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CORRELATION BETWEEN HIGH SENSITIVITY C-REACTIVE PROTEIN AND GLYCOSYLATED HAEMOGLOBIN IN DIABETICS, PREDIABETICS AND NON-DIABETICS.

Diabetology

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ABSTRACT

Background- Estimation and association of high-sensitivity C-reactive protein (hs-CRP) and glycated haemoglobin (HbA1c) in diabetic patients has been studied extensively. The objectives were to estimate and correlate hs-CRP with HbA1c and also to correlate hs-CRP and HbA1c with body mass index (BMI) and waist-hip ratio(WHR) in diabetic, pre-diabetic and non-diabetic group. **Methodology-** The cross sectional comparative study was done on 93 patients of which 30 were known diabetic, 33 prediabetic patients with family history of diabetes mellitus, obesity and hypertension and 30 non-diabetic patients without family history of diabetes mellitus, obesity and hypertension. Anthropometric measurements were taken and body mass index (BMI) and waist hip ratio(WHR) were calculated. Levels of serum highly sensitive C reactive protein (hs-CRP) and glycated haemoglobin (HbA1c) were estimated in all the groups. **Results-** Although statistically insignificant, mean BMI and hs-CRP were higher in pre-diabetic group and WHR was higher in diabetic group (P>0.05). Mean HbA1c was significantly high in diabetic (P<0.01). Significant positive correlation was found between hs-CRP and HbA1c in prediabetic groups (r=0.3545; p=0.0429). BMI was significantly correlated with HbA1c in diabetics and pre-diabetics (r=-0.408, P=0.025; r=0.452, P=0.008 respectively). **Conclusion-** Risk of developing T2DM in near future can be predicted by estimating hs-CRP and BMI of an individual. However, estimation of WHR and HbA1c can contribute significantly in glycemic management to avoid the further complications among diabetic patients.

KEYWORDS

C-reactive proteins, diabetes mellitus, inflammation, glucose intolerance, pre-diabetic.

INTRODUCTION

India ranks second in the prevalence of diabetes mellitus after China. [1] The International Diabetes Federation (IDF) has stated that in 2015, around 415 million people had Diabetes mellitus (DM) of which, India accounted for 69.1 million people. IDF has also predicted the rise in this number to be around 642 million by the year 2040. [1]In India, the prevalence of DM ranges from 5–17%. The urban regions and the southern most parts of the country appear to be the major contributors.[2]Rapid social and cultural changes such as increased urbanization, changes in diet and lifestyle, reduced physical activity, and ageing population has resulted in an increase in the prevalence of DM.[3]Indians are also reported to have a greater degree of insulin resistance and a greater genetic predisposition to diabetes.[4] Insulin resistance (IR) contributes widely to the development of type 2 DM (T2DM).[5] Hyperglycemia may lead to micro and macro vascular complications or inflammation if the blood sugar is not controlled.[6] In addition, inflammation has been shown to play a key role in the pathogenesis of T2DM.[7] Previous researches have reported the relation between some inflammatory biomarkers (PAI-1, IL-6, fibrinogen and High sensitivity C-reactive protein(hs-CRP)) and the development of T2DM.[8-10]Also, increase in serum hs-CRP level inT2DM and impaired glucose tolerance (IGT) has been studied which can be considered as an indicator for the development of T2DM.[8-11] Although WHO recommends the conventional oral glucose tolerance test (OGTT) as the gold standard, estimation of glycated hemoglobin (HbA1c) and fasting plasma glucose (FPG) are simpler, cost effective and convenient diagnostic methods used to diagnose T2DM.[8,12-15]The association of anthropometric measurements such as body mass index (BMI) and waist-hip ratio(WHR) with the development of DM has also been reported.[16-19]Similar studies among prediabetic patients which would be beneficial in preventing the onset are limited and present an area for research. Based on this premise, the study was designed to estimate and correlate hs-CRP with HbA1c in diabetics, prediabetics and non-diabetic individuals and to correlate hs-CRP and HbA1c with anthropometric measurements such as BMI and WHR in the three groups.

