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Correlation of serum ferritin and hs-CRP with HbA1C in patients with type 2 diabetes mellitus

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Abstract

Introduction: The prevalence of type 2 diabetes mellitus is rising rapidly worldwide. Systemic inflammatory activity is closely related to pathogenesis of insulin resistance in type 2 diabetes mellitus. Inflammatory biomarkers like high-sensitivity C- reactive protein (hs–CRP) and serum ferritin, and Glycated haemoglobin (HbA1c) could be a useful tool for assessing risk of developing diabetic complications in diabetic subjects. This research has been done to see how inflammatory biomarkers such as serum ferritin and high sensitive C-reactive protein correlate with HbA1c in type 2 diabetics.

Aims and objectives: Aim: To estimate serum ferritin, high sensitive C - reactive protein, glycated haemoglobin in patients with type 2 DM. Objectives: 1) to evaluate the levels of serum ferritin and high sensitive C - reactive protein in type 2 diabetic subjects. 2) To assess the correlation of serum ferritin and high sensitive C - reactive protein with HbA1c.

Materials and methods: This Hospital-based observatio nal cross - sectional study was conducted in Assam Medical College & Hospital, Dibrugarh for One year. Diagnosed cases of type 2 diabetes mellitus age between 40-70 years and those who gave written consent were included in the study. History of illness like acute and chronic infection and inflammation, known case of malignancy, gastro-intestinal bleed, known case of CKD and CLD, iron and copper metabolic disorders, diabetic patients with history of iron deficiency anaemia, known hemoglobinopathies, the hemoglobin level to specify the cut off for anaemia were <12g/dl in male and <11g/dl in female, pregnant women, history of smoking, blood transfusion within period of 03 months and not giving consent were excluded from the study. After obtaining

the Institutional Ethics Committee approval, cases were enrolled for the study. Detailed relevant history was taken, and clinical examinations were performed. Routine blood and urine examinations along with LFT, KFT, TSH, HbA1C, hs –CRP, S. ferritin, Fasting and post-prandial blood sugar estimations were done.

Results: Total 80 type 2 Diabetes mellitus patients were included in our study. Majority of subjects (42. 5%) belong to 50-59 years of age with mean age 53.13±8.02. Males (57. 5%) were more common than females (42. 5%). The mean HbA1c level of type 2 diabetes mellitus with ferritin level 17.09 - 464 ng/ml was 6.80 ± 5.47, those patients with ferritin level > 464 ng/ ml were having mean HbA1c level of 1.03±10.10. Statistically significant positive correlation (R-value = 0.24 & p-value = 0.029) has observed between HbA1c level and serum ferritin levels in T2DM patients.

The mean serum hs-CRP level of type 2 diabetes mellitus patients with HbA1c level <8% was 6.05±5.96 mg/L, those patients with HbA1c level 8-10% were having mean serum hs-CRP level of 6.63±5.07 mg/L and those patients with HbA1c level of >10% were having mean serum hs-CRP level 14.82±11.82 mg/L. Statistically significant positive correlation (r= 0.46 & p < 0.0001) observed between HbA1c level and serum hs-CRP levels in T2DM patients.

Conclusion: Strong association between serum ferritin and high-sensitivity C - reactive protein, and glycated hemoglobin was observed in our study.

Inflammatory biomarkers such as high-sensitivity C-reactive protein and ferritin are strongly and independently linked to type 2 diabetes mellitus and associated complications.

Keywords: Type 2 Diabetes, HbA1c, serum ferritin, hs-CRP]

Introduction

Diabetes Mellitus, a dysglycemic Metabolic Syndrome, is a spectrum of metabolic disorders characterized by hyper glycemia as a result of impaired insulin secretion, glucose utilization, and glucose synthesis.[1] The majority of diabetic cases fall into two main broad categories, depending on the under lying patho genic abnormalities: Type 1 DM, which is characterized by absolute insulin deficiency due to immune-mediated pancreatic beta-cell destruction, and Type 2 DM, which is characterized by peripheral insulin resistance and insufficient pancreatic beta-cell secretory response. Gestational diabetes, mono genetic diabetes, and diabetes from secondary causes are the remaining subtypes.[2] Although the prevalence of both type 1 & type 2 diabetes mellitus is increasing world wide, the prevalence of type 2 diabetes mellitus is rising much more rapidly, presumably because of increasing obesity, reduced activity levels as countries became more industrialized and the aging of population.[3]

