BJMHR
British Journal of Medical and Health Research
Journal home page: www.bjmhr.com

# Association of Fasting Plasma Glucose with Hs-CRP and Some Other Cardio Metabolic Parameters in Middle Aged Bangladeshi Population

**Rehnuma B*[1], Eva SN[2], Ibrahim M[1], Nasir TA[1]**
*1. Clinical Biochemistry, Lab Medicine Department, Apollo Hospitals Dhaka.*
*2. Biochemistry, Lab Medicine Department, United Hospital Ltd, Dhaka*

## ABSTRACT

Type 2 diabetes is not one disease but rather a heterogenous group of syndromes characterized by elevation of fasting blood glucose. Highly sensitive C-reactive protein (Hs-CRP) is an acute phase reactant and a sensitive marker of inflammation. Hyperglycemia can potentially promote the production of Hs-CRP. The aim of this study was to correlate the association of fasting blood glucose with Hs-CRP and some other cardio metabolic concentrations. A total number of 355 adults, age 30-60 yrs, subjects were recruited in the study. Of them 192 subjects was non diabetic (control) group and 163 was diabetic (study) group. Vital statistics were taken along with measurement of blood glucose, triglyceride, total cholesterol, high density lipoprotein, low density lipoprotein and Hs-CRP levels. Data were analyzed using statistical Package for Social Program (SPSS) for Windows version 17. In comparison to non diabetic subjects, diabetic are significantly older (P=0.001), have higher BMI (P=0.001), higher waist hip ratio (P=0.042) and higher body fat mass% (P<0.0001). Systolic blood pressure is high in diabetic subjects but not statistically up to significant level but diastolic blood pressure is high (P=0.016). In biochemical parameters Triglyceride (P=0.001) and Hs-CRP (P<0.001) are significantly higher and High Density lipoproteins (HDLs) are significantly lower (P=0.030) in diabetic subjects. Anthropometric parameters are found to be high in diabetic subjects compared to non diabetic subjects. High level of Hs-CRP, Triglyceride and low level of HDL-c is also observed in diabetic subjects. Literature is reviewed accordingly.

**Keywords:** High sensitive C-reactive protein (Hs-CRP), Diabetes mellitus, biochemical parameters, Lipids.

*Corresponding Author Email: planet_behterin@yahoo.com
Received 26 August 2015, Accepted 03 September 2015,

Please cite this article as: Rehnuma B *et al*., Association of Fasting Plasma Glucose with Hs-CRP and Some Other Cardio Metabolic Parameters in Middle Aged Bangladeshi Population. British Journal of Medical and Health Research 2015.

## INTRODUCTION

Diabetes is a metabolic disorder with inappropriate hyperglycemia either due to an absolute or relative deficiency of insulin secretion or reduction in the biologic effectiveness of insulin or both. It is also associated with disturbances concerned with carbohydrate, protein and fat metabolism. The decreased uptake of glucose into muscle and adipose tissue leads to chronic extracellular hyperglycemia which result in tissue damage and chronic vascular complications[1, 2]. C-reactive protein (CRP) is an inflammatory marker whose expression is markedly up regulated during inflammation[3]. It is the acute phase protein synthesized in the liver and regulated to a large extend by proinflammatory cytokine interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α)[4, 5]. Recent prospective studies have demonstrated that subjects with low grade inflammation have a higher risk of cardiovasular diseases[6-8]. Several lines of evidence suggest that elevation of CRP may reflect not only local inflammation at atherosclerotic lesions but also systemic abnormalities related to insulin resistance, such as increase in fasting insulin, body mass index (BMI), systolic blood pressure and triglyceride (TG) as well as decrease in high density lipoprotein cholesterol (HDL-c)[9, 10, 11]. Among several markers of inflammation, Hs–CRP is found to be significant in people with diabetes. Hyperglycemia is an associated factor to the increase of serum CRP levels in un-controlled type II diabetic subjects[12]. Several studies demonstrate that Hs-CRP remained a significant predictor of diabetes risk even after adjusting with body mass index, family history of diabetes mellitus, smoking and other factors [13]. In people with diabetes, CRP levels is highest tertile (> 0.28 mg/dl) were associated with a 2 fold increase in CV mortality after adjusting for age, sex and glucose tolerance tests[14, 15, 16]. Hypertensive patients with Diabetes had higher levels of Hs-CRP, a circulating inflammatory marker, than normal subjects. This finding suggests that patients with two associated diseases have a more active inflammatory CRP; a pentameric protein produced by the liver has emerged as the ‘golden marker for inflammation’. Studies have shown high level of Hs-CRP in subjects with type 2 diabetes mellitus and dyslipidemia. The present study was thus conducted with an aim to see the relationship of high sensitivity CRP (Hs-CRP) levels with various anthropometric as well as metabolic parameters in subjects with and without diabetes.

