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Comparative Study on Crp An Inflammatory Biomarkers in Type 2 Diabetes Mellitus

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ABSTRACT

Background:The main objective of this study is to prove that CRP level is higher in T2DM cases comparing to non-diabetic which may lead to heart disease among the patients
Methods: A cross-sectional study was conducted from November 2023 to May 2024, using the blood samples of the patients of type II diabetes mellitus patients, analysed in Agappe nephlometer for CRP and Beckman coulter AU480 for blood sugar and HbA1c.
Results:A total of 100 patients samples are taken for Hba1c, CRP, FBS&PPBS for the study of High level CRP in Diabetic Patients. Out of the 100 apparently (Diabetic 50 sample Non-Diabetic 50 sample) patients
Conclusions:The study concludes that the Type II Diabetes Mellitus patients have increased Crp level than the Non-Diabetic patients.It can be concluded from the study that raised levels of plasma CRP in type 2 diabetic patients may contribute to ongoing atherosclerotic processes leading to the development of coronary heart disease in these patients and this can be used as a early marker of development of atherosclerosis in patients with diabetes mellitus.

Keywords: CRP, Diabetes, Increased CRP, Inflammation, Biomarker, hs-CRP

1. INTRODUCTION

Type 2 diabetes mellitus (T2DM) accounts for around 90% of all cases of diabetes. In T2DM, the response to insulin is diminished, and this is defined as insulin resistance.A number of prospective cohort studies and nested case–control studies have reported that CRP is associated with increased risk of developing type 2 diabetes (T2D).

Type 2 diabetes is an inflammatory atherothrombotic condition associated with a high prevalence of cardiovascular disease. You are more likely to develop type 2 diabetes if you are not physically active and are overweight or have obesity. Extra weight sometimes causes insulin resistance and is common in people with type 2 diabetes.

FBS(FASTING BLOOD SUGAR)&PPBS(POST PRANDIAL BLOOD SUGAR) ;

FBS- It is a blood glucose test that measures your blood sugar after an overnight fast (not eating).
Normal range : 70-110mg/dl
PPBS - It is a blood glucose test that measures your blood sugar levels two hours after a meal.
Normal range : 80-140mg/dl

Glycated Haemoglobin A1C ;

The hemoglobin A1C (HBa1C)is a highly sensitive and accurate blood test for diagnosing type 2 diabetes. It measures your average blood sugar level over a two- or three-month period to determine whether it is consistently high.The value must be below 5.7 %. Anyone with an HbA1c value of 5.7 % to 6.4 % is considered to be prediabetic, while diabetes can be diagnosed with a HbA1c of 6.5% or highe In patients with type 2 diabetes, low grade inflammation is reflected by increased plasma levels of several biomarkers of inflammation such as C-reactive protein (CRP).

C-REACTIVE PROTEIN (CRP) :

CRP was discovered by Tillett and Francis in 1930.The test is based on the reaction between patient serum containing CRP as the antigen & the corresponding antibody coated to the treated surface of latex particle. The coated particles enhance the detection of an agglutinate reaction when antigen is present in the serum being tested. A sensitive marker of systemic inflammation has been shown to be increased in patients with type 2 diabetes mellitus. In addition, CRP levels are elevated in individuals with features of the metabolic syndrome and with cardiovascular disease.

Your liver releases more CRP into your bloodstream if you have inflammation in your body. CRP is synthesized by the liver in response to factors released by macrophages and fat cells (adipocytes). It is a member of the pentraxin family of proteins.High levels of CRP may mean you have a serious health condition that causes inflammation.People with higher sugar diets have more inflammatory markers in their blood, including C-reactive protein as a marker .Inflammation could be caused by different types of conditions, such as an infection or autoimmune disorders like rheumatoid arthritis or inflammatory bowel disease.

C-Reactive Protein (CRP) analysis is performed on the basis of two methods:

1. Standard/Conventional CRP test.
2. high sensitivity CRP test (hs-CRP).

The (Conventional/Standard)CRP test measures a wide range, so it is often used to check for early inflammation and infection. However, it is less sensitive at low range, CRP-(hs) test can detect protein at lower concentration (due to more sensitive) which makes it more effective than conventional CRP test method in diagnosis.High sensitivity-Crp Value can be converted to Standard CRP value by following equation;Standard CRP[Ls-CRP (mg/dL)]= high sensitivity [(hs)-CRP (mg/L)] X 9.2 .(For simplicity, a conversion factor of 10 may be used.