The mechanisms under lying chronic inflammation's ability to cause type 2 diabetes are unknown. It is known, however, that adipose tissue may produce and release the key pro-inflammatory cytokines tumour necrosis factor-alpha (TNF-α), interleukin-1 (IL-1) and interleukin-6 (IL-6) and that inflammatory markers are linked to body fat mass. Multiple metabolic processes associated to insulin resistance, including regulation, reactive oxygen species, lipoprotein lipase action, and adipocyte function, is influenced by pro-inflammatory cytokines and acute phase reactants.[4]

C-reactive protein (CRP) is an acute-phase protein, which is an inflammatory marker synthesized and released by the liver under the stimulation of cyto kines.[5]It has emerged as the golden marker for inflammation. Plasma levels of hs-CRP provide a sensitive marker of an increased inflammatory activity in

the arterial wall. It is a strong biomarker of inflammation in the progression of various diseases like coronary heart disease, cancer, diabetes, and others. The hs-CRP test is a highly sensitive quantification of CRP.[4]

Serum ferritin is an acute phase reactant and marker of iron stores. Ferritin regulates blood iron levels by releasing iron if the blood has a low iron concentration and it can help to store excess iron if the blood and tissues have a high iron concentration. The increased levels of ferritin in the blood reflect both the involvement of inflammation and independent actions of excess iron.[1]Studies have shown that serum ferritin was proportional to serum glucose concentration, diastolic blood pressure, HDL cholesterol, and insulin resistance. In fact, the higher the ferritin levels, the higher the incidence of type 2 diabetes mellitus.[6]

Glycated haemoglobin (HbA1c) a minor haemoglobin derivative is one parameter that provides an index of blood glucose control in a collective sense[7].The quantity of HbA1c formed is directly proportional to the average plasma glucose concentration that the red blood cell is exposed to during its 120-day life span. It is a reliable indicator of long-term hyper glycemia and the measure Ment of HbA1c% helps in identifying the risk of develop ping diabetic complications.

Systemic inflammatory activity is closely related to patho genesis of vascular athero sclerosis, insulin resistance in type 2 diabetes mellitus. Hence inflammatory biomarkers could be a useful tool for assessing risk. The greatest evidence to date supports the use of high-sensitivity C-reactive protein (hs–CRP) as an independent predictor of increased cardiovascular disease risk in non-diabetic and diabetic subjects.[1]

As a result, the goal of our research is to see how inflam matory biomarkers such as serum ferritin and high sensitive C-reactive protein correlate with HbA1c in type 2 diabetics.

Aims and objectives

Aim

To estimate serum ferritin, high sensitive C - reactive protein, glycated haemoglobin in patients with type 2 DM.

Objectives

1) to evaluate the levels of serum ferritin and high sensitive C - reactive protein in type 2 diabetic subjects.

2) To assess the correlation of serum ferritin and high sensitive C - reactive protein with HbA1c.

Materials and methods

This Hospital-based observational cross-sectional study was conducted in Assam Medical College & Hospital, Dibrugarh for One year (1st June 2020 to 31st May 2021).

Study population

All diagnosed cases of Type 2 Diabetes mellitus attending Medicine OPD, Diabetic OPD, or admitted in the Department of Medicine in Assam Medical College & Hospital, Dibrugarh were enrolled for the study.

Inclusion criteria

Diagnosed cases of type 2 diabetes mellitus age between 40-70 years and those who gave written consent were included in the study.

Exclusion criteria

History of illness like acute and chronic infection and inflammation, known case of malignancy, gastro-intestinal bleed, known case of chronic kidney disease, known case of chronic liver disease, iron and copper metabolic disorders, diabetic patients with history of iron deficiency anaemia, known hemo globino pathies, the hemo globin level to specify the cut off for anaemia were <12g/dl in male and <11g/dl in female, pregnant women, history of smoking, blood transfusion within period of 03

months and not giving consent were excluded from the study.

Sample size

Considering the standard deviation of serum ferritin to be 43.84 ng/ml as per study done earlier by Faiza et al[8] and estimate to be made within 10 ng/ml of true value with 95% confidence interval, the sample size for the present study is calculated and rounded off to be 80.

