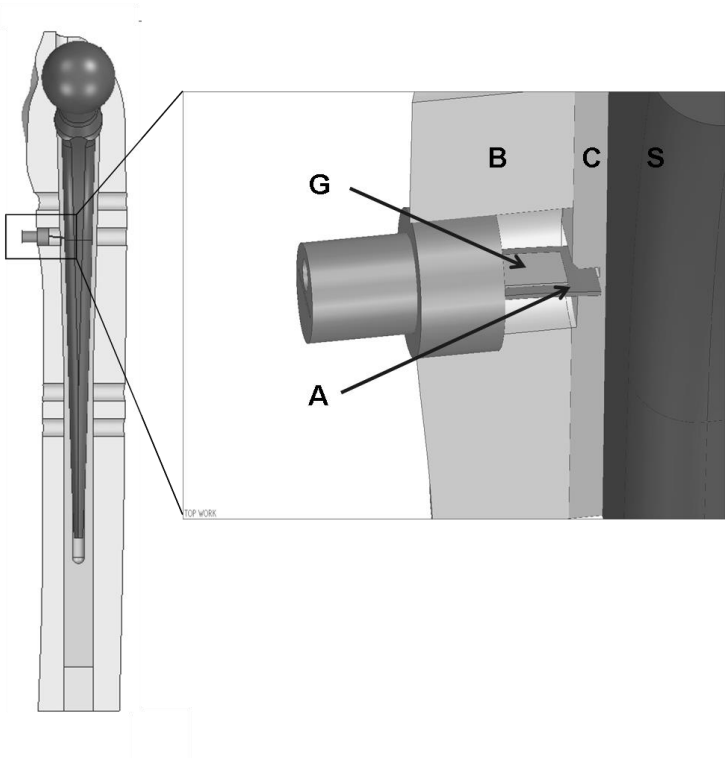


Fig. 3 Strain gauge. The aluminum plate onto which the strain gauge was pasted was inserted in the cement through the proximal posterior hole in the composite femur. The displacement of the aluminum plate represented the longitudinal displacement on the cement. A, aluminum plate; B, composite femur; C, cement; G, strain gauge; S, stem.

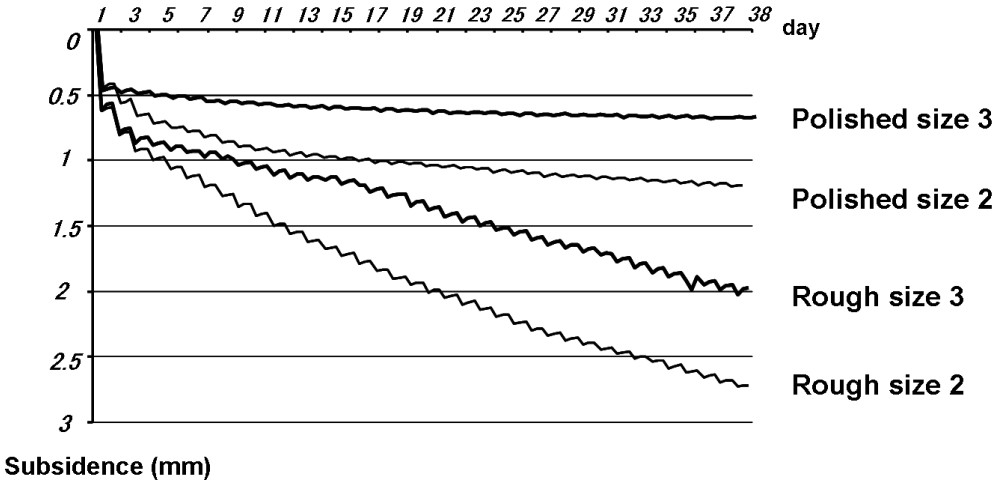


Fig. 4 Stem subsidence. All stems had subsided rapidly by 200,000 loading cycles. Afterward, subsidence for the polished stems converged slowly. However, subsidence after the early period was linearly progressive in the rough stems. The total amount of subsidence in the rough stems was more than two times that for the polished stems of the same size.