Methodology

The cross-sectional comparative study was conducted from October 2017 to May 2019. The study was approved by the Institutional Ethics and Research Committee (DMCK/139/2017) The purpose and details of the methods used in the study were explained to all the participants. A written informed consent was obtained prior to the study. A total of 93 patients between 25-70 years of age of which 30 were diabetic with clinically known type 2 diabetes mellitus (DM), 33 with family history of DM, Obesity and Hypertension (considered as pre-diabetic) and 30 healthy non-diabetic patients without family history of DM, Obesity and Hypertension (as controls) were included. Patients with insulin dependent diabetes mellitus (IDDM) and with chronic inflammatory diseases such as rheumatoid arthritis (RA), Osteoarthritis (OA), systemic lupus erythematosus (SLE), autoimmune diseases, tuberculosis, stroke, hepatic or renal diseases, malignancy or undergoing chemotherapy/radiotherapy and pregnant women were excluded.

Anthropometric measurements such as height, weight, hip and waist girth of all the patients were recorded to calculate body mass index(BMI) and waist hip ratio(WHR). Fasting venous blood was collected (5ml) and levels of Glycated Hemoglobin (HbA1c) and high sensitivity C – Reactive Protein (hs-CRP) were estimated by high performance liquid chromatography Method, Immunoturbidimetric or Latex Method respectively. [20,21]

Statistical Analysis- All the data collected was statistically analyzed in R software (3.6.1). Kruskal-Wallis Test was used to find significant difference between the three groups. In the presence of significant difference between the three groups, post hoc analysis (multiple comparison) was performed by Dunn-test. Correlations were assessed by Pearson correlation test.

RESULTS-

Demographic and clinical data of all the participants is given in table 1.

Table 1- Demographic And Clinical Data Of Sample (n=93)

Variables	Diabetics (n=30)	Pre-diabetics (n=33)	Non-diabetics (n=30)
Mean age (years)	53.3 ± 7.05	49 ± 10.43	41.3 ± 9.53
Gender			
Male	20	15	13
Female	10	18	17
Mean BMI (kg/m2)	25.73±3.37	26.85±4.65	24.98±3.96
Variables	**Diabetics (n=30)**	**Pre-diabetics (n=33)**	**Non-diabetics (n=30)**
Mean WHR	0.91±0.11	0.89±0.15	0.88±0.15
Mean hs-CRP (mg/L)	2.68 ± 1.45	3.96 ± 5.27	1.89 ± 1.08
Mean HbA1c (%)	9.59 ± 2.29	6.06 ± 0.25	5.25 ± 0.21

BMI- Body Mass Index; WHR- Waist Hip Ratio; hs-CRP- Highly Sensitive C-Reactive Protein; HbA1c- Glycated Hemoglobin

Table 2- Shows biochemical parameters and anthropometric parameters in diabetic, pre-diabetic and non-diabetic subjects.

Parameters	Groups	No. of Subjects(N)	Mean± SD	SEM	95% CI
BMI	1	30	25.739±3.37	0.61	24.47-27.06
	2	33	26.85±4.65	0.8	25.20-28.49
	3	30	24.985±3.967	0.72	23.50-24.465
WHR	1	30	0.908±0.11	0.02	0.86-0.95
	2	33	0.8857±0.15	0.026	0.83-0.94
	3	30	0.8806±0.155	0.028	0.57-1.19
HbA1c	1	30	9.59±2.29	2.292	8.737-10.45
	2	33	6.06±0.25	0.044	5.976-6.157
	3	30	5.25±0.209	0.038	5.17-5.328
hs-CRP	1	30	2.686±1.45	0.265	2.14-3.23
	2	33	3.96±5.27	0.917	2.09-5.83
	3	30	1.88±1.08	0.197	1.48-2.29

Values where expressed as Mean ±SD
Gr. 1= Diabetic, Gr.2= Pre-diabetic, Gr.3= Non-diabetic
SEM= Structural Equation Modeling.
SD= Standard Deviation
CI= Confidence Interval

Table no 3- Mean Values Of BMI, WHR, hs- CRP & HbA1c with Diabetic, Pre-diabetic patients and non- diabetics.

