Advances in Life Science and Technology
ISSN 2224-7181 (Paper) ISSN 2225-062X (Online)
Vol.36, 2015

Evaluation of Some Serum Biochemicals that Associated with Antioxidant Status in Periodontitis Patient in Relation with Gestational Diabetes

Dr .Khadija M. Ali[1] Dr. Bakhtiar M. Ahmed[2] Dr. Amal H.Aziz[1]
1. Department of Periodontology, College of Dentistry, Hawler Medical University, Erbil, Iraq
2. Department of Basic Sciences, College of Dentistry, Hawler Medical University, Erbil, Iraq

Abstract
Periodontal disease is inflammatory disease that characterized by oxidative stress and inversely associated with antioxidants. Gestational diabetes mellitus (GDM) occurs with variable severity in 3%-5% of all pregnancy may be associated with oxidative stress and impairment of antioxidant defense. In previous cross –sectional or case control studies,clinical periodontal disease has been associated with GDM .This study was carried out to assess the association between the periodontal disease and (GDM). 80 pregnant women were participated in this study, 40 of them were diagnosed with GDM. Full mouth periodontal examination with some serum biochemical that associated with antioxidant status: uric acid, bilirubin, and total protein parameters were performed for all participants. The results of the study showed a significant decrease in serum uric acid and bilirubin in periodontitis groupsas compared with non-periodontitis groups in both pregnant women with and without GD, while serum total protein decreasednon-significantly in periodontitis groups than in non-periodontitis. The results of this study support the hypothesis of the association of periodontal disease with GDM.
Keywords: Periodontitis, Gestational diabetes mellitus, serum antioxidants.

1. Introduction

Diabetes mellitus is a group of metabolic disease characterized by hyperglycemia resulted from defects in insulin secretion , insulin action, or both (ADA,2013).It is classified according to its etiology into; type 1,type 2,gestational diabetes (GDM) and other specific types(Negarato *et al*,2013).

Gestational diabetes is a condition of carbohydrate intolerance of varying severity hat begins or recognized during pregnancy (NIH, 2013).It may be related to oxidative stress and impaired antioxidant defenses(West 2000).Oxidative stress due to excessive Reactive oxygen species (ROS) and weakened antioxidant defense is casually associated with inflammation and inflammatory mediators (Singh *et al.*,2005).

Periodontal disease is a chronic inflammatory disease ,characterized by destruction of the tooth supporting structures (Pendyala *et al*.,2013), thatis initiated by sub-gingival plaque bio-film and an abnormal host response to specific bacteria and/or their products(Page and konrman,1997).The aberrant response is characterized by exaggerated inflammation, involving the release of excess proteolytic enzymes (Figueredo *et al.,*1999)and ROS by hyper-active/reactive neutrophils (Pendyala *et al.,*2013).

Many studies have been proved without a reason of doubt that periodontitis is an inflammatory disease that characterized by increased oxidative stress(Borges *et al*.,2007 and D'Aiuto *et al* 2010),and it is inversely associated with antioxidants(Iain *et al* .,2006 and Bijn *et al.,* 2014).

GDM occurs with variable severity in 3%-5% of all pregnancy and may be related to oxidative stress and impaired antioxidant defense (West, 2000).Overproduction of oxidizing molecules results in the progressive loss of pancreatic ß-cells depleting insulin levels (Soares *et al.,*2005).

Bilirubin, uric acid ,and total protein are considered a potent antioxidants (Prabhavathi *et al.,*2014, Abassi *et al.,* 2015, and Chaudhary *et al* 2015) ,having beneficial effects in diseases related to oxidative stress(Abraham *et al.,*2007 and Duann *et al.,* 2009).

Aim of the study

Association between periodontal disease and GDM remains a controversial topic, so the purpose of this study is to evaluate this association through the evaluation of some serum antioxidants: serum uric acid, bilirubin, and total protein in both pregnant women with and without GDM in relation to periodontal disease.