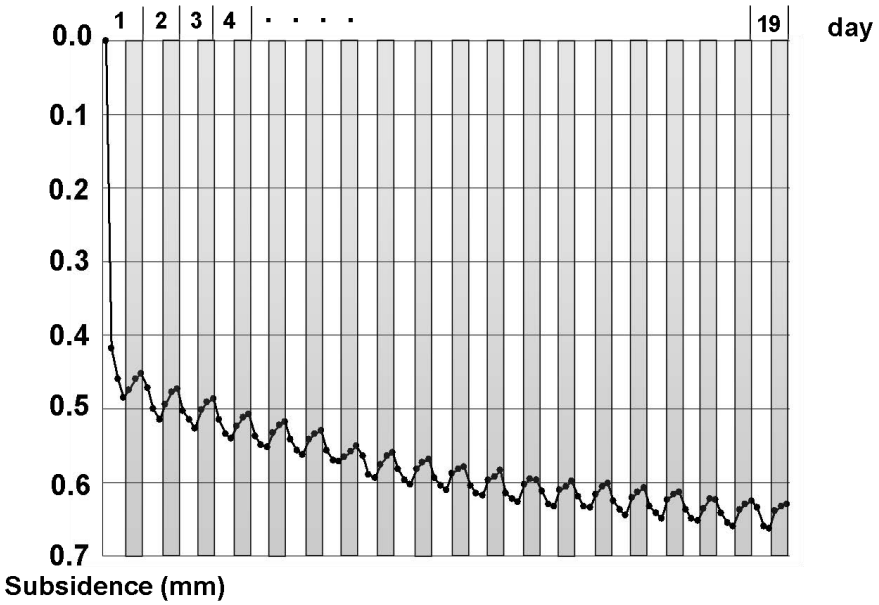
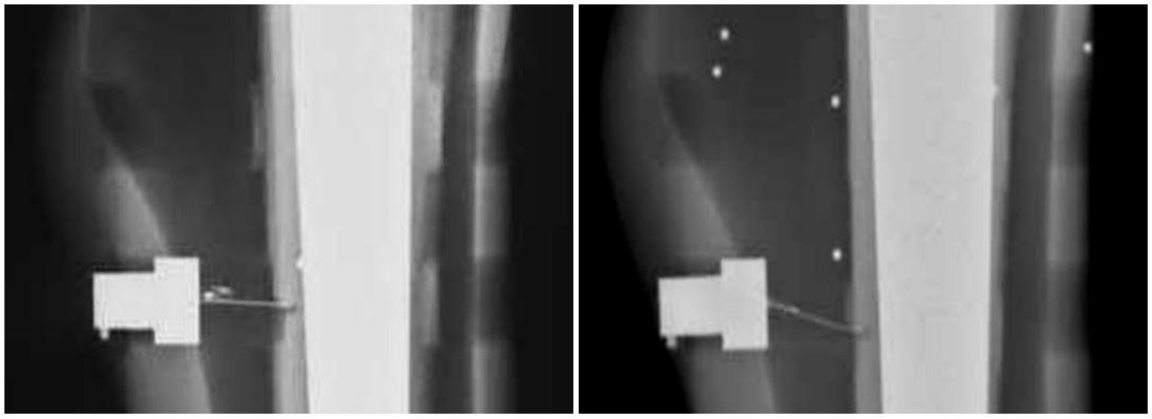
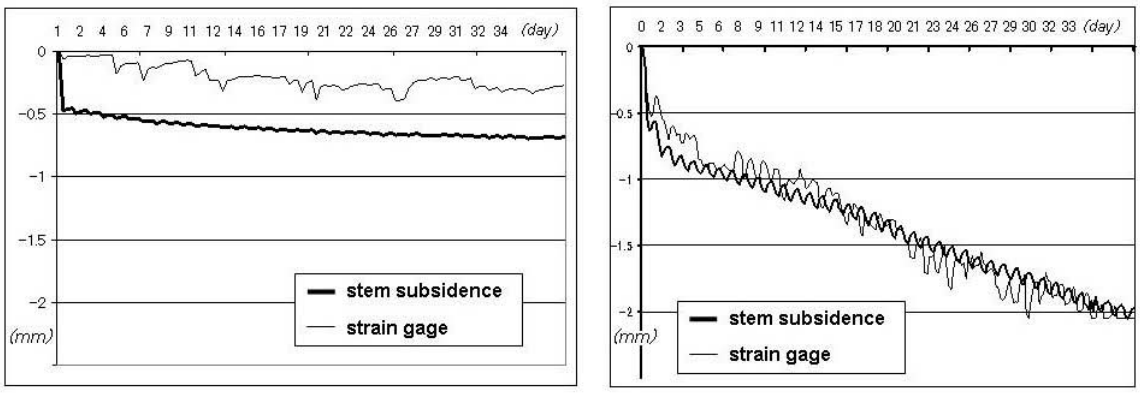


Fig. 5 Enlargement of stem motion during load and nonload in size-3 polished stems: displacement from original position between day 1 and day 19. The stem subsided during the load periods but rose up during the nonload periods. Other stems were also seen to have a similar zigzag motion, seen in Fig. 4



A **B**

Fig. 6A–B Radiographs of aluminum plates obtained after the experiment. (A) Polished stem. Less deformity of the aluminum plate was seen. (B) Rough stem. The aluminum plate was bent distally.



A **B**

Fig. 7A–B Stem subsidence and strain gage on the aluminum plate. (A) Polished stem. Cement movement was not synchronized with stem subsidence but recovered sometimes independently. (B) Rough stem. Cement subsidence was synchronized with stem subsidence.

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The Etiology and Prevention of Osteoporosis in Greek-O-Arabic (Unani) Medicine

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Abstract - Osteoporosis (pronounced as ahsteoporosis) is characterized by low bone mass with micro architectural deterioration of bone tissue leading to enhance bone fragility, thus increasing the susceptibility to fracture. Although exact numbers are not available, based on available data and clinical experience, 25 million Indians may be affected. Osteoporotic fractures in India occur in both sexes but are more common in females. It may occur at a younger age in India than in the West. The pharmacological interventions are expensive with limited or no cure promise, and the peak bone mass of the population can be increased significantly by appropriate and timely intervention in children. So, the public health measures that are efficacious, safe and cost-effective, must be adopted for the population at large. This calls the attention of the physicians of all the systems of medicine including Greek-o-Arabic (unani) system. Although, there is no description of osteoporosis in Greek-o-Arabic (unani) classical literature yet, the debility of body organs including bones is widely discussed. It is generally said that 'prevention is better than cure', so a specific prevention plan must be structured as per Greek-o-Arabic norms. Nevertheless, before making the prevention plan one must understand the Greek-o-Arabic etiopathology of the disease. Therefore, this work is an attempt to understand the underlying causes and risk factors of osteoporosis, and to construct a mighty prevention plan. To keep the Greek-o-Arabic spirit alive, the typical Greek-o-Arabic terms are not translated into English.