## MATERIALS AND METHOD

An invitation was made to the volunteer of the study through personal contact to report in the department of Biochemistry and Physiology, BIRDEM in fasting condition. Subjects reported were examined for their wellbeing. Purpose and nature of the study were explained to them. Consented respondents were give appointment for blood sampling. Detailed medical and

personal history was recorded on the day of blood sampling in a predesigned case record form.

**Anthropometric measurements and blood pressure recording**

Volunteer's height (in meter) and weight (kg), waist and hip (cm) circumference were taken following standard procedure. Cut-off values for BMI (normal <22.9 Kg/m2; overweight 23-27.5 and obese <27.5) and WHR (male-0.90 and female-0.80) were used as per WHO, 2004 guidelines for Asian population. Blood pressure (average of two independent measurements) was recorded using barometric Sphygmomanometer. Five milliliter of venous blood was drawn from each subject by vein puncture at fasting and drawn blood was allowed to clot. After 20 minutes samples were centrifuged at 3000 rpm for 10 minutes. Separated serum was aliquot in micro centrifuge tubes, labeled and preserved at (-30°C) for biochemical analyses.

**Biochemical methods**

Glucose was measured by (glucose-oxidase) and total cholesterol, triglyceride and HDL-c was measured (by enzymatic colorimetric) method using in the Biochemistry Aut-analyzer 'Hitachi 704' reagents of RANDOX Laboratories Ltd., UK. LDL- c was calculated using Friedwald formula. The method was not applied when triglyceride level exceeded 400 mg/dL. SGPT by UV spectrophotometric method, Serum creatinine by alkaline picrate method Serum Hs-CRP by enzyme linked immunosorbant assay (ELISA) method.

**Statistical methods**

Data were expressed as mean±SD and number (percent). Statistical analyses were performed using Statistical Package for Social Science (SPSS) for Windows Version 17. Two tailed P value <0.05 was taken as significant level.

**Recruitment criteria**

A total number of 355 volunteers aged 30-60 years finally recruited in this study. Subjects suffered from acute illness in the last three months, Pregnant and lactating mothers and subjects with secondary obesity, known primary hyperlipidemias, hereditary or systemic inflammatory diseases, on any regular medications or significant physical training program were excluded.

## RESULTS AND DISCUSSION

Mean age of the study subjects was 41.6 years. Of the total 355 subjects 163 (45.9%) were diabetic and 192 (54%) were non diabetic. Mean fasting sugar were 132.59 ± 53.12 (mg/dl) in diabetic subjects and 96.09 ± 26.23 (mg/dl) in normal subjects. Mean Hs-CRP were 4.8±3.4 in diabetic subjects and 2.5±2.9 in normal subjects. In figure 1, ROC curve also showing positive relation of BMI, Fat%, Waist circumference, Waist hip ratio for prediction of Fasting blood glucose. The anthropometric characteristics in relation to fasting blood

glucose of the study group were shown on the Table 1. In comparison with non-diabetic subjects, are significantly older (P=0.001), have higher BMI (P=0.001), higher waist hip ratio (P=0.042) and higher body fat mass% (P<0.0001). Systolic blood pressure is high in diabetic subjects but not statistically up to significant level but diastolic blood pressure is significantly high (P=0.016). The Biochemical characteristics in relation to fasting blood glucose of the study group were shown on the Table 2.