2. Subjects and method

2.1 Subjects:

Eighty pregnant women with age range of 22-32 years were included in this study who-attained diabetic scenter in maternity Hospital and pregnancy unit at health centers in Erbil city. These women were about 26-32weeks of gestation; according the last menstrual cycle or based on ultrasound examination. These pregnantwomen were divided into four groups:

The first group (G1) included 20 healthy pregnant women (control group). The second group (G2)

included 20 pregnant women with periodontal disease. The third group (G3) included 20 pregnant women with GDM. Finally the fourth group (G4) included 20 pregnant women with both GDM and periodontal disease. Ethical approval for this study was obtained from localized ethical committee.

Depending on the health document during pregnancy; the GDM pregnant women were diagnosed using oral glucose tolerance test (OGTT) basing on Carpenter and Constant criteria (Amiri *et al,* 2013).All the participants agreed to sign a consent form. Patients case history was recorded which included general information of the patient, medical history and drug history. Exclusion criteria included obese pregnant women (Body mass index more than 25 Kg/m2), pregnant women with systemic disease, and history of periodontal treatment in past 6months.

2.2 Methods:

Body mass index was calculated using the following formula (Park, 2005):BMI =Weight (Kg)/ (Height (m)^2.A full-mouth periodontal examination was performed for each pregnant woman by one periodontist. The measurements were taken at six sites per tooth (mesio-buccal, mesio-lingual, disto-buccal, disto-lingual, mid-buccaland mid-lingual), using manual UNC-15 periodontal probe and mouth mirror under ordinary light.

The periodontal status was diagnosed according to the clinical parameters only, avoiding using x- ray , since pregnant women cannot be exposed to radiographic examination. The clinical measures of periodontal conditions included; plaque index (PI), probing pocket depth (PPD)which represents the distance between the base of the pocket and the gingival margin, and clinical attachment level (CAL)which represents the distance between the base of the pocket and cement-enamel junction (Newman *et al*, 2012). Severity of PPD and CAL were estimated (total PPD/CAL divided by affected surface) (Bortold *et al*, 2003).

After periodontal examination, (5ml) Fasting blood sample was drawn from each subject, then the sample was centrifuged and the serum was separated, and transferred into a plain tube containing no anticoagulant and stored in an ice-box for transferring to chemical laboratory for the estimation of the following serum biochemical: glucose levels, HbA1c, uric acid, bilirubin, and total protein All biochemical parameters were determined by colorimetric methods using specific kits.

2.3 Statistical analysis:

Data were analyzed using the statistical package for social sciences (SPSS, Version 19). One way descriptive analysis was done to calculate mean ± SD. Analysis of variance (ANOVA) was used to compare among means of the studied groups. A post Hoc test (LSD) was used to find out significant differences between each two groups (out of the four study groups). A "P" value of ≤0.05 was considered statistically significant.

3. Results:

This study included 80 pregnant women that divided into four groups. The age, BMI, and gestational weeks were matched for these groups (table 1). The results showed that there were non-significant differences in the age ranges among the groups. In general the ages for all the groups were nearly in the range of (25.5 – 26) years. Regarding to the BMI values for the groups, the results indicated that non-significant differences in BMI values were found among the groups. In general the BMI values for all the groups were nearly24–25kg/m2.Concerning gestational weeks; a non-significant difference also was found among the groups (P >0.05).

The periodontal clinical parameters PPD, CAL are shown in figure (1); in which the PPD (G2 and G4:4.89±0.43, 5.45±0.5respectively) and CAL (G2 and G4:4.93±0.6, 5.58±0.43 respectively) were significantly higher in periodontitis groups when compared with non-periodontitis groups (PPD in G1 and G3:3.05±0.53,3.2±0.33,and CAL in G1 and G3 1.44±0.35, 1.53±0.42 respectively) for both pregnant women with and without GDM.

Figure (2) indicates the serum fasting glucose (SFG) levels for the groups. The results showed a significantlyhigh SFG levels in both GDM groups G3 andG4(154.30±38.38 and 165±11.68 mg/dl, respectively). Theblood sugar of these two groups were uncontrolled, this is according to their high serum HbA1c % values(7.21±0.8and 7.90±0.6 percentage respectively) as shown in figure (3).