A high level of hs-CRP in the blood has been linked to an increased risk of heart attacks. Also, people who have had a heart attack are more likely to have another heart attack if they have a high hs-CRP level. But their risk goes down when their hs-CRP level is in the typical range. [An hs-CRP test isn't for everyone.]The present study was conducted among the population of A. C. S. Medical Hospital Patients. This study shows the relatively high prevalence of C-Reactive Protein (CRP)and Glycated Hemoglobin A1C (HBA1C) values in the study population.

This study create the social awareness for the TypeII Diabetes patients to lower their sugar contents in their Essentials.

The present study was conducted on private medical college -CENTRAL LABORATORY, this study was conducted to show the association of CRP with other parameters and to prevent the development of Coronary Heart Diseases in CRP elevated patients.

2. METHODOLOGY

SAMPLECOLLECTION

Check if patient is Diabetic or Non-Diabetic or has a history of diabetics in previous cases. Prepare the equipment like gloves, labels, tourniquet, 22 gauze pad, alcohol sponge, adhesive strip Syringe/needle of (21-22 gauze) and appropriate colour collection tubes.

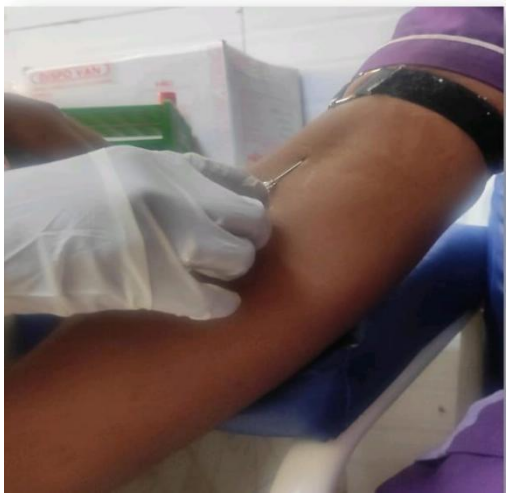


Figure 1: Obtaining Blood from a Superficial Vein of the Arm.

Blood can be collected by evacuated tube system, syringe method or butterfly method. Select the site student lying supine with ventral surfaces of both hands up, inspect the most suitable site. Put tourniquette 4" above the intended puncture site; ask patient to make a fist. The ante cubital area has basilic, cephalic and median cubital veins. Palpate the vein. If antecubital veins of either hand are unsuitable look for veins in forearm and hands. Rub the selected site with isopropyl alcohol pad in concentric circles working outward from the centre. Allow to dry for 30-60 seconds. While yournon-dominant hand stabilises the vein between index finger and thumb, put the needle with bevel upwards at 15° angle and enter skin and vein in direction of blood flow. Entry should be quick and smooth. Release tourniquette once required amount of blood fills the syringe/tube. Remove the needle and apply 2" x 2" sterile gauze pad and tape it. Label the specimen. The needle is destroyed in needle destroyer. If there is bleeding from venipuncture site, apply pressure and ask patient to raisethe hand above head for 3-5 minutes.
Approximately Evacuated blood sample in the respective tubes of EDTA tube for HbA1C,Serum Gel tube for CRP and Sodium Fluoride tube for Sugar tests.Then the EDTA blood sample was placed in the BECKHAM COULTER (Fully Automated Machine) after mixing with Hemolyzing Reagent. Sodium Fluoride tubes are also kept on Beckham Coulter Machine after centrifuging. CRP tests are measured in AGAPPE CRP ANALYZER.

3. SAMPLE PROCESSING

HbA1C Test Processing

- Anti-coagulated blood with proper anticoagulant like EDTA is taken
- Add 1000µl of Hba1c reagent with 10µl of patients sample by wiping the outer part of the tip.
- Mix it Gently with the help of pipette.
- Placed it in the racks and kept on the machine and observe the Results.

Figure 2: (a) Hemolyser (b) EDTA vaccutainer

CRP Test Processing

Sample from serum gel tube is taken

- A cuvette is taken and 150µl of CRP R_1 reagent is added and 5l of patient sample is mixed and kept for 30secs incubation.
- Then 150µl ofCRP R_2 reagent is added after the incubation then the results are observed afte 180secs(3mins).