**Table 1: Distribution of the study subjects by anthropometric variable (n=355)**

| Parameters | Diabetic subjects (163) | Non diabetic subjects (192) | P value |
|---|---|---|---|
| Age | 44.7±9.0 | 38.6±6.8 | 0.001 |
| Body Mass Index (BMI) | 25.7±3.1 | 24.1±3.2 | 0.001 |
| Waist Hip ratio (WHR) | 1.0±0.42 | 0.88±0.56 | 0.042 |
| Body Fat Mass % | 32.3±4.9 | 21.6±4.2 | <0.0001 |
| Systolic Blood Pressure | 116.4±7.3 | 113.7±7.6 | 0.613 |
| Diastolic Blood Pressure | 75.2±6.8 | 72.7±7.2 | 0.016 |

Results were expressed as mean±SD. Unpaired Student's t test was performed to compare between groups.

**Table 2: Distribution of the study patients by biochemical characteristics (n=355)**

| Parameters | Diabetic subjects (163) | Non diabetic subjects (192) | P value |
|---|---|---|---|
| Fasting glucose (mg/dl) | 132.59 ± 53.12 | 96.09 ± 26.23 | < 0.0001 |
| Triglycerides (mg/dl) | 213.5±109.5 | 162.6±97.7 | 0.001 |
| Total cholesterol (mg/dl) | 197.6±39.1 | 188.6±37.8 | 0.105 |
| HDL-c (mg/dl) | 34.2±6.8 | 36.5±7.4 | 0.030 |
| LDL-c (mg/dl) | 120.6±37.4 | 119.6±32.8 | 0.839 |
| Hs-CRP | 4.8±3.4 | 2.5±2.9 | <0.001 |

Results were expressed as mean ± SD .Unpaired Student's t test was performed to compare between groups.

HDL-c, (High density lipoprotein cholesterol), LDL-c, (Low density lipoprotein cholesterol) Hs-CRP, (High sensitive C-reactive protein)

Mean fasting sugar were 132.59 ± 53.12 (mg/dl) in diabetic subjects and 96.09 ± 26.23 (mg/dl) in normal subjects. Triglyceride (P=0.001) and Hs-CRP (P<0.001) are significantly higher and High Density lipoproteins (HDLs) are significantly lower (P=0.030) in diabetic subjects.

**Table 3: Pearson Correlation analysis of fasting blood sugar with age, BMI, triglyceride HDL-c, and Hs- CRP levels (n=355)**

| Variables (n=355) | Positive | Negative | P value |
|---|---|---|---|
| Age | 210 | | 0.003 |
| BMI | 163 | | 0.022 |
| TG | 294 | | <0.001 |
| HDL | | -150 | 0.034 |
| Hs-CRP | 201 | | 0.005 |

Results were expressed as Pearson correlation and statistical significance p.

BMI, Body mass index; TG, Triglyceride; HDL-c, High density lipoprotein cholesterol; LDL- c, Low density lipoprotein cholesterol.