Keywords : *osteoporosis, asbab, su-e-mizaj, su-etarkeeb, tafarruq-e-ittesal, mahiyat-al-marzi.*

GJMR-H Classification : *FOR Code: WB 55.U5*

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Aisha Aijaz [α] & Anis A. Ansari [σ]

Abstract - Osteoporosis (pronounced as ahsteoporosis) is characterized by low bone mass with micro architectural deterioration of bone tissue leading to enhance bone fragility, thus increasing the susceptibility to fracture. Although exact numbers are not available, based on available data and clinical experience, 25 million Indians may be affected. Osteoporotic fractures in India occur in both sexes but are more common in females. It may occur at a younger age in India than in the West. The pharmacological interventions are expensive with limited or no cure promise, and the peak bone mass of the population can be increased significantly by appropriate and timely intervention in children. So, the public health measures that are efficacious, safe and cost-effective, must be adopted for the population at large. This calls the attention of the physicians of all the systems of medicine including Greek-o-Arabic (unani) system. Although, there is no description of osteoporosis in Greek-o-Arabic (unani) classical literature yet, the debility of body organs including bones is widely discussed. It is generally said that 'prevention is better than cure', so a specific prevention plan must be structured as per Greek-o-Arabic norms. Nevertheless, before making the prevention plan one must understand the Greek-o-Arabic etio-pathology of the disease. Therefore, this work is an attempt to understand the underlying causes and risk factors of osteoporosis, and to construct a mighty prevention plan. To keep the Greek-o-Arabic spirit alive, the typical Greek-o-Arabic terms are not translated into English.

Keywords : osteoporosis, asbab, su-e-mizaj, su-e-tarkeeb, tafarruq-e-ittesal, mahiyat-al-marzi.

I. Introduction

Who defines osteoporosis as "The bone density that falls 2.5 standard deviation below the mean for young healthy adults of the same race and gender (also referred to as a T-score of -2.5)"1. According to WHO, osteoporosis is second only to cardiovascular disease as a global health care problem2. Worldwide, lifetime risk for osteoporotic fractures in women is 30-50%, in men risk is 15-30%3. One out of eight males and one out of three females in India suffers from osteoporosis, making India one of the largest affected countries in the world4. Experts say the number of osteoporosis patients is approximately 26 million (2003 figures) with the numbers projected to increase to 36 million by 20135.

Realizing the burden of this disease on health professionals, the Greek-o-Arabic classical literature was explored in the light of modern etiological parameters, so that the exact pathology of the disease can be understood. This etiopathogenesis was availed to construct the Greek-o-Arabic prevention plan of the disease.

Causes of osteoporosis in Greek-o-Arabic (unani) medicine

Asbab (causes): According to Ibn Sina, there are four *asbab* (causes) of all the diseases namely *asbab-e-maddi, asbab-e-souriya, asbab-e-fayeliya and* asbab-e-tamamia6.

a) Asbab-E-Souriya

These are the *asbab* related to *Mizaj, Quwa* and *tarakeeb*

Mizaj: While discussing the causes of weakness of members (*aza*), Ibn Sina mentioned *su-e-mizaj* (persi-stent intemperament) as an important factor. He says "The causes of weakness of members include the per-sistent intemperament especially the cold one while the hot intemperament although enfeebles and benumbs an organ by corrupting the temperament of pneuma (rooh). Dry intemperament prevents the faculties from pen-etrating the organ by becoming thick. "Moist intem-perament produces weakness by relaxing the organs and obstructing the passage".

As the patients of osteoporosis do not show the signs of dominance of any *khilt*, therefore this *su-e-mizaj* must be *su-e-mizaj sada*. The primary qualities like cold and dryness show the properties of retention and holding and in this disease there is increased porosity of bones due to excessive depletion of bone mass, therefore, this *su-e-mizaj* must be *su-e-mizaj haar* or *su-e-mizaj ratab* or may be *su-e-mizaj haar ratab*.

Quwa: Poor nutrition and malabsorption are the definite causes of Ca and vitamin D deficiency predisposing osteoporosis1. This indicates that there is a malfunction of *quwwat-e-ghazia* in such a way that the *quwwat-e-jaziba, masika*, and *hazima* become weaker and *quwwat-e-dafia* becomes stronger than normal. The genetic factors are the major determinants of peak skeletal mass and density. Peak bone mass is often lower among individuals with a family history of

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osteoporosis1. Studies have suggested that a major genetic component responsible for bone mass may be linked to polymorphism in the gene for vitamin D receptor (VDR)7. This genetic predisposition of osteoporosis indicates that there must be some dysfunction of *quwwat-e-tanasuliya* that manifests as this disease.

Tarakeeb: An attenuation of texture (*su-e-tarkeeb*) of the constituting fibres of an organ leads to weakness of the organs. Ibn Sina says in this context, "the looseness of the texture in the fibres of an organ leads to weakness. Special feature of this is that the person has no pain or discomfort"6.

Hence, *su-e-tarkeeb* is one of the important causes of osteoporosis in which the micro-structure of bones is disrupted without any pain or discomfort.

b) Asbab-E-Maddiya

These include the *arkan*, *arwah, akhlat* and *aza:*

Arkan (ustuqissat): Ibn Sina says in *Al-Qanoon* that "the physicians must learn from physics that the primary elements are four and no more"6. These are *arz, maa, hawa* and *naar* as proposed by Aristotle. Each of these *arkan* bears the primary qualities and show specific characteristics. Ibn Sina says "in nature, the earth serves the purpose of making the objects firm and stable. Water has its being in the universe so that moulding of forms, shaping of coutures and attempering may become easy. In nature the purpose of air is to impart porosity, lightness and ability to rise upward". Hence, the cause of increased porosity of bones in osteoporosis may be because of the dominance of *ustuqis-e-hawa* (air) in the human body.