The serum uric acid for the groups, are shown in figure (4).The results showed that; serum uric level was significantly lower in periodontitis group (G2), while its levels were high in G3. Serum bilirubin decreased significantly in periodontitis groups than non-periodontitis (Figure 5).While serum total protein decreasednon-significantly in periodontitis groups than in non-periodontitis as shown in (Figure 6).

4. Discussion

Chronic periodontitis is an inflammatory disease that affects the supporting tissues of teeth, it is initiated by specific bacteria within the plaque bio-film and progresses due to an abnormal inflammatory –immune response to those bacteria (Iain *et al.,* 2006). The aberrant response is characterized by exaggerated inflammation, involving the release of excess proteolytic enzymes and reactive oxygen species (ROS)by the hyper-active

/reactive neutrophils (Pendyala *et al*, 2013).

Oxidative stress is reported in periodontitis both locally and peripherally (serum) (Iain *et al.,* 2006).Oxidative stress, through the production of reactive oxygen species (ROS) and reactive nitrogen has been proposed as the root cause underlying the development of insulin resistance, β-cell dysfunction, impaired glucose tolerance (Maharjan *et al* 2008) .Oxidative stress due to excessive ROS and weakened antioxidant defense is causally associated with inflammation and inflammatory mediator(Singh *et al* 2005) .

More recently ,periodontitis has been recognized as a risk factor for certain systemic diseases where low-grade inflammation within the peripheral circulation is associated with the etiology of that disease or its progression(Iain *et al*2006).In previous cross-sectional or case-control studies, clinical periodontal disease has been associated with gestational diabetes mellitus(Dasanayake*et at* 2008) , therefore important to examine serum antioxidant concentrations in periodontal health/disease ,to determine whether serum antioxidant concentrations were associated with altered relative risk for GDM .In this study the serum level of uric acid, bilirubin and total protein were measured as these biochemicals considered as antioxidant agent (Prabhavathi *et al* 2014, ,Abassi *et al* 2015, Chauthary *et al* 2015).

Gestational diabetes is a disturbance of the glucose homeostasis in pregnancy. In gestational diabetes there is increased oxidative stress leading to generation of free radicals(Sujata *et al,*2012).

The result of this study showed that the pregnant women in group (1) and (3) are free from periodontitis while those in group (2) and (4) having periodontitis depending on measuring PPD and CAL. In this study a group of antioxidant measured due to the fact that antioxidant work in concert rather than from in isolation, by recycling each other from their oxidized counter parts.Therefore, measuring individual species imposes limitations(Iain *et al* 2006).

The level of uric acid, in this study was found to be decreased in pregnant women with periodontitis comparing to pregnant women free of periodontitis, this may be due to the decrease in the level of antioxidant agents as response to oxidative stress that resulted from periodontitis.This finding was in agreement with the results obtained by Sreeram *et al* 2013 who work on periodontitis generally. While Zieboltz *et al*.,2007 found that there is no significant differences in serum uric acid level between subjects with periodontitis and those without periodontitis . In pregnant women with GDM, the results showed that uric acid levels would be elevated, this could be explained by the fact that the hyperuricaemia may be a protective response, capable of opposing harmful effects of free radical activity and oxidative stress (Waring *et al*.,2000).

Bilirubin has been recognized as a substance with potent antioxidant properties (Libor Vitek, 2012) .The results of our study showed a negative association between bilirubin and periodontitis as its level increased in pregnant women free of periodontitis with and without GDM compared to pregnant women with periodontitis with and without GDM. The pregnant women with GDM showed a decrease in the level of bilirubin than pregnant women without GDM.This result may be attributed to the fact that both periodontitis and GDM is related to oxidative stress and impaired antioxidant defense(Borges *et al.,* 2007, D'Aiuto*et al.*2010).Our finding of depleted serum bilirubin in pregnant women with GDM and periodontitis(group4)compared to the other groups, supports this possibility and suggests that periodontitis has negative effect on the already compromised oxidative state of pregnant women with GDM.