Ethical clearance

Ethical clearance was obtained from the institutional ethics committee (human) before starting the research.

Informed consent

All the study participants were given an explanation of the study and informed written consent was taken from them or their attendants before enrolment into the study.

Case definitions

The criteria for the diagnosis of diabetes mellitus, as laid down by the American Diabetes Association, 2020 are as follows:

FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 hours. *

(OR)

Two-Hour Plasma Glucose ≥200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water. *

(OR)

HbA1c ≥6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay. *

(OR)

In a patient with classic symptoms of hyper glycemia or hyper glycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).

* In the absence of unequivocal hyper glycemia, diag nosis requires two abnormal test results from the same sample or in two separate test samples.

B) Diagnosis of type 2 diabetes mellitus

Type 2 diabetes mellitus was diagnosed empirically in the absence of features suggestive of Type 1 diabetes mellitus. In cases where there was doubt in clinically differentiating between the two, Fasting C peptide levels and fasting Insulin levels were done.

Method of data collection

Data was recorded in a predesigned and pretested proforma. Data included a detailed history, general and systemic examination and required investigations.

History Taking

An elaborate history was taken in each patient with special reference to the points concerning diabetes mellitus e.g. increased thirst or dryness of mouth, increased hunger or reduced appetite, frequent urination at night time, malaise and weakness, abdominal pain, leg pain or leg ulcers, reduced vision, dizziness or black-outs, chest discomfort, chest pain or shortness of breath, reduced vision. Past history was elaborated, with emphasis on the history of hyper tension, TIA, CVA, angina or MI, nephropathy, and thyroid disorder. In the family history, subjects were enquired about a history of diabetes, dyslipidemia, hyper tension, stroke, heart disease in the family, and whether the subject's father, mother, or grandparents were affected by diabetes mellitus or not. Regarding drug history, the history of anti-diabetic drugs – oral hypoglycemic or insulin was elucidated. History of NSAIDs, Aminoglycosides, am phot ricin B, cyclophosphamide, cyclosporine, etc. was also enquired and documented.

Clinical Examination

A detailed general physical examination was carried out with special emphasis on weight, height, BMI, abdominal

circumference, nutritional status, pallor, icterus, cyanosis, pedal edema (pitting and non-pitting), jugular venous pressure, pulse and blood pressure.

Systemic examination was done with weightage on every system affected by diabetes. Examination of the cardiovascular system was done to find evidence of coronary artery disease, evidence of heart failure, heart murmurs, etc. The nervous system examination was done, with emphasis on the cranial nerves, motor system, sensory system, and the autonomic nervous system. A 10 g mono filament test was also done in every subject for diagnosing neuropathy. Fundoscopy was done to gather evidence of retinopathy in every subject. The respiratory and gastrointestinal systems were also meticulously examined in each patient.

Anthropometric measurement

Weight

Weight was measured in Kg using a bathroom weighing scale which was adjusted to zero before each measure Ment. The patients were asked to stand on the scale bare footed with minimal clothing and look straight ahead without touching anything. Weight was recorded to the nearest 100 g.

Height

Patients were made to stand against a wall and height was measured using an inelastic measuring tape to the nearest 0.1 cm.

Body Mass Index was calculated using the formula:

$$BMI=\frac{Weight\ in\ kg}{(Height\ in\ meters)^2}$$

Laboratory investigations

Complete Blood Count, LFT, Serum sodium, serum potassium, fasting lipid profile, Uric Acid, Blood Urea, Serum creatinine, Thyroid function test were done in the Pathology and Bio chemistry Laboratory in Assam Medical College and Hospital, Dibrugarh. eGFR was calculated using the CKD- EPI formula.

Urine routine examination

It was done especially for sugar and albumin using Uro Color 2 Urine Test Strips.

Estimation of Urinary Albumin-Creatinine Ratio

It was estimated using System reagent for the quantitate Ve determination of Microalbumin (MALB) in urine on Beckman Coulter AU analyzers.

Estimation of 24 hours urinary protein

It was estimated by quantitative estimation of 24-hour urinary protein excretion.