Anthropometric & biochemical parameters	Groups	Count	(Mean ±SD)	P Value		
				DM	PDM	NDM
BMI	Diabetic	30	25.74± 3.37	-	0.28	-
	Pre-diabetic	33	26.85± 4.41	-	-	0.09
	Non-diabetic	30	24.99± 3.97	0.43	-	-
WHR	Diabetic	30	0.91+0. 11	-	<0.000 1**	-
	Pre-diabetic	33	0.89+0. 15	-	-	<0.000 1**
	Non-diabetic	30	0.88+0. 16	<0.00 01**	-	-
hs-CRP	Diabetic	30	2.69±1. 45	-	<0.000 1**	-
	Pre-diabetic	33	4.71±5. 25	-	-	<0.000 1**
	Non-diabetic	30	1.88±1. 08	<0.00 01**	-	-
HbA1c	Diabetic	30	9.59±2. 29	-	<0.000 1**	-
	Pre-diabetic	33	6.06±0. 25	-	-	<0.000 1**
	Non-diabetic	30	5.25±0. 21	<0.00 01**	-	-

No significant difference was observed in mean BMI among the three groups (P>0.05). But, there was significant difference in mean HbA1c, WHR and hs-CRP among the three groups(P<0.01) (table 3). Further, Dunn test revealed significant differences in mean HbA1c between diabetic and pre-diabetic(P<0.001), pre-diabetic and non-diabetic (P<0.001) and non-diabetic and diabetic patients(P<0.001).

Table no 4- Correlation between different parameters with their groups

Parameters	Groups	r Value	P value	95% CI
hs-CRP and BMI	1	0.23	0.2	-0.13-0.55
	2	0.32	0.07	-0.025-0.59
	3	0.27	0.13	-0.09-0.58
hs-CRP and WHR	1	-0.23	0.21	-0.54-0.14
	2	-0.17	0.32	-0.49-0.17
	3	-0.13	0.48	-0.47-0.24
HbA1c and BMI	1	-0.4	0.025	-0.67-0.05
	2	0.45	0.01	-0.129-0.688
	3	0.076	0.01	-0.29-0.42
HbA1c and WHR	1	0.38	0.034	0.050-0.65
	2	-0.12	0.49	-0.44-0.23
	3	-0.12	0.5	-0.46-0.24
HbA1c and hs-CRP	1	0.16	0.37	-0.2-0.49
	2	0.35	0.042	0.012-0.62
	3	-0.14	0.43	-0.48-0.22

r = Correlation coefficient, **P<0.05 considered statistically significant,** CI= Confidence Interval

No significant correlation was seen between BMI and hs-CRP in any group (P>0.05). A significant correlation was also noted between BMI and HbA1c of both diabetic, pre-diabetic patients and non-diabetic control (r=0.40, P=0.03; r=0.45, P=0.01; r=0.76, P=0.01 respectively). No significant correlation was seen between WHR and hs-CRP in any of the groups (P>0.05). However, there was a significant positive correlation between WHR and HbA1c (r=0.38, P=0.034). Positive correlation was found between hs-CRP and HbA1c in diabetic and pre-diabetic groups (r=0.16; r=0.35 respectively). This correlation was statistically significant in the pre-diabetic group (P=0.04).

DISCUSSION

Diabetes Mellitus is one of the leading causes of morbidity and mortality worldwide. It has a resounding impact on the metabolism of the individual. Hyperglycemia increases concentration of end products resulting from advanced glycation. Further, this end product activates macrophages and increases the oxidative stress. This in turn induces inflammation and induces the synthesis of cytokines such as Interleukin-1, 6 and tumor necrosis factor(TNF) which in turn leads to increase in the serum hs-CRP level among diabetics. [22-24] Elevation in the level of serum hs-CRP also seems to be associated with cytokines derived from adipose tissue. [25] The possible role of adipose tissue leading to inflammation in diabetic and pre-diabetic patients is poorly understood. Studies imply that increase in hs-CRP level among pre-diabetic patients marks the disease process. [26]. Level of HbA1c increased significantly in diabetic patients compared to pre-diabetic and non-diabetic patients. [27-28] HbA1c estimation has gained importance due to the inconvenience associated with OGTT and measuring fasting blood glucose. It also has a huge advantage in that it signifies the average blood glucose level of over 8-12 weeks. The fact that it does not need any special preparation (fasting) and can be performed any time of the day has made it the method of choice in the diagnosis of diabetes. Although, the importance of HbA1c in the diagnosis and management of Diabetes is established, it is not routinely used in many parts of the world. [29]

Although not statistically significant, positive correlation was found between hs-CRP and HbA1c in the diabetic and pre-diabetic group which can be attributed to the association of hyperglycemia and inflammation. [26,30-31]