Regarding total protein the results of this study showed that there is a slight decrease in levels of total protein in pregnant women with GDMand periodontitis than those without GDM and periodontitis, but the difference was non-significant. This result also could be explained by the fact that the level of this antioxidant decreased due to the oxidative stress and weekend antioxidant defense that is associated with inflammatory conditions, such as; GDM and periodontitis. The findings of this study coincide with the results of a studies measured total protein in subjects with and without periodontitis (Zieboltz *et al .,* 2007 and Rajesh *et al* .,2015),and pregnant women with and without GDM (Moastafavie *et al* 2003), where they didn't find statistic differences in total protein between those groups.

The relation between periodontal disease and pregnancy can be explained as the periodontal disease is a slowly progressive disease (Newman *et al*, 2012), which induces local and host immune response and is able to produce transient bacteremia (Garcia *et al*, 2000, Amar and Han, 2003).The link between pregnancy and periodontal inflammation has been known for many years, as a result of alteration in the composition of sub-gingival plaque that occurs during pregnanacy (Newman *et al*, 2012). Viable bacteria and bacterial products (e.g., lipopolysaccharide) from sub-gingival plaque and pro-inflammatory cytokines (TNF-α, IL-6, and C-reactive protein) from inflamed periodontal tissue, can enter circulation and trigger maternal systemic inflammatory response (Garcia *et al*, 2000, Amar and Han, 2003). It is known that pancreatic beta cell destruction can result from pro-inflammatory imbalance created by sustained elevations of cytokines (Moller, 2000), therefore maternal chronic periodontal disease could induce sustained systemic inflammatory response that may result in a state of insulin resistance with progressive loss of pancreatic β–cell depleting insulinlevels (Soares *et al.* 2005,Xiong*et al*, 2009).Furthermore, Reactive oxygen species (ROS) disrupt transmission pathways between the insulin receptor and the glucose transport system leads to on insulin resistance(:Kalaivanam *et al*., 2006).

5- Conclusion:

The results of this study supports the hypothesis of association between periodontal disease with GDM through the alteration of some serum antioxidants , such findings could serve as an alarm to treat periodontal disease in pregnant women carefully ,which might be effective in reducing GDM risk, as periodontitis is treatable ;more ever preventable.