Table 3 presents the results of the Pearson's correlation analysis with fasting blood glucose and other high risk variables and it showed a significance positive correlation with age (r=0.210, P=0.003) , BMI(r= 0.163, P=0.022 ), Triglyceride ( r=0.294 , P<0.001 ), and Hs-CRP ( r=0.201, P=0.005) and a negative correlation with HDL-c (r=-0.150, P=0.034). High sensitive C-reactive protein (Hs-CRP) has been a subject of interest among the researchers in recent times. By definition it is the detection of very low level of CRP in the blood using sensitive ELISA or immune turbidometry method. Usually CRP is present in the blood of healthy person at a very low level. It is widely regarded that CRP is the biochemical marker of ongoing inflammatory process and long been used to evaluate prognosis by the clinicians. Detection of very low level of CRP 'Hs-CRP' in the blood has been regarded as the presence of subclinical inflammation. Diabetes mellitus (DM) is characterized by metabolic abnormalities including hyperglycaemia, elevated Triglycerides, low HDL-c, and central obesity. C-reactive protein progressively increased as fasting glucose levels increased. These relationships did not show threshold effects, and Hs-CRP levels apparently rose even with the fasting glucose levels corresponding to the normal range of the fasting glucose category (75-115 mg/dl, 4.1-6.0 mmol/l). This result was in agreement with what previously reported by Doi Y et al[17]. Studies on western populations have shown low grade systemic inflammation indicated by elevated Hs-CRP to be one of the mechanisms by which hyperglycemia and other known risk factors such as obesity, smoking and hypertension contribute to cardiovascular disease in diabetes mellitus[13, 16]. However, the nature and extent of inflammation was seen to vary depending on ethnic, cultural and environmental background of a particular population. There are few studies of Hs-CRP in Bangladesh, a very high-risk group for diabetes, subclinical inflammation and other cardio metabolic disorders. The main focus of the present study was to show the significant increase of Hs-CRP in subjects with Type 2 diabetes of Bangladeshi origin and explore its relationship with fasting blood sugar levels. It demonstrates that the mean±SD Hs-CRP levels are 4.8±3.4 in diabetic subjects and 2.5±2.9 in healthy subjects. Although the number of subjects was relatively small, it gives an approximate baseline data for the Bangladeshi population. In previous studies on the same population [19] found mean Hs-CRP 1.8 (mg/l) in healthy controls and 4.0 (mg/l) in type2 DM patients. Another case control study found Hs-CRP mean 2.14± 0.13 in healthy controls of Bangladesh[20]. Persistent and mild elevations in Hs-CRP levels in Bangladesh could be due to increased exposure to repeated infections. The present study showed a significance increase of Hs-CRP in subjects with diabetes, Hypertension, obesity and dyslipidaemia (Table 1 and

2). Elevated blood sugar level has been implicated in the inflammatory process and pathogenesis of metabolic disorders. Levels of Hs-CRP are significantly elevated in individuals with increasing blood sugar and are associated with measures of adiposity. The predominant role of adiposity on the regulation of the inflammatory response is not surprising. Adipose tissue is in itself a source of CRP and a major producer of interleukin-6, a key stimulator of CRP secretion. In obesity, adipose tissue contains an increased number of resident macrophages and T cells, which interact closely adipocytes to modulate the inflammatory response. Both cross sectional and prospective studies have documented substantial evidence in this regard [10, 12, 18]. Previous reports show that hyper Triglyceridemia and Diabetes mellitus are positively associated with CRP levels[21, 26]. Both carbohydrate and lipid metabolism are interconnected with their physiological pathways. Obviously alteration in one affects the other. Clinical study, on tribal population of Andhra Pradesh, showed a strong link between serum sugar and lipid levels in diabetic patients [28]. Similar results were also reported by Idogun et al.[29] and Albrki et al.[30] in different population it appears that, Asian's genetic composition makes them more susceptible for diabetes and associated Cardiovascular Diseases (CVD). Of course dietary factors and physical activity also contribute significantly. Gotto [31] has found that increased Triglyceride itself can induce CVD in normal as well as in diabetic patients and raised Triglyceride with hyperglycaemia support atherogenic state[27]. Besides this, parallel increase in it worsens these complications by increasing serum LDL-C and decreasing HDL –c [27, 28]. In addition, excess fat consumption may result in increased fat depot in liver, muscles and visceral organs that promote lipogenesis and leads to obesity. Thus our results showed increased values of Hs-CRP, Fasting blood sugar, Triglyceride and decreased value of HDL-c again indicating an increased possibility of ischemic heart disease in our sample population. In conclusion, the present study showed that Hs-CRP has a strong association with diabetes in middle aged Bangladeshi population. It is also concluded that age, body mass index, abdominal obesity and high body fat% have strong association with diabetic individuals and high levels of Hs-CRP groups predicts the high risk of diabetes mellitus type 2. It is also observed that Hs-CRP levels are the sensitive marker for inflammation. Moreover this study also concludes that elevated Hs-CRP level significantly different with different age groups of diabetes mellitus individuals.