Although the difference was not statistically significant, BMI was high in pre-diabetic and diabetic patients (P=0.28). This concurs with the previous study reporting the connection of BMI with DM and stating that overweight and obese people are at a risk of diabetes. [16] Despite this, there was no significant correlation between BMI and hs-CRP in pre-diabetic patients (r=0.32, P=0.07). However, BMI significantly correlated with HbA1c of both diabetic, pre-diabetic patients and non-diabetics control (r=-0.40, P=0.025; r=0.45, P=0.01; r=0.076, P=0.01 respectively). This contradicts previous reports. [32]

Despite being considered the most reliable anthropometric factor in detecting the risk of diabetes, WHR didnot significantly correlate with hs-CRP in any of the groups (P>0.05) However, a significant correlation of WHR with HbA1c in diabetic patients was noted. [33-34] All

the above findings indicate that estimation of hs-CRP, HbA1c and BMI could help in determining the risk of developing DM.

CONCLUSION

Mean BMI and hs-CRP are comparatively higher in pre-diabetic patients while mean WHR and HbA1c are higher in diabetic patients. Evaluation of these factors can contribute towards identifying the risk of developing DM among individuals and management of blood sugar levels among diabetic patients to reduce complications.

REFERENCES

1. International Diabetes Federation. IDF Diabetic Atlas 7th Edition. [Internet] Available from: http://www.idf.org/idf-diabetes-atlas-seventh-edition Accessed 30 Aug 2016
2. Tripathy JP, Thakur JS, Jeet G, Chawla S, Jain S, Pal A, Prasad R, Saran R. Prevalence and risk factors of diabetes in a large community-based study in North India: results from a STEPS survey in Punjab, India. Diabetology & metabolic syndrome. 2017 Dec;9(1):8.
3. Mendenhall E, Shivashankar R, Tandon N, Ali MK, Narayan KMV, Prabhakaran D. Stress and diabetes in socioeconomic context: a qualitative study of urban Indians. Soc Sci Med. 2012;75(12):2522–9.
4. Mohan V. Why are Indians more prone to diabetes? J Assoc Physicians India. 200452:468–74
5. Tutuncu Y, Satman I, Celik S, Dinccag N, Karsidag K, Telci A, Genc S, Issever H, Tuomilehto J, Omer B. A comparison of hs-CRP levels in new diabetes groups diagnosed based on FPG, 2-hPG, or HbA1c criteria. J Diabetes Res. 2016;2016.
6. Saudek CD, Kalyani RR, Derr RL. Assessment of Glycemia in Diabetes Mellitus: Hemoglobin A. JAPI. 2005; 53.
7. Naik M, Kanjani I, Co-Relation of High Sensitivity C-Reactive Protein (hs-CRP) with HbA1C in Patients with Type 2 Diabetes Mellitus, Int J Sci Res (IJSR), 2018,7(1): 952-54
8. Genuth S, Alberti KG, Bennett P, Buse J, DeFronzo R, Kahn R, Kitzmiller J, Knowler WC, Lebovitz H, Lernmark A, Nathan D. Follow-up report on the diagnosis of diabetes mellitus. Diabetes care. 2003 ;26(11):3160-8.
9. De Rekeneire N., Peila R., Ding J., et al. Diabetes, hyperglycemia, and inflammation in older individuals: the health, aging and body composition stud. Diabetes Care. 2006;29(8):1902–1908.
10. Trpkovic A, Stanimirovic J, Resanovic I, Otasevic P, Jevremovic D, Djordje R, R Isenovic E. High Sensitivity C-reactive Protein and Cardiovascular Risk Prediction. Current Pharmaceutical Analysis. 2015 Feb 1;11(1):60-5.
11. Schmidt M. I., Duncan B. B., Sharrett A. R., et al. Markers of inflammation and prediction of diabetes mellitus in adults (Atherosclerosis Risk in Communities study): a cohort study. The Lancet. 1999;353(9165):1649–1652.
12. The International Expert Committee. International expert committee report on the role of the A1C assay in the diagnosis of diabetes. Diabetes Care. 2009;32(7):1327–1334.
13. World Health Organization. World Health Statistics 2011. Geneva, Switzerland: WHO Press; 2011.