Method of sample collection

Under aseptic precautions about 6 ml of fasting venous blood was drawn from ante-cubital vein of study subjects using a sterile dis posable syringe. Of that, 4 ml was collected in plain vacutainer and 2 ml into EDTA containing vacutainer.

Plain vacutainer containing 4 ml of blood was subjected for centrifugation and the serum was separated. The bio chemical parameters were analyzed by immune-metric assay and High-performance liquid chromatography.

Estimation of blood glucose

GOD/POD method (Glucose oxidase and Peroxidase Method) was used to estimate blood glucose.

Estimation of glycated hemoglobin (HbA1c)

Estimated by chromatographic separation by ion-exchange HPLC of whole blood preferably, fresh and collected in EDTA vial.

Estimation of serum ferritin

Serum samples were analyzed by Immunometric method. Reference range: <17.09ng/ml-low; 17.09-464ng/ml-Normal; >464ng/ml-High

Estimation of high sensitive CRP

Serum samples were analyzed by Quantitative ELISA method.

Statistical analysis

The data collected was tabulated in Microsoft Excel Worksheet 2010 and computer-based analysis was performed using the Statistical product and service solutions (SPSS) 20.0 software (SPSS, Chicago, Illinois, USA). Results on continuous measure ments are presented as mean ± standard deviation and are comp a red using student ‘s t-test and Analysis of Variance (ANOVA). Were the

p-value was found significant ($p< 0.05$) in ANOVA among 3 groups, post hoc analysis was done to find out the significance between 2 individual groups.

Discrete data are expressed as number (%) and analysed using Chi square test and Fisher ‘s exact test. Pearson ‘s correlation coefficient (r) was used to measure the correlation among continuous variables. For all analyses, statistical signifi cance was fixed at 5% level ($p<0.05$).

Results and observations

Total 80 type 2 Diabetes mellitus patients were included in our study. The results and observations are illustrated below.

Table 1: age wise distribution of study populations

Age(years)	Number(n=80)	Percentage (%)
40-49	26	32.5
50-59	34	42.5
60-69	16	20
≥70	4	5
Total	80	100.00
Mean ± S.D.= 53.13±8.02		

Table 1 shows that the majority of subjects belong to 50-59 years of age (42.5%) followed by age group 40-49 years (32.5%), 60-69 years (20%), and ≥ 70years (5%). The mean age for the study subject was 53.13±8.02.

Fig 1: gender wise distribution of the study populations

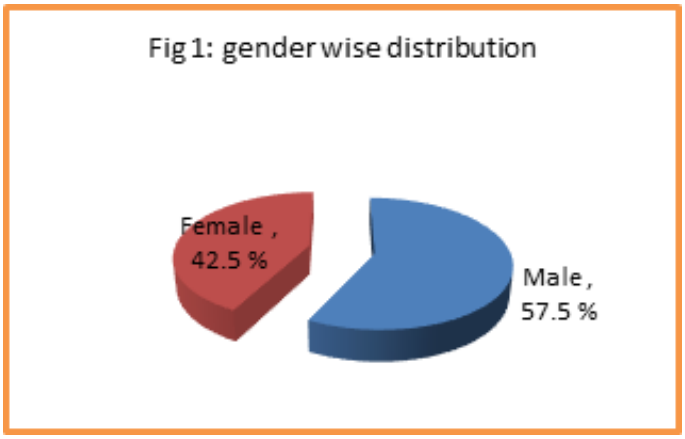


Fig 1: Shows that males (57.5%) were more common than females (42.5%) with the male: female ratio 1.35:1.

Table 2: BMI level of study populations

BMI (kg/m^2)	Number (n=80)	Percentage (%)
Underweight (<18.5)	1	1.25
Normal (18.5-24.99)	58	72.5
Overweight (25-29.99)	14	17.5
Obese (≥30)	7	8.75
Total	80	100
Mean ± S.D.= 22.69±3.91		

Table 2 shows that the majority of subjects lie in the normal BMI level group (72.5%), and the remaining study subjects lie in the overweight age group (17.5%). 8.75% individual lies in the obese group and 1.25% individual lies in underweight group. The Mean BMI level of the study subject was 22.69±3.91.