References

1- American diabetes association: Diabetes care. (2013). 36, supplement 1, S67-S74.
2- Negarato CA, Tarizia O, Jovanovic L, Chinellato L M. (2013). Periodontal disease and diabetes melletes; J Applo Sci. 21(1):1-12
3- NIH Consensus Development Conference on Diagnosing Gestational Diabetes Mellitus.(2013). 29, (1).
4- West IC (2000).Radicals and oxidative stress.Diabet Med: 17: 171-80.
5- Singh U, Devaraj S and Jiala l (2005) Vitamins E, oxidative stress, and inflammation. *Annual Review of Nuutrition* 25 151-174.
6- PendyalaG, ThomasB, and Joshi S.(2013).Evaluation of total antioxidants capacity of saliva in type 2 diabetic pateints with and without periodontal disease: A case control study; *N Am J Med Sci.*5(1):51-57.
7- Page RC, Kornman K. (1997) The pathogenesis of human periodontitis: an introduction .*Periodontol 2000.;*14:9-11.
8- Figueredo CM, Gustafsson A ,Asman B, Bergstrom K. (1999).Increased release of elastate from in vitro activated peripheral neutrophils in patients with adult periodontitis.*J Clin Periontol*;26:206-11.
9- Borgest I Jr, MorieraEA, FilhoDW, deOliveiraTB, da Silva MB, Frode TS. (2007).Proinflammatory and oxidative stress markers in pateints with periodontal disease,Mediators.2007:45794.
10- D'Aiuto F, Nibali L, Parkar M, Patel K, Suvan J, Donnos N. (2010). Oxidative stress,systemic inflammation and sever periodontitis. *J Dent Res,89(11):1241-46.*
11- Iain L.C., Mike R, Dietrich T.(2006).The prevalence of inflammatory periodontitis is negatively associated with serum antioxidant concentration .*J. Nutr;*137:657-664.
12- Biju Thomas[1], Amita Rao[1], Ballamajalu Rajendra Prasad[1], Suchetha Kumari(2014). Serum levels of antioxidants and superoxide dismutase in periodontitis patients with diabetes type 2. J Indian Soc Periodontol;18(4):451-455
13- Soares AF, GuichardantM, CozzoneD, Bernoud N, Bouzaidi N, Lagarde M,and Geloen A.(2005).Effects of oxidative stress on adiponectin secretion and lactate production in 3T3-L1adipicytes.*Free Radic.BiolMed*;38:882-889
14- Prabhavathi K, Kundur M, Shashidar KN,and Harish R. (2014). Serum total bilirubin levels in diabetic retinopathy- A case control study .IOSR *Journal of pharmacy,*4(8):01-06.
15- Abbasi A, PetronellaE, CorpeleijinE, Ron T.,Gansevoort,RijkO,HansL,HarstP,RonaldP,NavisG,BehroozZ,Stephan J.(2015).Bilirubin as apotential causal factor in type 2 diabetes risk :a Mendelian randomization study. *Diabetes;*64(4):1459-1469.
16- Chaudary N, Chapagain NS, Baral RK, TimilsinaS., and Tiwari S.(2015).Evaluation of oxidative stress and antioxidant in pateints with type 2 diabetes mellitus and its correlation with glycosylated hemoglobin.Int J Med Health Sci;4(1):7-11.
17- Abraham NG, AsilaA, Drummond G, Peterson S.(2007).Hemeoxygenase-1 gene therapy :recent advances and therapeutic applications. *Curr Gene Ther*;;7:89-108.
18- Duann P, Lianos EA. (2009).GEC-targeted HO-1 expression reduces proteinuria in glomerular immune injury.*Am J Physol Renal Physiol;*297:F629-638.
19- Amiri FN, Basirat B, Omidvar S, Sharbatdaran M,Tilakin KH, and Pouramir M.(2013).comparison of the serum iron,ferritin level and total iron-binding capacity between pregnant women with and without gestational diabetes .*J Nat Sci Biol Med ;*4(2):303-305.
20- Park S (2005).PARK's text book of preventive and social medicin.18th Edition.Banarsidas B hanotpublishers.1167, Prem Nagar, Jabalpur, 482 001(India):317-318.
21- Newman MG, Taki HH, Klokkevold PR. (2012). Carranza'scinical periodontology 11[Th] edition
ELSEVIER SAUNDERS, pages: 160,353,410,415.
22- Bortold P, Ishikawa I., and DeDeios N (2003). Current trends in periodontal diagnosis, disease Recognition and management; Proceedings of the 5th Asian pacific society of periodontology meeting ,Cebu.the Philippines.1-2 December
23- Maharjan BR, Jha JC, Adhikari D, Vishwanath P, Baxi J, Alurkar VM , Singh PP.A study of oxidative stress, antioxidant status and lipid profile in diabetic patient in the western region of Nepal .Kathmandu University Medical J2008; 21(6):16-22.
24- A.P. Dasanayake1, N. Chhun, A.C.R., Tanner, R.G., Craig, M.J. Lee, A.F. Moore1, and
R.G. Norman1 Periodontal Pathogens and Gestational Diabetes Mellitus *J Dent Res*. 2008 April ; 87(4): 328–