14. World Health Organization Europe. The European Health Report 2009: Health and Health Systems. Copenhagen, Denmark: WHO Regional Office for Europe; 2009.
15. Speeckaert M., Van Biesen W., Delanghe J., et al. Are there better alternatives than haemoglobin A1c to estimate glycaemic control in the chronic kidney disease population? Nephrol Dial Transplan. 2014;29(12):2167–2177
16. Ni Mhurchu C, Parag V, Nakamara M, Patel A, Rodgers A, Lam TH. Body Mass index and risk of diabetes mellitus in the Asia-Pacific region. Asia Pac. J. Clin. Nutr. 2006:15(2): 127-133
17. Cheng CH, Ho CC, Yang CF, Huang YC, Lai CH, Liaw YP. Waist-to-hip ratio is a better anthropometric index than body mass index for predicting the risk of type 2 diabetes in Taiwanese population. Nutr Res. 2010; 30:585–93
18. Hajian-Tilaki K, Heidori B. Is waist circumference a better predictor of diabetes than body mass index or waist-to-height ratio in Iranian adults? Int J Prev Med. 2015; 6:5
19. Altayeb NM. Evaluation of High Sensitive C Reactive Protein Level in Type II Diabetic Sudanese Patients in Khartoum State (Doctoral dissertation, Sudan University of Science and Technology)2015.
20. Estimation of HbA1c by HPLC assay by use only with the Bio-Rad D-10 Hemoglobin Testing System, run on HPLC
21. Estimation of hs-CRP by immunoturbidimetric assay by using Cobas c 311/501 analyzers: (CRPHS: CAN 217 product analysis sheet)
22. Gohel MG, Chacko AN. Serum GGT activity and hs-CRP level in patients with type 2 diabetes mellitus with good and poor glycemic control: An evidence linking oxidative stress, inflammation and glycemic control. J Diabe Metabolic Dis. 2013;12:56.
23. Kashinakunti SV, Rangappa M, Kallaganada GS. International J Biochem Res Rev. 2016;11(4): 1-8.
24. Yan SF, Ramasamy R., Naka Y, Schmidt AM. Glycation, Inflammation, and RAGE. A Scaffold for the Macrovascular Complications of Diabetes and Beyond. Circ Res. 2003; 93: 1159–1169
25. Alexandraki K, Piperi C, Kalofoutis C, Alaveras A, Kalofoutis A. Inflammatory process in type 2 diabetes: The role of cytokines. Ann N Y Acad Sci. 2006; 1084: 89-117
26. Ravish H, Mohan Kumar R. To study the Serum levels of hs-CRP in Pre-diabetes Mellitus patients and to compare that of normal subjects. JEBMH, Dec.2015; 55(2):8806-8809
27. Emily Downward (2018): New (More Moderate) Guidelines for HbA1c Levels. Available from- https://type2diabetes.com/news/new-guidelines-hba1c-levels/
28. Joe Leech, Dietitian (2018): HbA1c and The "Normal" HbA1c Range: Explained for Complete Newbies.[Internet] Available from-https://www.dietvsdisease.org/normal-hba1c-range/.
29. World Health Organization. Use of glycated haemoglobin (HbA1c) in diagnosis of diabetes mellitus: abbreviated report of a WHO consultation. World Health Organization; 2011.
30. Takashi Motomura, Maki Okamoto, Tetsuhiro Kitamura et al., 2009: Effects of Pitavastatin on Serum Lipids and High Sensitivity C-Reactive Protein in Type 2 Diabetic Patients. Journal of Atherosclerosis and Thrombosis, March 2009; 16(5):546-552
31. Sarinn apakom V and Wanicagool W, (2008). Association between hs-CRP and HbA1c in overweight type 2 diabetic female patients, The FASEB Journal. 2008; 22:1098-3
32. Geetha Bhaktha, Manjula Shantaram, Shivananda Nayak, Nagendra S: Relationship of hs-CRP level in Diabetic Persons Free From Micro and Macrovascular Disease. Int. J. Res. Dev. Pharm. L. Sci., 2014, 3(4), 1070-1073 .
33. Vazquez G, Duval S, Jacobs DR Jr, Silventoinen K. Comparison of body mass index, waist circumference, and waist/hip ratio in predicting incident diabetes: a meta.analysis. Epidemiol Rev. 2007; 29:115-28.
34. Huxley R, Barzi F, Lee CM, Lear S, Shaw J, Lam TH, Caterson I, et al. Waist circumference thresholds provide an accurate and widely applicable method for the discrimination of diabetes. Diabetes Care. 2007; 30(12):3116-8.