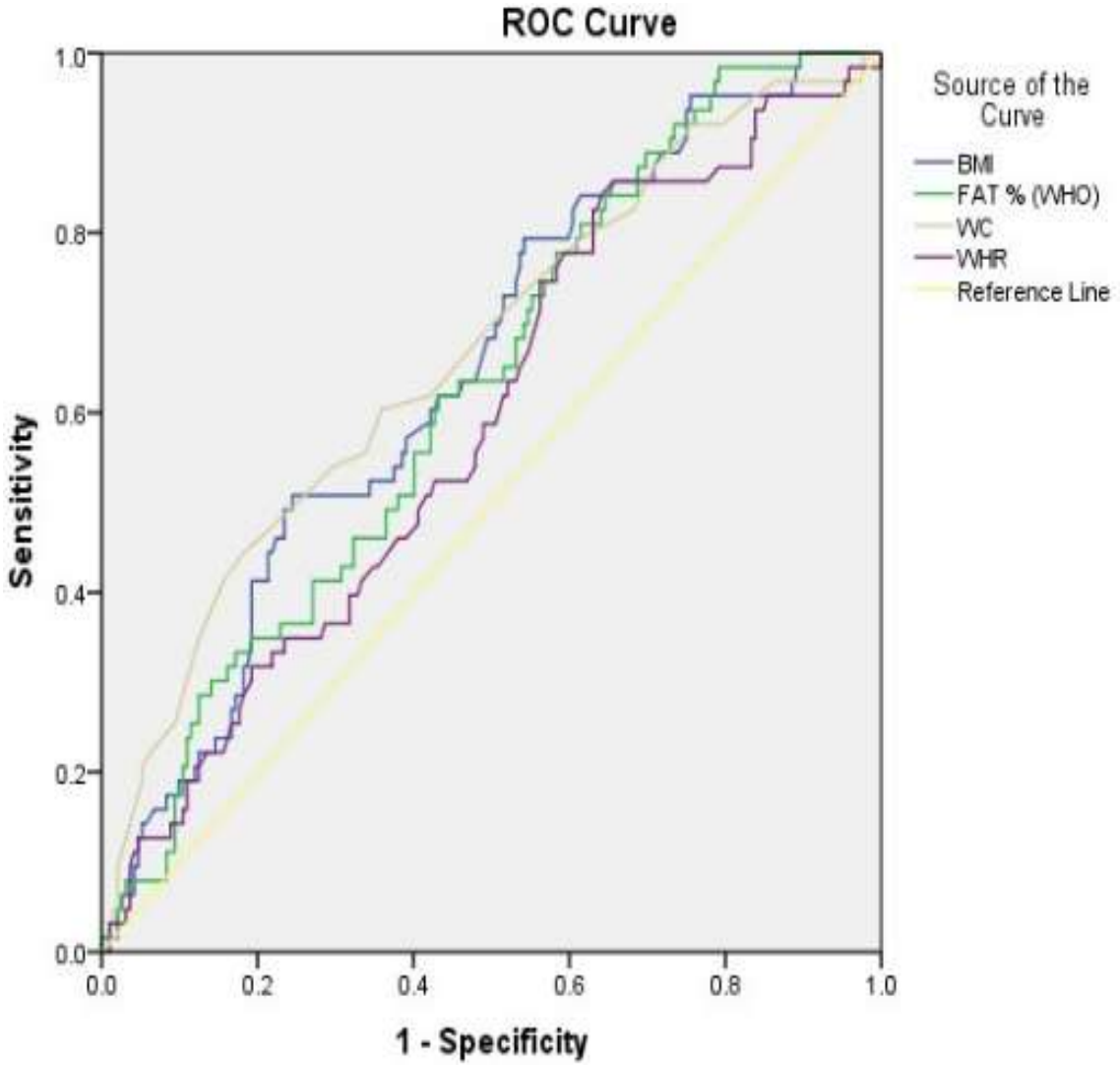


**Figure 1: ROC curve of BMI, Fat%, Waist circumference, Waist hip ratio for prediction of Fasting blood glucose**

## CONCLUSION

We demonstrated the significant association of low grade inflammation as indicated by elevated Hs-CRP levels with type 2 diabetes mellitus. It was also concluded that advanced age, obesity and dyslipidaemia were the major correlates of higher Hs-CRP levels. To help the type 2 diabetic patients from the very beginning in respect of the prognostic view of macro vascular risk, estimation of serum Hs-CRP in the early stage may be a positive enthusiastic intervention. Further studies are required to evaluate Hs-CRP as a predictor of deranged cardiovascular risk factors and to explore the influence of obesity, sugar, lipids and other modulators on its elevation.