Arwah: Intemperament, dissipation or dispersion of pneuma can cause weakness of organs. It can occur by itself, following any kind of depletion, fever, pains or by foul smell, putrid water, and diffusion of poisonous effects in air6.

Akhlat: There is a strong correlation between *akhlat-e-moharrika* (hormones) and osteoporosis. Bone remodelling is regulated by several circulating hormones including oestrogens, androgens and parathyroid hormone. In addition, estrogen receptor α (ERα) gene polymorphisms may also be associated with BMD in Indian women and may influence some determinants of bone metabolism resulting in accelerated age related bone loss8.

Estrogen deficiency causes bone loss by activating new bone remodelling sites and increasing bone reabsorption by osteoclasts. Thus, in the estrogen deficient states as menopause, bone loss is increased. In males, it is associated with testosterone deficiency. Hyperparathyroidism bone reabsorption is increased leading to bone loss and decreased BMD.

Aza: In osteoporosis, *Aza-e-mufrida-izam* (bo-nes) are diseased and become light, porous and liable to fractures. In this disease *quwwat-e-ghazia* is weak-ened indicating *zof-e-jigar* and its *aza-e-khadima*. Weak-ness of *quwwat-e-tanasulya* indicates the dysfunction of *khusyatain.*

c) Asbab-E-Fayeliya

These causes are divided into two groups:

1) *Asbab-e-sitta zaruria*

These are six essential factors of life

i. *Hawa*

Faasid hawa is one of the important causes of dissipation of pneuma and intemperament of members making them weak.

ii. *Makool-wa-mashroob*

Mal-nutrition or low dietary intake of Calcium, phosphorous, vitamin D, K and C is the main cause of osteoporosis. Also low protein intake is associated with lower peak bone mass during adolescence and lower BMD in elderly. Modest vitamin D deficiency [25-hydroxyvitamin D levels <50nmol/L] leads to compensatory hyperparathyroidism and is an important risk factor for osteoporosis and fractures1.Peak bone mass may be impaired by inadequate calcium intake during growth, leading to increased risk of osteoporosis in later life. In adults, insufficient calcium intake induces secondary hyperparathyroidism and increases the rate of remodelling of bones. Excess of alcohol (>2units/day) especially in younger age group increases the risk. Some studies indicate that soft drinks containing phosphoric acid may increase the risk of this disease1. Thus, it can be said that *ghiza-e-qalil-al-taghzia, radi-al-kaimoos* is the cause of osteoporosis.

iii. *Harkat-wa-sukun badani*

Physical inactivity such as prolonged bed rest and paralysis results in significant bone loss1. This indicates that *sukun-e-badani mufarrat* is one of the important factors of osteoporosis.

iv. *Istafragh-wa-ehtibas*

In renal diseases, kidney can't properly generate calcitriol from calcidol which is the storage form of calcium. This increases the excretion of calcium in urine. Thus, i*stafragh-e-ghair tabayi* increases the risk of osteoporosis.

2) *Asbab-e-ghair zaruria*

These are discussed below:

i. *Mulk Wa Balad*

While osteoporosis can occur in all the countries of the world, Europeans and Asians are more commonly involved.

ii. *Jins*

This disease can occur in males but females are more commonly involved.

iii. *Asnaan*

Osteoporosis is the disease of *sinn-e-kahulat* commonly occurring between 50-70 years of age.

iv. *Adaat*

Smoking over a long period has detrimental effects on bone mass. These effects may be mediated directly by toxic effects on osteoblasts or indirectly by modifying estrogen metabolism, likewise chronic heavy drinking of alcohol predispose to osteoporosis.

v. *Umoor-e-ghariba*

Advia (drugs) like glucorticoids, anti convulsant, l-thyroxine, anti-coagulants, proton-pump inhibitor and thiazolidinediones when administered may decrease bone mass. Amraz like endocrinal disorders, malabsorptions, rheumatological disorders, haematological disorders and genetic diseases predispose osteoporosis.

d) Asbab-e-tamamia

In osteoporosis *fail-e-taghzia* of *izam* is deranged leading to porosity and weakness of bones.

i. *Mahiyat-al-marzi (pathogenesis)*

Osteoporosis is the disease of izam (bones). In the beginning there is *su-e-mizaj haar ratab sada* and *tahlil-e-ruh* due to various *asbab*, leading to *zof-e-jigar*. This manifests in *zof-e-quwwat-e-ghazia*. The weakness of *quwwat-e-ghazia* lead to inadequate bone formation while *quwwat-e-dafia* increases the bone reabsorption resuting in decreased peak bone mass. This condition manifests in *su-e-tarkeeb.* In osteoporosis not only the bone density is decreased, but the micro-archtechture of bone is also distrupted. The weaker spicules of trabecular bone breaks resulting in "Microcracks". This is an obvious form of *tafarruq-e-ittesal-e-dakhili*. Such porous bones get fractured easily on fall causing *tafarruq-e-ittesal khariji*.

ii. *Prevention plan (Tahaffuz)*

The Greek-o-Arabic prevention plan of osteoporosis is made keeping the causative factors in mind. The salient features of this plan are discussed below:

Living at a place with proper ventilation and adequate supply of healthy air (*hawa-e-jayyadul jawahar)* devoid of any pollution.