333.
25- Sujata M, Anitha M, Paraveen S, Suresh.S., Kanakannavar , Vishwanatha H.L.(2012).A Study of oxidative stress in gestational diabetes mellitus .An observational study at tertiary centre.Asian journal of medical research.1(1):17-21.
26- Sreeram M., Suryakar AN., Dani NH., Kalkarni MB.(2013).Is periodontitis associated with decreased glomerular filteration rate with oxidative stress as an important link?. *IOSR-JDMS*; 12(3):41-47.
27- Zieblotz D., Gesa C., Horneker E., Rainer F.(2007).Periodontal findings and blood analysis of blood donors :Pilot study. *Revista Românà De Stomatologie; LIII* (3):151-157.
28- Waring W S., Webb D S., Maxwell S R.(2000).Uric acid as a risk factor for cardiovascular disease. *Q J Med*; 93:707-13.
29- Libor Vitek. (2012).The role of bilirubin in diabetes metabolic syndrum,and cardiovascular diseases.Frontiers in pharmacology.3(55):1-7.
30- Rajesh KS., Sporthi KH., Hegde S., and Arun Kumar MS.(2015).Evaluation of systemic inflammatory markers in clinically healthy subjects and chronic periodontitis pateints. *J of Dent and Med Sci*;14(3):1-6.
31- Moastavie E., Nakhjavani M. , and Niroomanesh SH.(2003).Hypomagnesaemia and gestational diabetes .Iranian Journal of endocrinology and metabolism ;5(2):111-119.
32- Garcia RI, Henshaw MM, Krall EA (2000). Relationship between periodontal disease and systemic health; Periodontol. 25:21–36.
33- Amar S, Han X (2003). The impact of periodontal infection on systemic diseases; Med Sci Monit.9:RA291–299.
34- Moller DE (2000) Potential role of TNF-alpha in the pathogenesis of insulin resistance and type 2 diabetes; Trends Endocrinol Metab. 11:212–217.
35- Xiong X, Karen E, Elkind-Hirsch, VastardisS, Delaroza R, Prijian G, Buekens P (2009). Periodontal disease is associated with gestational diabetes mellitus: a case-control study; J Periodontol. 80(11):1742–1749.
36- Kalaivanam K.N, Dharmalingam M, Marcus S.R.(2006).Lipid Peroxidation in type 2 Diabetesmellitus, *Int. J Diab Dev Ctries.*;26(1):30-32

Table (1): Characteristics of the studied groups, including; age, BMI, and gestational week

Variables	Groups	N	Mean	SD	p (ANOVA)	Significance by LSD
AGE	G1 **G2** **G3** **G4**	20 20 20 20	26.15 26.25 25.80 26.10	4.31 3.64 4.05 3.61	.986	NA
MI	**G1** **G2** **G3** **G4**	20 20 20 20	24.73 24.57 24.79 24.83	.34 .36 .41 .27	.106	NA
WEEKS	**G1** **G2** **G3** **G4**	20 20 20 20	29.13 28.87 28.65 28.36	1.33 1.32 1.98 1.50	.450	NA

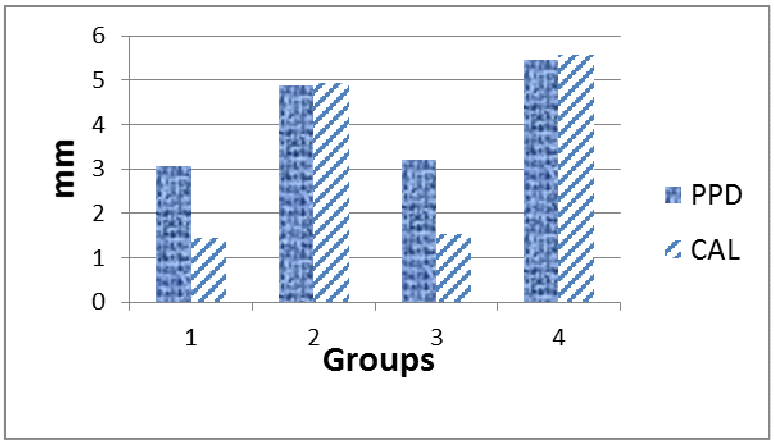

Figure (1): The clinical measures of periodontal conditions including; probing pocket depth (PPD) and clinical attachment level (CAL).