Figure 3: AGAPPE CRP ANALYZER

FBS&PPBS Test Processing

- The requirements are same as that of EDTA except centrifuging process.
  Fasting samples are collected with proper 12 hrs of fasting day before night.
- Post prandial samples ae taken after 2hrs of consuming food.
  Sodium fluoride anticoagulated samples are taken and centrifuged for 15 mins at 3000rpm.
- Samples are kept in racks and placed in BECKHAM COULTER (Fully automated machine) ahter checking for any lysed samples.
- Then the results are observed.

Figure 4: Sodium Flouride

An automated Biochemical fully automated analyzer is used for performing more tests at single time by saving time consumption than semi automated.the machine is maintained at cooling temperature and proper Quality control maintenance at regular intervals for proper results.
Test parameters are saved in the particular softwares and easy to take prints of the results in the system without any mistakes.

4. RESULTS

A total of 100 patients samples are taken for Hba1c, CRP, FBS&PPBS for the study of High level CRP in Diabetic Patients. Out of the 100 apparently (Diabetic 50 sample Non-Diabetic 50 sample) patients of ACS Medical college

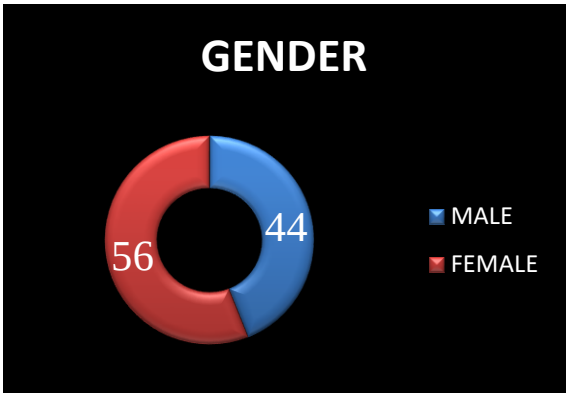


Table: 1

GENDER	FREQUENCY
MALE	44
FEMALE	56

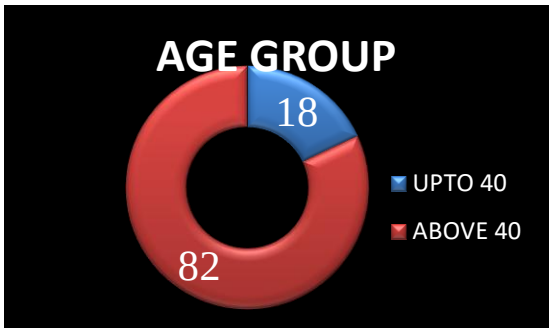


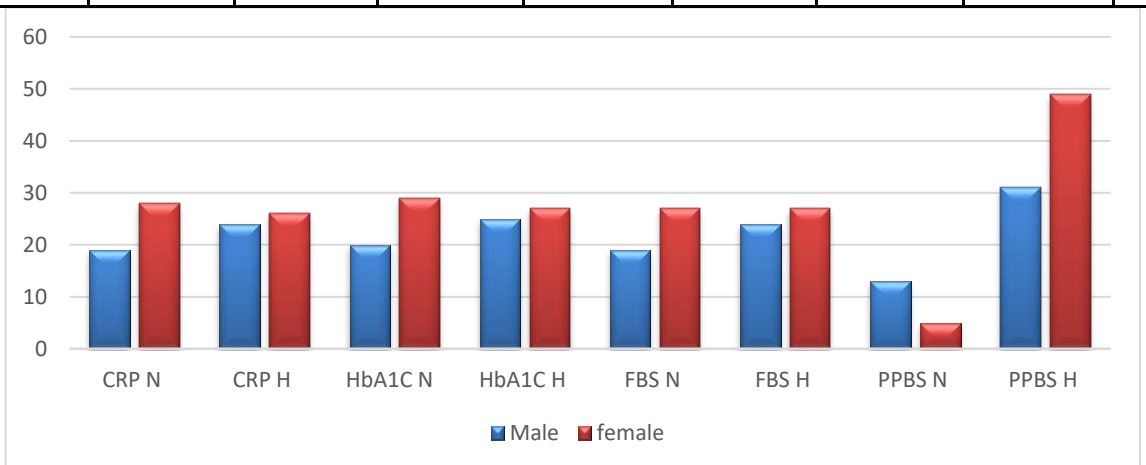
Table: 2

AGE GROUP	FREQUENCY
UPTO 40	18
ABOVE 40	82

DIABETIC & NON-DIABETIC PATIENTS BASED ON GENDER

Table: 3

Gender	CRP N	CRP H	HbA1C N	HbA1C H	FBS N	FBS H	PPBS N	PPBS H
Male	**19**	**24**	**20**	**25**	**19**	**24**	**13**	**31**
Female	**28**	**26**	**29**	**27**	**27**	**27**	**05**	**49**



Graph 1

HbA1C N = HbA1C Normal
HbA1C H = HbAIC Elevated
FBS N = FBS Normal
FBS H = FBS Elevated