## ACKNOWLEDGEMENT

We acknowledge the important contribution of the volunteers, laboratory staff, Biomedical Research Group of BIRDEM, to make this work possible. Special thanks to the Diabetic

Association of Bangladesh (BADAS) for financial support. But of all we are grateful to all the subjects who participated in the study.

## REFERENCES

1. Brownlee M and Cerami A (1981). Biochemistry of the complications of diabetes mellitus. Annu rev; Biochem, 50, 385-432
2. Luscher TF, Creager MA, Bckman JA, Cosentino F (2003). Diabetes and vascular disease: Pathophysiology, Clinical consequences and medical therapy: Part II. Circulation, 108 (13), 1655-1661.
3. Schultz DR, Arnold PI (1990). Properties of four acute phase proteins: C-reactive protein, serum amyloid a protein, alpha 1-acid glycoprotein, and fibrinogen. Semin Arthritis Rheum, 20,129-147
4. Li SP, Goldman ND (1996). Regulation of human C-reactive protein gene expression by two synergistic IL-6 responsive elements. Biochemistry, 35, 9060-9068
5. Uhlar CM, Whitehead AS (1999). Serum amyloid A the major vertebrate acute-phase reactant. Eur J Biochem, 265, 501-523
6. Kuller LH, Tracy RP, Shaten J, Meilahn EN (1996). Relation of C-reactive protein and coronary heart disease in the MRFIT nested case-control study. Multiple Risk Factor Intervention Trial. Am J Epidemiol,144, 537-547
7. Ridker PM, Cushman M, Stampfer MJ, Tracy RP, Hennekens CH (1997). Inflamation, aspirin, and the risk of cardiovascular disease inapparently healthy men. N Engl J Med, 336, 973–979.
8. Sato H, Miida T, Wada Y Hasegawa H, Kuroda T, Narita I, Nakano M, Gejyo F (2007). Atherosclerosis is accelerated in patients with long-term well-controlled systemic lupus erythematosus (SLE). Clin Chim Acta, 385, 35-42
9. Yudkin JS, Stehouwer CD, Emeis JJ, Coppack SW (1999). C-reactive protein in healthy subjects: associations with obesity, insulin resistance, and endothelial dysfunction: a potential role for cytokines originating from adipose tissue? Arterioscler Thromb Vasc Biol,19, 972-978
10. Ridker PM (2003). Clinical application of C-reactive protein for cardiovascular disease detection and prevention. Circulation, 107, 363-369
11. Hanyu O, Miida T, Kosuge K, Ito T, Soda S, Hirayama S, Wardaningsih E, Fueki Y, Obayashi K, Aizawa Y (2007). Preheparin lipoprotein lipase mass is a practical marker of insulin resistance in ambulatory type 2 diabetic patients treated with oral hypoglycemic agents. Clin Chim Acta, 384,118-123