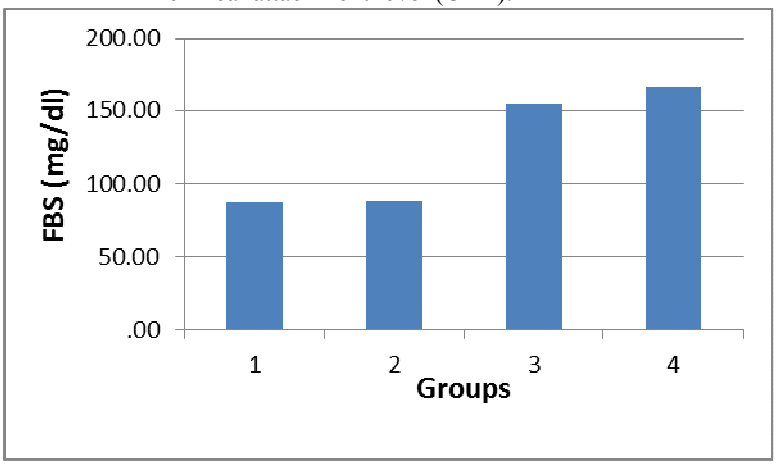

Figure (2): Serum fasting glucose levels for the groups.

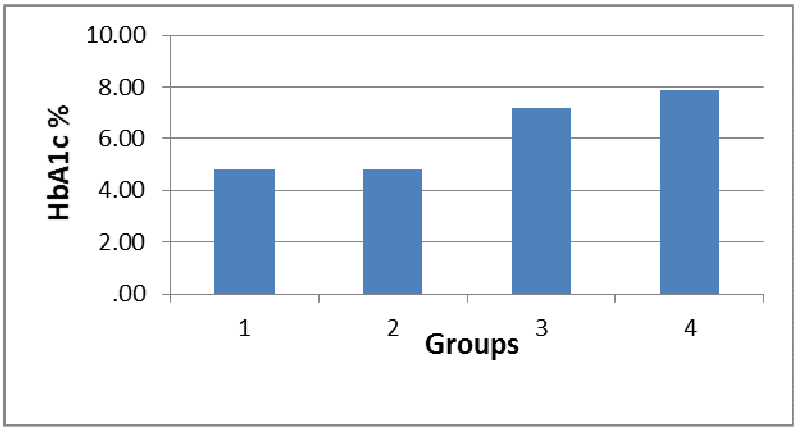

Figure (3): The percentage of glycosylated hemoglobin (HbA1c %) for the groups.

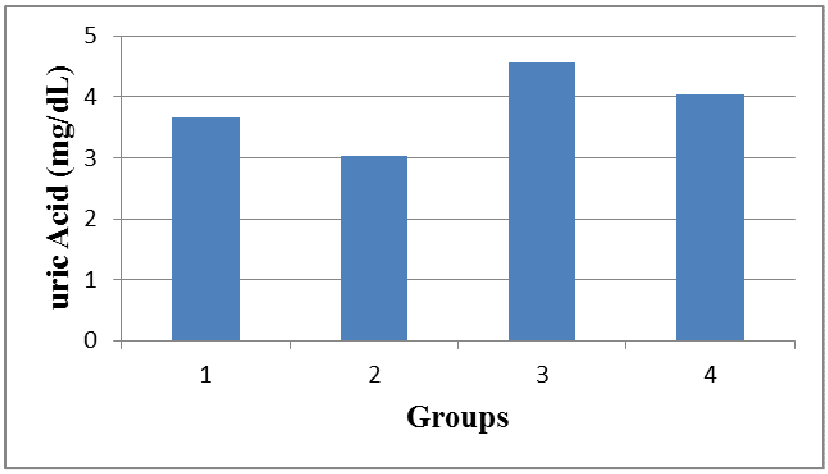

Figure (4): Serum uric acid levels for the groups.