PPBS N = PPBS Normal
PPBS H = PPBS Elevated
CRP N = CRP Normal
CRP H = CRP Elevated

A total of 100 participants were taken for Non-diabetic patients and Type II Diabetic patients. Out of the 100 apparently (males 44 sample females 56 sample) patients of ACS Medical hospital made up of 19 male and 28 male samples had low CRP , Elevated CRP levels had 24 male and 26 females (100 samples).Elevated HbA1C levels had 25 males and 27 females , Lower HbA1C levels had 20 males and 29 females(100 samples). Elevated FBS levels are 24 males and 27 females,Lower levels are 19 males and 27 females (100samples). Elevated PPBS levels are 31 males and 59 females,Lower levels are 13 males and 5 females (100 samples).

Diabetic & Non- Diabetic patients Mean Range;

Graph: 2

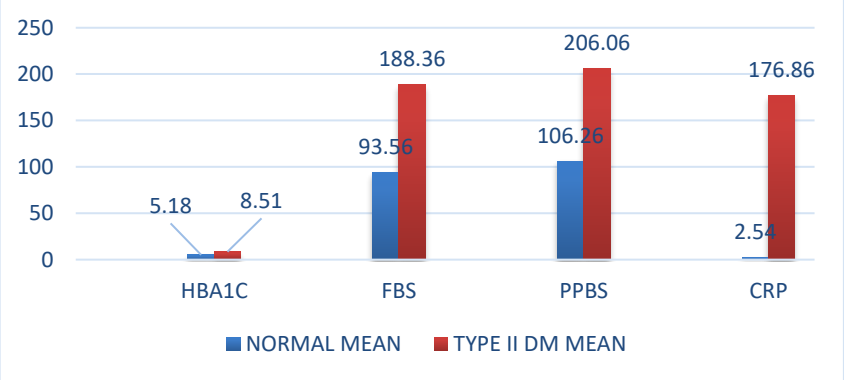


Table: 4Demographic, clinical and biochemical characteristics of the two Groups

Parameters	GROUP-A	GROUP-B	p-value
	Mean+SD	Mean+SD	
HbA1C(%)	5.18+0.53	8.51+ 2.51	< 0.05
FBS(mg/dL)	93.56 + 11.16	188.36 + 76.75	< 0.05
PPBS(mg/dL)	106.26 + 18.48	206.06 + 67.93	< 0.05
CRP(mg/L)	2.54 + 1.51	176.86 + 66.44	< 0.05

- **significant p value = <0.05**
- **NS = Non-significant**
- Similarly, levels of CRP were also found to be significantly higher (P< 0.05) in patients of Group B (Type-II Diabetic Mellitus patients) as compared to Group A.

Table 5 Correlation of CRP with Different Parameters in Studied Groups

PARAMETER	CRP	
	r	p-value
AGE(yrs)	0.063	NS
FBS (mg/dl)	.361*	<0.05
PPBS (mg/dl)	.361*	<0.05
HBAIC (%)	.361*	<0.05

***(p-value<0.05)**

shows the association of CRP with various parameters in the studied population as a whole. There was a positive significant (P<0.05) association of CRP with FBS,PPBS and HBA1C in both the studied groups.