Taking balanced diet containing all the essential nutrients including vitamins and minerals in adequate amount i.e. taking *ghiza-e-kaseer-al-taghzia jayyad-al-kaimoos* like *maul lahm*, *beza neem barisht* and *lahm-e-tayyur*. Avoiding all the junk foods, cold drinks and alcohol beverages will also help.

Achieving a higher peak bone mass in adolescent is possible by exercise. jogging, walking or stair climbing at 70-90% of maximum efforts three times a week may increase bone density by 5% in 9 months i.e. maintaining the level of *hakat-wa-sukun badani tabayi* is beneficial. Epidemiologic data reveals that when exercise is initiated in adult life the peak bone mass increases by 1-2% in <2 years duration. But, excess physical activity can cause damage to bones. Many marathon runners developed severe osteoporosis in later life. In females, heavy exercise can lead to decreased estrogen levels predisposing osteoporosis.

Quitting bad habits like smoking and alcohol drinking. Avoiding the *muzir advia* and curing the *muzmim amraz* in time can slow down the progress of the disease.

Taking Greek-o-Arabic (unani) calcium preparations orally like *kushta sadaf* (50mg OD) and *khamira marwareed* (4gm OD) can provide organic calcium which may be helpful in preventing the disease.

II. Conclusion

After above discussion, now the Greek-o-Arabic definition of osteoporosis can be presented

"Osteoporosis *(takhalkhul-e-izam)* is that *marz-e-murakkab* of *izam* in which *su-e-mizaj, su-e-tarkeeb* and *tafarruq-e-ittesal* occur simultaneously but gradually, leading to *takhalkhul* and *zof* making them liable to *kasar*". Its various causes are *ghalba-e-unsur-e-hawa, su-e-mizaj haar ratab, qillat wa kasrat-e-akhlat-e-moharrika, zof-e-jigar and khusyatain, fasad-wa-tehlil-e-ruh, zof-e-quwwat-e-ghazia wa tanasulya and nuqsan-e-fail-e-taghzia-e-izam* etc. it's *asbab-e-badia* (environmental causes) are *faasid hawa*, *ghiza-e-qalil-al-taghzia, radi-al-kaimoos, sukun-e-badani mufarrat, istafragh-e-ghair tabayi, balad-e-maghrabi, jins-e-moannas, sin-e-kahulat and adviyat* and *muzmin amraz*.

Its *mahiyat-al-marzi* includes the *su-e-mizaj haar ratab sada* and *tehlil-e-ruh*. That results in *zof-e-quwwat-e-ghazia wa tanasuliya* followed by *su-e-tarkeeb* leading to *tafarrq-e-ittesal dakhili* making the bones liable to *kasar*.

This disease can be prevented by residing in *hawa-e-jayyad al jawahar*, eating *ghiza-e-kaseer-al-taghzia jayyad-al-kaimoos*, maintaining the *tabayi* level of *hakat-wa-sukun badani*, and by taking Greek-o-Arabic calcium supplements.

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Assessment of Knowledge of ICDS Women Beneficiaries in District Budgam of Kashmir Region Regarding Prenatal Care

By Rajni Dhingra & Iffat Ghani
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Abstract - Prenatal care is universally considered important for women and children. This study aims to assess the knowledge of women beneficiaries of ICDS centres related to prenatal care belonging to district Budgam of Kashmir region. Nursing mothers (NM), Pregnant women (PW) and Mother of children beneficiaries (MCB age 6 months-3years) were included to assess and compare the their awareness levels. A total of 600 women beneficiaries were randomly selected from four blocks of district Budgam (150 from each block). The results of the study revealed that majority (79.1%) of the respondents were aware of the importance of medical consultation during pregnancy and about 48.6% were fully aware with appropriate time of consultation. Almost all respondents were aware of weight monitoring during pregnancy but not about its significance. Respondents were also aware about the doses and time schedule of TT vaccination during pregnancy. Basic pre-natal care components are effective means to prevent range of pregnancy complication and reduce maternal mortality. The findings indicate that there is need for enhancement of intervention educational programme in ICDS regarding importance of prenatal care and service for the healthy birth outcome and mothers' well being.

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I. Introduction

In many developing countries ,complications of pregnancy and child birth are leading causes of death among women of reproductive age.The maternal health situation in the country has been staggering despite several changes in a rapidly evolving socioeconomic environment. The roles and responsibilities of primary care physicians have also been revised continuously in this context. Under their leadership, different cadres of health workers have been appointed to address the problem. As deadline for Millennium Development Goals (2015) is approaching, the need for improving the standard of maternal care is more than ever. In the last decade, as per the National data, health indicators including utilization of antenatal care services were as poor as 60% in rural India. Keeping in view the gap between the target and reality, National Rural Health Mission (NRHM) was launched in April 2005, to improve the rural health care delivery system and health status of the people. Accredited Social Health Activists (ASHA) were introduced at the village level for motivating the beneficiaries to utilize the antenatal care services provided by the government health facilities. Under supervision of Auxillary Nurse Midwives (ANM) and physicians at primary health care level, ASHA were planned to play the role of a connecting bridge between community and first level government health sector. These groups of health care providers, along with Anganwadi workers (AWW), build the base line of rural health services in the country. They, under the Mission, seek to provide universal access to equitable, affordable and quality maternal health care, as well as to bring about an improvement in the health status of the pregnant women belonging to underprivileged sections of the society. (Roy et al, 2013). Overall maternal mortality is much more prevalent in rural India, where the UN estimates the MMR to be 619. (Maternal Mortality in India- Report, 2008). ICDS (Integrated Child Services Scheme) is one of the centrally sponsored schemes with one of its important components of services responsible for overall improvement of health of expectant mothers by providing nutrition and health care during pregnancy and health education through their AWCs (Anganwadi centers) in collaboration with Primary Health Centres (PHC) particularly in rural areas. It delivers services at Anganwadis (AW village centres) right at the doorsteps of the beneficiaries to ensure their maximum participation. It utilises local women as honorary village level workers for delivery of the package of services (Tandon, 1993). The fact that more than 100,000 women in India are estimated to die every year from pregnancy and child birth related causes reinforces the importance of ensuring that all pregnant women receive adequate antenatal care during pregnancy and that deliveries takes place under the supervision of trained medical personnel in a hygienic environment. Antenatal care provide an opportunity for a variety of preventive intervention during pregnancy, including tetanus toxoid injection and educating women about nutrition, safe delivery and post partum care. (Swamy et al, 1993). An assessment of composite measure for antenatal care utilization was undertaken by Bloom, Lippeveld and