Table 3: hs-CRP level in study populations

hs-CRP (mg/L)	Number(n=80)	Percentage (%)
<1	3	3.75
01-3.0	15	18.75
>3.0	62	77.50
Total	80	100.00
Mean ±S.D. =8.05±7.89		

Above table 3 shows that in 77.50% study populations, serum hs-CRP level was found out to be >3.0 mg/L followed by 18.75% in 01-3.0 mg/ L, and 3.75% in <1mg/ L. The mean serum hs-CRP level was 8.05 ± 7.89 mg/ L.

Table 4: HbA1c level of study populations

HbA1c (%)	Number(n=80)	Percentage (%)
<8	31	38.75
8-10	33	41.25
>10	16	20
Total	80	100
Mean ±S.D. =8.63±2.12		

Above table 4 shows that the majority of study subject lies in HbA1c level 8-10% (41.25%) followed by HbA1c level <8% (38.75%) and HbA1c level>10% (20%). The mean HbA1c level was found out to be 8.63± 2.12.

Table 5: serum ferritin level in study populations

Serum ferritin (ng/ ml)	Number(n=80)	Percentage (%)
<17.9	0	0.00
17.9-464	66	82.50
>464	14	17.50
Total	80	100
Mean ±S. D =348.53±148.69.		

Table 5 shows that 82.50% study subject lies in ferritin level 17.9 - 464 ng/ml followed by ferritin level >464 ng/ml (17.50%). No subject has a ferritin level of less than <17.9 ng/mL. The mean serum ferritin level was 348. 53 ± 148.69.

Table 6: hs-CRP level according to duration of diabetes

Duration of diabetes (years)	hs-CRP level(mg/L)			R-value	p-value
	<1	01-3.0	>3.0	0.225	0.045
0-5	3	0	9		
06-10	0	14	36		
11-15	1	0	13		
16-20	0	0	4		
>20	0	0	0		

Table 6 shows that the distribution of hs-CRP according to the duration of diabetes was seen maximum number of cases (n=50) with duration of 06-10 years. The mean duration of diabetes was 9.16±3.58 years. (r=0.225, p=0.045).

Table 7: ferritin level according to duration of diabetes

Duration of diabetes (in years)	Ferritin level(ng/ml)			R-value	p-value
	<17.9	17.9-464	>464		
0-5	0	11	1	0.259	0.020
6-10	0	46	4		
11-15	0	8	5		
16-20	0	2	3		
>20	0	0	0		

From above table 7, it is seen that the distribution of serum ferritin according to the duration of diabetes was observed maximum number of cases (n=50) with duration of 06 – 10 years (r=0.259, p=0.020).

Fig 2: Chronic complications of diabetes

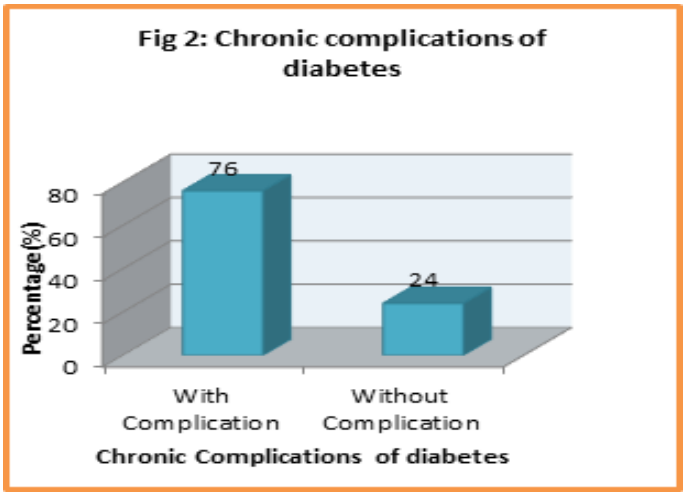
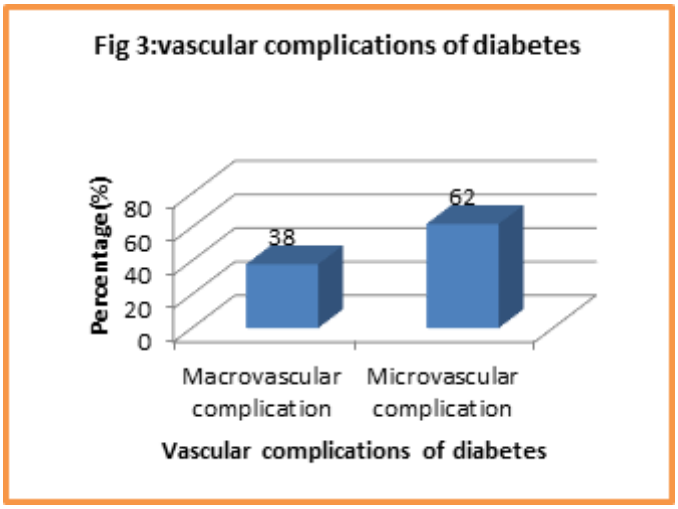