5. DISCUSSION

Elevated levels of C-reactive protein (CRP) in individuals with Type 2 Diabetes Mellitus (T2DM) highlight a complex interplay between chronic inflammation and metabolic dysfunction. T2DM is characterized by insulin resistance, where cells become less responsive to insulin, leading to elevated blood sugar levels. This metabolic disturbance triggers a cascade of inflammatory responses within the body. CRP, synthesized primarily in the liver in response to interleukin-6 and other pro-inflammatory cytokines, emerges as a key player in this inflammatory cascade. Its levels rise in response to systemic inflammation, serving as a biomarker of the body's immune response.

In T2DM, this chronic, low-grade inflammation not only exacerbates insulin resistance but also contributes to the development and progression of cardiovascular diseases (CVD). Endothelial dysfunction, a consequence of prolonged inflammation, compromises the function of blood vessel walls, promoting the formation of atherosclerotic plaques. These plaques can narrow arteries and increase the risk of heart attacks, strokes, and other cardiovascular complications.

Moreover, the inflammatory milieu in T2DM extends beyond the cardiovascular system, affecting various metabolic pathways and exacerbating insulin resistance. Adipose tissue dysfunction further contributes to the release of inflammatory mediators, perpetuating the cycle of inflammation and metabolic dysregulation.

Understanding the role of CRP in T2DM goes beyond its utility as a biomarker; it provides insights into the underlying pathophysiological mechanisms driving both metabolic and cardiovascular complications. Targeting inflammation through lifestyle modifications, such as regular exercise and a healthy diet, as well as pharmacotherapy, including statins and anti-inflammatory agents, represents a promising approach to managing T2DM and reducing the associated cardiovascular risk.

In conclusion, the elevated CRP levels observed in T2DM underscore the intricate relationship between inflammation and metabolic dysfunction, highlighting the importance of comprehensive management strategies that address both aspects of the disease. By targeting inflammation, clinicians can potentially improve outcomes and reduce the burden of cardiovascular complications in individuals with T2DM.

CRP, synthesized primarily in the liver in response to cytokines like interleukin-6, serves as a sensitive marker of systemic inflammation. Its levels rise in tandem with the inflammatory burden, reflecting the degree of immune activation and tissue damage. In individuals with T2DM, this elevation in CRP levels not only signifies the presence of inflammation but also plays a pivotal role in the pathogenesis of associated complications, particularly cardiovascular diseases (CVD).

The link between elevated CRP levels and increased cardiovascular risk in T2DM is well-established. Chronic inflammation promotes endothelial dysfunction, initiating a cascade of events that contribute to the formation of atherosclerotic plaques. These plaques can lead to arterial stenosis, thrombosis, and ultimately, cardiovascular events such as heart attacks and strokes.

Moreover, the inflammatory milieu in T2DM extends beyond the vasculature, impacting various metabolic pathways and exacerbating insulin resistance. Adipose tissue dysfunction further exacerbates the release of pro-inflammatory cytokines, perpetuating a vicious cycle of inflammation and metabolic dysregulation.

Understanding the role of CRP in T2DM goes beyond its utility as a biomarker; it serves as a sentinel for the intricate interplay between inflammation and metabolic dysfunction. Targeting inflammation through lifestyle interventions, such as weight management, regular exercise, and dietary modifications, as well as pharmacotherapy, including statins and anti-inflammatory agents, represents a multifaceted approach to mitigating cardiovascular risk in T2DM patients.

In summary, the elevation of CRP levels in T2DM underscores the critical importance of addressing inflammation as a key component of comprehensive management strategies. By targeting inflammation, clinicians can potentially reduce the risk of cardiovascular complications and improve outcomes in individuals with T2DM.

6. CONCLUSION

- The study concludes that the Type II Diabetes Mellitus patients have increased Crp level than the Non-Diabetic patients.
- It can be concluded from the study that raised levels of plasma CRP in type 2 diabetic patients may contribute to ongoing atherosclerotic processes leading to the development of coronary heart disease in these patients and this can be used as a early marker of development of atherosclerosis in patients with diabetes mellitus.
- Effective Camps and Awareness programs are recommended among the Type II Diabetes Mellitus patients for preventive measures.
- In this study patients of the private . Medical Hospital patient population comparatively Diabetic patients had Elevated CRP levels are higher than the non-diabetic patients.

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