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Wypiji (1999) at Varanasi, Uttar Pradesh, India. Results showed that demarcating women's antenatal care status based on a simple indicator — two or more visits versus less — marked a large amount of variation in care received. Logistic regression analyses were conducted to examine the effect of antenatal care utilization on the likelihood of using safe delivery care, a factor known to decrease maternal mortality. After controlling for relevant socio-demographic and maternity history factors, women with a relatively high level of care had an estimated odds of using trained assistance at delivery that was almost four times higher than women with a low level of care. Similar results were obtained for women delivering in a health facility versus at home. This strong positive association between level of care obtained during pregnancy and the use of safe delivery care may help explain why antenatal care could also be associated with reduced maternal mortality. In another study, it was found that women attending ANC (Antenatal care) at least twice were more likely to have a live birth. Women attending for two ANC visits (but not more than two) were more likely to have a healthy weight baby (Brown et al, 2008). Another such study in India assessed that the characteristics of sample households for pregnant women were broadly in proportion to the characteristics of the all Indian population. About 89% of the pregnant women availed visits of which 62% has received three or more ANC visits. Those receiving the second dose of TT or booster dose were about 78%. About 73% of the pregnant women received IFA tablets during their pregnancy. About 53% of the pregnant women had full package of ANC i.e availed three or more ANC visits, both the doses of TT/ booster and IFA tablets. The proportion of pregnant women who availed full ANC package was lower in rural areas as compared to urban areas, higher for literate women as compared to illiterate women. The proportion of institutional deliveries managed by hospitals and health centres was about 41%, it being higher among literate women and in urban area (Singh and Yadav, 2009). Mothers who receive late (defined as beginning in the third trimester of pregnancy) or no prenatal care are more likely to have babies with health problems. Mothers who do not receive prenatal care are three times more likely to give birth to a low weight baby, and their baby is five times more likely to die (MCH Bureau, 2005). A study conducted in Karachi to assess the knowledge of women on obstetrical complication and care, has shown that the half of the sample population (married women of reproductive age) had no antenatal care in their last pregnancy and 75% of them delivered at home. It was also indicated in the findings that the women were having poor knowledge on pregnancy related complication. Only 5% of the women perceived absent / decreased fetal movements as a danger sign of pregnancy, other reported danger signs included premature uterine contraction by 3%, premature rupture of membrane by 3% and convulsion by 13% (Hassan and Nissar, 2002) prenatal care benefits all expecting mother and their unborn. Rather than decreasing, rates of low birth weight (LBW) babies and preterm births have risen and are now the highest they have been in more than three decades. Babies born too small or too early are at higher risk for death and for both short and long term health problems (Swamy et al, 2008).

a) Turmoil and Antenatal Care

Children exposed to negative shocks in-utero, or early in life, have higher mortality rates, lower birth weights and are shorter for their age. These shocks can include recessions, famines, droughts, and disturbed conditions. A new dimension to these external shocks are armed conflict. Kashmir province in J&K State has witnessed armed conflict since 1990. Official census reports (Census of India 2001, 2011) and reports based on the National Family Health Survey (NFHS-1997) draw a positive picture for the entire state of Jammu and Kashmir in terms of mortality rates, fertility and vaccination programmes etc. However, during pregnancy the access to health services including vaccinations, prenatal and antenatal care, and micro nutrients needed for the foetus development, is usually limited because of armed conflict. Stress experienced by expecting women due to disturbed socio-political environment during pregnancy changes the production and distribution of hormones, including intrauterine growth hormones.In addition, stress can also reduce the gestation time of the foetus. In a study, it was also revealed that exposure to violence in utero and early in life has adverse impacts on children's age–adjusted height (z-scores). It was found that children more affected by the insurgency were 0.9 to 1.4 standard deviations smaller compared with children less affected by the insurgency. The effect was found stronger for children who were born during peaks in violence. A robust finding in the health literature is that shorter children perform worse in schools, in jobs and are sicker throughout their life (Parlow, 2012).