Fig 2: Shows that 76% type 2 diabetes mellitus patients had chronic vascular complications whereas 24% were without any complication.

Fig 3: Type 2 DM with vascular complications



Above fig 3 shows that 62.00 % of study subjects had micro vascular complications and 38.00 % had macro vascular complications.

Table 8: Pearson's correlation coefficient in type 2 dia be tic subjects

Parameters	R-value	P-value	significance
Serum ferritin and FBS	0.427	<0.0001	Highly significant
Serum ferritin and HbA1C	0.245	0.029	significant
Serum hs-CRP and FBS	0.199	0.076	Not significant
Serum hs-CRP and HbA1C	0.305	0.006	significant
Serum hs-CRP and LDL	0.277	0.013	significant

*Karl Pearson's coefficient of correlation: p< 0.01= S (Significant), p< 0.001=HS (Highly significant) and p> 0.05=NS (Not significant)

From table 8, it is observed that there was a highly significant (p < 0.001) positive correlation existed between fasting blood sugar & ferritin. Significant positive correlation between Serum ferritin and HbA1c (p=0.029) was also seen. There was correlation found between hs-CRP & fasting blood sugar (p=0.076). Signifi can't positive correlation between hs-CRP & HbA1c, and hs -CRP & LDL. (p<0.05) also noted.

Table 9: Relationship between serum ferritin and HbA1c level in type 2 diabetes mellitus patients

Ferritin level (ng/ ml)	Mean HbA1C (%)	SD	p-value
<17.09	-	-	0.029
17.09-464	6.80	5.47	
>464	11.03	10.10	

From above table 9, it was found that the mean HbA1c level of type 2 diabetes mellitus patients with ferritin level 17.09-464 ng/ml was 6.80±5.47, those patients with ferritin level > 464 ng/ml were having mean HbA1c level of 11.03 ± 10.10. Statistically significant positive correlation (R-value=0.24 & p-value= 0.029) has observed between HbA1c level and serum ferritin levels in T2DM patients.

Table 10: Relationship between serum hs-CRP and HbA1c level in type 2 diabetes mellitus patients

HbA1C level (%)	Mean hs-CRP	SD	p-value
<8	6.05	5.96	<0.0001
8-10	6.63	5.07	
>10	14.82	11.82	

Post-Hoc Test:	
<8 vs 8-10	: p=0.039
<8 vs>10	: p=0.046
8-10 vs>10	: p=0.967

From above Table 10,it was found that the mean serum hs-CRP level of type 2 diabetes mellitus patients with HbA1c level <8% was 6.05±5.96 mg/L, those patients with HbA1c level 8-10% were having mean serum hs-CRP level of 6.63±5.07 mg/L and those patients with HbA1c level of >10% were having mean serum hs-CRP

level 14.82±11.82 mg/L. Statistically significant positive correlation (r= 0.46 & p < 0.0001) observed between HbA1c level and serum hs-CRP levels in T2DM patients.

Discussion

Age distribution

In our study, it was seen that majority of subjects belong to 50-59 years of age (42.5%), followed by 40-49 years of age (32.5%),60-69 years of age group (20%), ≥70 years of age group (5%). The mean age for the study subject was 53.13±8.02.

Raj S et al.[9] (2013) found that the mean age of study population was 54.3±9.2 years. Ramesh, et al.[4] (2019) found that 16% subjects were in the age group of 36- 45 years, 40% subjects in the age group of 46-55 years and 44% subjects in the age group of >56 years. Nazan Erenoglu Son *et al.* [10] (2019) in their study found that the mean age of the of the group was 59.96±11.26 years.