12. Martha RM and Fernando GR (1999). Increased levels of CRP in Non-controlled Type II diabetic subjects. Journal of Diabetes and its complications, 13, 211-215.
13. Pradhan AD, Manson JE, Rifai. N, Burning JE, Ridker PM (2001). C-reactive protein, interleukin 6 and risk development type 2 diabetes mellitus. JAMA, 286, 327-334.
14. Chiriboga DE, Ma Y, Li W, Stanek E, Hebert JR, Merriam PA, Rawson ES, Ockene IS (2009). Seasonal and gender variation of the high sensitivity C - reactive protein in healthy adults: A Longitudina study. Clinical Chemistry, 55, 313-321.
15. Jager A, Van Hinsberg VW, Kostense PJ, Emeis JJ, Yudkin JS, Nijpels G, Dekker JM , Heine RJ, Boutee LM,Stehouwer CD (1999). Von-Willebrand factor, CRP and five year mortality in diabetic subjects: The Hoorn study. Arteioscler Throm.vasc. Biol, 12, 3071-3080
16. Pfutzner A, Forst T (2006). High-sensitivity C-reactive protein as cardiovascular risk marker in patients with diabetes mellitus. Diabetes Technol Ther, 8(1), 28-36.
17. Doi Y, Kiyohara Y, Kubo M (2005). Relationship between C-reactive protein and glucose levels in community-dwelling subjects without diabetes: the Hisayama Study. Diabetes Care, 28(5),1211-3.
18. Maryam Tohidi, Masumeh Hatami, Farzad Hadaegh1, Maryam Safarkhani, Hadi Harati, Fereidoun Azizi (2010). Lipid measures for prediction of incident cardiovascular disease in diabetic and nondiabetic adults: results of the 8.6 years follow-up of a population based cohort study. Lipids in Health and Disease, 9,1-9
19. Ismat Ara (2009). Association of high sensitive C-reactive proyein with insulin sensitivity in non obese type 2 diabetic subjects, (Thesis) BIRDEM.
20. Awan z.a, Naveed a.k, Malik m.m and Naveed a (2008). Evaluation of C - reactive protein and Interleukin – 6 as Markers of Coronary Heart Disease. ANNALS, 14, 50-56
21. Pick up JC, Maltock MB, Chusney GD, Burt D (1997). NIDDM as a disease of the innate immune system, association of acute phase reactatnts and interleukin-6 with metabolic syndrome X. Diabetologia, 40,1286-1292.
22. Chambers JC, Eda S, Bassett P, Thomson SG, Gallimor JR, Pepys MB, Kooner JS, KarimY (2001). CRP, insulin resistence, central obesity and CHD risk in Indian and Asian from the UK compared with European whites. Circulation, 104 (2), 145-50
23. Visser M, Bouter LM, Mc Quillan GM, Wener MH (2000). Elevated CRP levels in over weight and obese adults.JAM Med. Assoc, 282, 2131-2135
24. Barinas M E, Cushman M, Meilan EN, Tracy RP, Kuller LH (2001). Serum levels of CRP are associated with obesity; weight gain and hormone replacement therapy in healthy post menopausal women. Am.J Epidemiol, 1094-1101.

25. Frohlich M, Imhof A, Berg G, Hutchinson WL, Pepys MB, Boeing H, Muche R, Brenner H. Koenig W (2000). Association between C- reactive protein and features of the metabolic syndrome: a population - based study. Diabetic CarE, 23, 1835-1839.
26. Abha Gupta, Dilip Kumar, Satyam Rajvanshi, Arvind Kumar, TVS Arya (2015). To study the association of high sensitivity C-reactive protein with newly diagnosed DM type 2. JIACM 2015, 16(1), 12-5
27. Haffner SM (2003). Insulin resistance, inflammation, and the prediabetic state. Am J Cardiol, 18, 18-26.
28. Samatha P, Venkateswarlu M, Siva Prabodh V (2012). Lipid Profile Levels in Type 2 Diabetes Mellitus from the Tribal Population of Adilabad in Andhra Pradesh, India. Clin Diagnos Res, 6, 590-2.
29. Idogun ES, Unuigbe EI, Ogunro PS, Akinola OT, Famodu AA (2007). Assessment of the serum lipids in Nigerians with type 2 diabetes mellitus complications. Pak. J. Med. Sci. (Part 1), 2, 708-12.
30. Albrki WM, Elzouki AN Y, EL-Mansoury ZM, Tashani OA (2007). Lipid profiles in Libian type 2 diabetes. J Sci Appls, 1, 18-23.
31. Gotto AM (1998). Triglyceride as a risk factor for coronary artery disease. Jr Am J Cardiol, 82, 22-5.