Addressing maternal health means ensuring that all women receive the care they need to be safe and healthy throughout pregnancy and child birth. Prenatal care is an essential first step in child's life. Children and the unborn have a special place in all societies and their needs are frequently considered a high priority, but in reality their needs may frequently, for various reasons go unnoticed. One reason among them is the poor knowledge of pregnant women regarding the care or antenatal care which may directly affect an unborn child. The major components of prenatal care include the diagnosis and treatment of any health complication counselling about diet, avoidance of drugs etc. Comprehensive prenatal care may prevent complications of pregnancy, which can have life time

effects and reduce premature labor and neonatal mortality. Keeping above factors in view the present study was taken with the purpose to determine the knowledge of women beneficiaries related to prenatal care with the objectives.

II. Objectives of the Study

The present research was undertaken with following objectives.

- To study the extent of knowledge among sample women beneficiaries of ICDS belonging to rural areas of district Budgam regarding prenatal care.
- To compare the knowledge level related to prenatal care among woman beneficiaries across groups (Pregnant woman, Lactating mothers and mothers of child beneficiaries) related to prenatal care.

III. Methodology

The sample comprised of 600 registered women beneficiaries of AWCs out of which 150 were nursing mothers, 150 were pregnant women and 300 were mothers of child beneficiaries (age group 6months-3years). Data was collected in the year 2011 from January2011-June 2011.

a) The Sample

The sample has been drawn from Kashmir, an area affected by armed conflict has been selected for this study.Among the districts, Budgam has been selected for the study which has eight blocks and about 593 villages. The total population of the district is 7.35 lacs with gender ratio 0f 830/1000 and literacy rate 57.98% (2011). Out of eight blocks of district Budgam, sample was collected from four blocks (Budgam, Nagam, Chadoora and B.K.Pora) in a representative manner. For sampling a list of Anganwadi centres (AWCs) was obtained from the office of Project Officer of ICDS of each block.After obtaining the list of Anganwadi centres from each block,the centres were selected by random sampling technique using lottery method. The maximum number of child beneficiaries in the age group 6months-3years registered in an AWC is 25 which can vary depending upon the population covered under the centre.Out of 25,only 5 mothers of child beneficiaries were purposively selected from the each AWC from the attendance register maintained for this group of beneficiaries.Similarly the maximum number of nursing mothers and pregnant women registered in an AWC is 06,but the number of both the groups of beneficiaries is not always equal.For the present study a total of 5 women beneficiaries from both the groups were purposively selected from the attendance register maintained by the AWW.Beneficiaries having children in the age group (0-6months) fall in the category of nursing mothers, whereas, beneficiaries having children in the age group (6months-3years) were considered as mothers of child beneficiaries.

b) Tools Used

In order to collect the data a self devised Interview Schedule.

i. *Interview Schedule*

After going through different review material, an Interview Schedule was prepared which was pretested on 25 women beneficiaries belonging to all finalised.

The interview schedule comprised of

a. General Profile of respondents.
b. Pregnancy and Prenatal care.
   i. Consultation during pregnancy.
   ii. Appropriate timing for consultation.
   iii. Knowledge about weight monitoring.
   iv. Vaccination and its importance during pregnancy.

c) Procedure of data collection

The data was collected by visiting the beneficiaries either at home or at AWC whichever was feasible for them.Before approaching the beneficiaries AWW of concerned area was informed who also helped in locating the beneficiaries and sometimes accompanied the researcher while collecting data.

IV. Results and Discussion

The results of the present study have been discussed under three categories

Table 1 : Knowledge related to consultation during pregnancy

Demographic Character	Pregnant (PW) (n= 150)		Nursing (NM) (n=150)		Mothers (MCB) (n=300)		All Beneficiaries (n=600)		χ^2 Analysis
	f	%	f	%	f	%	f	%	
(a) Consultation During Pregnancy									
Private clinic	24	16	25	16.6	40	13.3	89	14.8	10.8_6
Mid- wife	--	--	--	--	2	0.66	2	0.3	
PHC / Hospital	124	82.6	115	76.6	234	78.0	473	79.1	
No consultation required	2	1.3	10	6.6	24	8.0	36	6.0	
Total	150	100.0	150	100.0	300	100.0	600	100.00	
(b)Appropriate Time for Consultation									
From beginning	84	56.0	76	50.6	131	43.6	291	48.6	14.0_{6*}
II Trimester	48	32.0	42	28.0	94	31.3	184	30.6	
IIItrimester	16	10.6	22	14.6	51	17.0	89	14.8	
Not Necessary	2	1.3	10	6.6	24	8.0	36	6.0	
Total	150	100.0	150	100.0	300	100.0	600	100.0	
(c)Knowledge about significance of weight Monitoring									
To Check growth of foetus.	46	30.6	50	33.3	89	29.6	185	30.8	1.7_6
To control weight	16	10.6	20	13.3	37	12.3	73	12.1	
Advised by AWW	1	0.6	1	0.6	1	0.3	3	0.5	
Unaware about its significance	87	58.0	79	52.6	173	57.6	339	56.5	
Total	150	100.0	150	100.0	300	100.0	600	100.00	

Column percentage ** denotes highly significant $p \leq 0.01$,*Significant $p \leq 0.05$ df is in subscripts of x^2 values

Pregnant women absolutely need good prenatal care.It is essential to ensure not only the health of mothers,but also the health and well being of the baby.The first prenatal visit starts at one month and continues till delivery as per the doctor's advice.Table-1 (a) reveals that majority of selected Kashmiri respondents (79.1%) were in favour of medical consultation during pregnancy either at Primary Health Centre or Government Hospital,whichever was easily accessible to them ,while as only small proportion(6%) did not find it necessary to consult a doctor during pregnancy .Statistically no significant difference ($p>0.05$) was observed among the groups.