Gender distribution

We encountered more males (57.5%) than females (42.5% with male: female ratio was 1.35:1.

Ramesh et al.[4] (2019) have found 57% males and 43% females with the male: female ratio 1.33:1.

Jagannatha S et al.[1](2016) observed that out of 50 type 2 diabetic subjects studied, 38 were males and 12 were females.

Body mass index distribution

We encountered normal BMI in 72.5% and overweight in 17.5% of study populations.8.75% individual were in the obese group whereas 1.25% individual were in under weight group. The mean BMI level of the study subject was 22.69±3.91.

Jagannatha s et al.[1](2016) found that the mean BMI (kg/m2) of study subject was 22.2 ± 3.62. Raj S et al.[9] (2013) observed the mean BMI of diabetic subject was 24.28 kg/m2.

Type 2 diabetes mellitus with macro vascular compli cation and microvascular complication distribution

We observed microvascular complication in 47.50% and macro vascular complications in 28.75% of the study population.

Maulee Hiromi Arambewela et al.[11] (2018) encountered macro vascular complication in 13.7%, and micro vascular complication in 74% while 10.5% had both macro and micro vascular complications.

Serum hs-CRP level among type 2 diabetes mellitus patients

In our study, we observed that 77.50% had serum hs-CRP level > 3.0 mg/ L, 18.75% had 01-3.0 mg/ L level, and 3.75% of study subject had <1mg/L. The mean serum hs-CRP level was 8.05±7.89 mg/L.

Ramesh et al.[4] (2019) observed that, out of 77 diabetic subjects 7 (9%) patients had low hs-CRP levels, 15 (20%) had intermediate and 55 (71%) had high hs-CRP levels. Gupta et al.[12]2018) found that out of 50 diabetic patients ‘s 42 (84%) had hs-CRP>3mg/L (high risk).

Serum ferritin level among type 2 diabetes mellitus patients

In our study, it was found out that 82.50% study subject were in ferritin level 17.9-464 ng/ml followed by 17.50% in ferritin level >464 ng/ml. No subject has a ferritin level of less than <17.9 ng/mL. The mean serum ferritin level was 348.53±148.69. Lian long et al.[13] (2020) found that the majority of study subject (85.15%) were in serum ferritin level within 10-299.9ng/ml (reference range).

Faiza et al.[8] (2014) in their study observed mean serum ferritin level 233.11±43.84 ng/ml.

HbA1c level among type 2 diabetes mellitus patients

In our study, it was found out that the majority of study subjects had HbA1c level 8-10% (41.25%) followed by HbA1c level <8 (38.75%) and HbA1c level >10% (20%). The mean HbA1c level was 8.63± 2.12. Jagannatha et al.[1]

(2016) observed the mean HbA1c % among cases was 8.59 ± 1.83. Khan et al.[14] (2012) found the mean HbA1c % among cases was 8.45+ 0.76. Nazan Erenoglu Son et al.[10](2019) in their study found the mean HbA1c % to be 9.09±2.73. According to Gupta et al.[12](2018), the mean HbA1c% among cases was 7.95 ± 0.84.

Pearson's correlation between fasting blood sugar, hs-CRP, ferritin, & HbA1c in type 2 diabetic subjects:

In our study, highly significant (P < 0.001) positive correlation existing between fasting blood sugar & ferritin was observed. There was significant positive correlation between Serum ferritin and HbA1c (p=0.029). There was correlation found between hs-CRP & fasting blood sugar (p=0.076). There was significant positive correlation hs-CRP & HbA1c, hs-CRP & LDL. (p<0.05).

According to Gupta et al.[12] (2018), hs-CRP levels positively correlated with FBS(r=+0.8), HbA1c(r=+0.9), TG(r=+0.6) and LDL(r=+0.6) with p-value<0.001.

Jagannatha s et al.[1](2016) also observed that hs-CRP levels positively correlated with FBS(r=+0.3), hs-CRP and HbA1c(r=0.4).

According to Harikrishnan et al.[15](2018), Serum ferritin levels positively correlated with FBS(r=0.5), ferritin and HbA1c(r=0.9) with p-value <0.001.