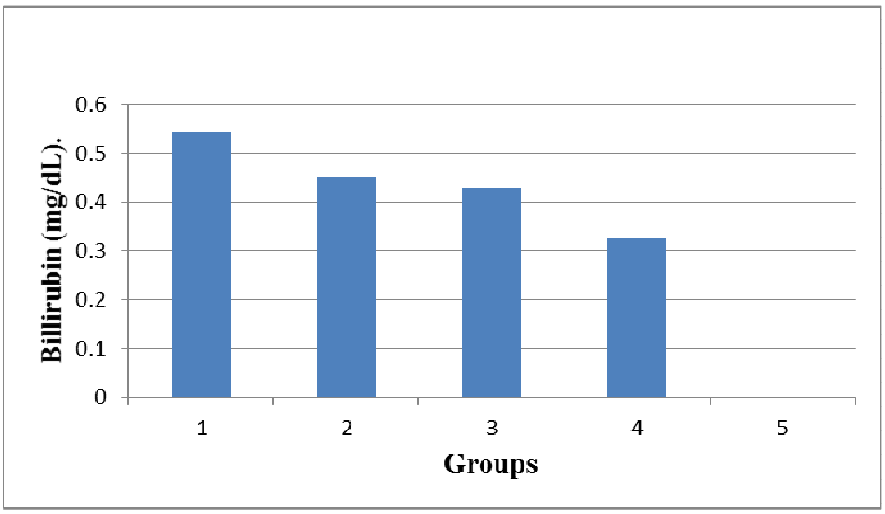

Figure (5): Serum bilirubin levels for the groups.

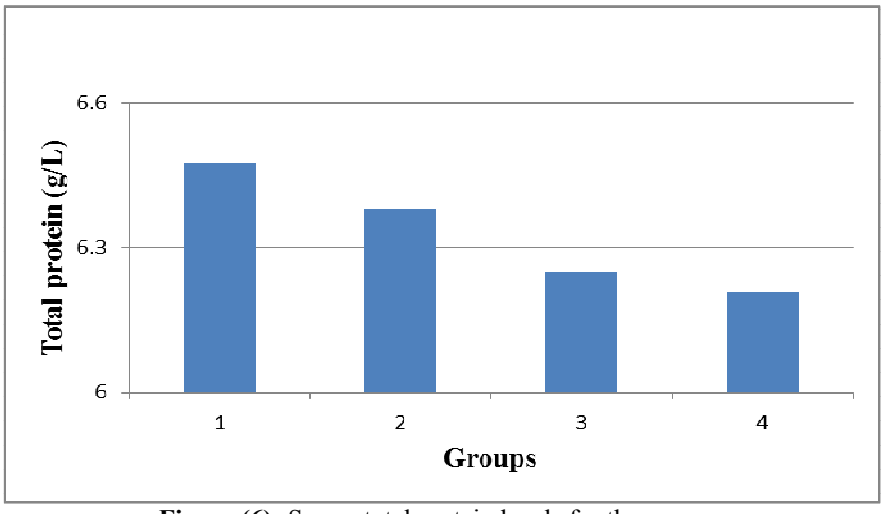

Figure (6): Serum total protein levels for the groups.

The IISTE is a pioneer in the Open-Access hosting service and academic event management. The aim of the firm is Accelerating Global Knowledge Sharing.

More information about the firm can be found on the homepage:
http://www.iiste.org

CALL FOR JOURNAL PAPERS

There are more than 30 peer-reviewed academic journals hosted under the hosting platform.

Prospective authors of journals can find the submission instruction on the following page: http://www.iiste.org/journals/ All the journals articles are available online to the readers all over the world without financial, legal, or technical barriers other than those inseparable from gaining access to the internet itself. Paper version of the journals is also available upon request of readers and authors.

MORE RESOURCES

Book publication information: http://www.iiste.org/book/

Academic conference: http://www.iiste.org/conference/upcoming-conferences-call-for-paper/

IISTE Knowledge Sharing Partners

EBSCO, Index Copernicus, Ulrich's Periodicals Directory, JournalTOCS, PKP Open Archives Harvester, Bielefeld Academic Search Engine, Elektronische Zeitschriftenbibliothek EZB, Open J-Gate, OCLC WorldCat, Universe Digtial Library , NewJour, Google Scholar