With respect to awareness regarding appropriate time for consultation during pregnancy, it is clear from table (b) that majority (48.6%) of the Kashmiri beneficiaries under study were of the opinion that first prenatal visit should be started from the first trimester.Some (14.8%) women beneficiaries found it safe to start consultation in III Trimester if it is second pregnancy or if there is no complication or problem faced by pregnant women. The difference among the groups was statistically found significant ($p<0.05$).

Gaining weight is a positive sign that you are giving your baby what it needs to develop. There are two reasons for the weight gain during pregnancy, to nourish the developing foetus and to store up reserves for

breastfeeding. For awareness regarding importance of weight gain, table (c) reveals that out of entire rural sample population from Kashmir majority (56.5%)were unaware about the significance of weight monitoring,while as a good percentage (30.8%) was also found fully aware of its significance,Ithough such difference in groups was statistically found insignificant.($p>0.05$).

Table 2 : Vaccination During Pregnancy

Variable	Pregnant (PW) (n= 150)		Nursing (NM) (n=150)		Mothers (MCB) (n=300)		Total (n=600)		χ^2 Analysis
	f	%	f	%	f	%	f	%	
Awareness about T.T vaccine during pregnancy									
Once during pregnancy	4	2.6	--	--	7	2.3	11	1.8	59.3_4**
Twice	127	84.6	97	64.6	148	49.3	372	62.0	
Thrice	19	12.6	53	35.3	145	48.3	217	36.1	
Total	150	100.0	150	100.0	300	100.0	600	100.0	
Doses of TT to be given									
Each dose in each Trimester	20	13.3	22	14.6	58	19.3	100	16.6	6.6_4
All doses in first two trimester	92	61.3	84	56.0	149	49.6	325	54.2	
All doses in 2nd two trimester	38	25.3	44	29.3	93	31.0	175	29.0	
Total	150	100.0	150	100.0	300	100.0	600	100.0	
Importance of TT									
Prevents infection	19	12.6	23	15.3	34	11.3	76	12.7	7.7_6
Safety of mother& child.	40	26.6	27	18.0	81	27.0	148	24.6	
Safety of Child only	3	2.00	6	4.0	15	5.0	24	4.0	
As per Doctor's advice	88	58.6	94	62.6	170	56.6	352	58.6	
Total	150	100.0	150	100.0	300	100.0	600	100.0	

Column percentage df is in subscripts of x^2

*denotes significant $p<0.05$, **denotes highly significant $p<0.001$

Vaccination is considered to be essential during pregnancy to give protection against infection to both foetus and the mother.Data from the table 2(a) reveal that all the Kashmiri rural women under study were aware that Tetnus Toxoid (TT) vaccination is to be taken. Only a small percentage (1.8%) of women beneficiaries were unaware about the importance of TT vaccination because they had taken only one dose of TT because of carelessness or lack of awareness about its importance during pregnancy.There was a highly significant difference among the groups statistically ($p<0.000$).

Similarly with reference to knowledge of selected Kashmiri rural women regarding the doses of TT given during pregnancy it is clear from the table(b) that majority(54.2%) women beneficiaries believed that all doses should be given in the first two trimesters.16.6% were of the opinion that each dose should be given in each trimester.No significant difference in knowledge among the groups was statistically found ($p>0.05$).

Further it is observed from table(sec-c) that although all the Kashmiri rural women were aware about TT vaccination during pregnancy, but the majority (58.6%) was not aware about the reasons for importance of TT during pregnancy. Only a small proportion (12.4%) of respondents were fully aware about importance of TT. All the groups were almost equally aware about its importance with no significant difference in knowledge among the group ($p>0.05$).

V. Summary and Conclusion

The findings reveal that the knowledge of respondents about maternal health care, including the number and timing of antenatal and pre natal care was moderate, but there were still many aspects of pre natal care where the knowledge was lacking and in which respondents need to be made aware of. These included doses of Tetnus Toxoid and significance of weight monitoring.

Table; 3 presents the comparison between previous studies and the present studies in this area and the present research conducted on rural women in a remote district affected by armed conflict.

Table 3 : Comparison between Previous and Present Study

Name,Year and Place	Previous Studies	Present Study
el-Sherbini AF,el-Torkey MA, Ashmawy AA,Abdel-Hamid HS(1993)Assuit Egypt Ishra and Fatin (2012)Iraq,Baghdad Hasnain S and Sheikh NH(2007)Lahore, Pakistan Mattos et al (2005)Brazil	• 30.5% were aware about prenatal care (PNC) • 25% lacked basic & essential knowledge • 50% of PW were having inadequate knowledge about PNC. • 32% of women were having poor knowledge about TT vaccination. • Out of total sample 2.8% were not aware about PNC. • 92.1% were well aware about importance of TT vaccination.	• 48.6% were aware about PNC. • Only 6% sample women were having no knowledge regarding PNC. . • 62% Kashmiri sample women were well aware about TT vaccination. • 24.6% women beneficiaries from sample Anganwadi centres of district Budgam were well aware about importance of TTvaccination. • 58.6% unaware about importance of TT vaccination.

Better understanding of various aspects of antenatal care must be ensured by ICDS workers and Health care workers at grass root levels for improving the foetal and maternal health indicators. The results of the study point to need for enhanced efforts on the part of ICDS workers for aiming at educational intervention for women beneficiaries of ICDS centres.

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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.

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

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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.

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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.

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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).

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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.

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(Free of charge) from the following website:

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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.

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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.

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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
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- 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.

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- Shape the theory/purpose specifically - do not take a broad view.
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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.
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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
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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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