Padmaja et al.[16] (2015) in their study also found high (r=0.62, r=0.66) positive correlation between serum ferritin and HbA1c of females and males respectively in diabetic group (p-value=< 0.01).

Ferritin and hs-CRP level according to duration of diabetes

We encountered a positive correlation between ferritin and duration of diabetes (r=0.259, p=0.020).

In our study, the patient who had a longer duration of diabetes had raised levels of hs-CRP as shown in which showed a positive linear correlation with r=0.2 and P-value=0.04 (statistically significant).

Ritu Gupta et al.[17] (2020) observed that there was a positive correlation between hs-CRP and duration of diabetes (R-value=0.20, p-value=0.044). Poonam et al.[18] (2017) also found that, serum ferritin was significantly related to the duration of diabetes (p<0.05). Pramila devi et al.[19] (2013) also observed that as duration of diabetes increases there was increase in serum ferritin levels compared to recent onset.

Relationship between serum ferritin and HbA1c level in type 2 diabetes mellitus patients

In our study, it was found out that the mean HbA1c level of type 2 diabetes mellitus patients with ferritin level 17.09-464 ng/ml was 6.80±5.47, those patients with ferritin level > 464 ng/ml were having mean HbA1c level of 11.03±10.10. There was a statistically significant positive correlation (R-value=0.24 & p-value= 0.029) observed between HbA1c level and serum ferritin levels in T2DM patients.

Nazan Erenogluson et al.[10] (2019) observed that the serum ferritin values increased significantly with increase ing HbA1c % values, with p-value highly signifi can't <0.001.

Borah M et al.[20] (2016) found that the serum ferritin levels significantly increased in diagnosed cases of type 2 diabetes mellitus in comparison with the age and gender matched healthy individuals (p value<0.01).

A strong positive correlation was found between HbA1c % and serum ferritin levels and the correlation was found to be statistically significant (p<0.01), which is com parable to our study.

Sharma A et al.[21](2020) observed that Serum ferritin had a positive correlation with HbA1c (r=0.85). The mean Serum ferritin was significantly higher (p<0.01) (189.61 ± 156.99 ng/ml) in diabetic patients when compared to controls (88.74 ± 47.28 ng/ml). According to Raj S et al.[9]

(2013), serum ferritin was significantly related to HbA1c (r=0.209, p<0.05), which is comparable to our study.

Relationship between serum hs-CRP and HbA1c level in type 2 diabetes mellitus patients

In our study, it was found that the mean serum hs-CRP level of type 2 diabetes mellitus patients with HbA1c level <8% was 6.05±5.96 mg/L. Patient with HbA1c level 8-10% had mean serum hs-CRP level of 6.63±5.07 mg/L and HbA1c level of >10% had mean serum hs-CRP level 14.82±11.82 mg/L. Statistically significant positive correlation (r= 0.46 & p < 0.0001) observed between HbA1c level and serum hs-CRP levels in T2DM patients. According to King D.E et al.[22](2003), for each level of HbA1c, the percent of elevated CRP was as follows: <7, 48.9%; 7–8.9, 45.4%; 9–10.9, 60.7% and ≥11, 70.6%. Overall, 51.5% of participants had elevated CRP. In unadjusted analyses, increasing HbA1c was significantly associated with a higher percent of patients with elevated CRP levels (p< 0.05).

Gupta et al.[12](2018) also observed significant positive correlation (p-value <0.0001) between HbA1c and hs-CRP, which is comparable to our study. Ramesh, et al[4](2019) found that the mean of HbA1c of type 2 DM subjects with hs-CRP of >3mg/L is 8.90+ 1.24 (p=0.004).

Limitations of the study

Sample size of our study was small. Due to the cross-sectional nature of the study, we could not follow up the patients to look complications. Association of these bio markers in non-diabetic patients could not be ascertained as there were no controls.

Further scope of the study

The high levels of hs-CRP and ferritin as bio markers for predicting in type 2 diabetes and associated compli cations are demo nstrated in this study.

Future studies may also consider inclusion of inter leukins (IL - 1 and IL-6) as additional bio markers in a large number of participants to reduce data variability and enhance statistical significance.

Conclusion

In our study, we have observed that there is strong association between fasting serum glucose, ferritin, high-sensitivity C-reactive protein and glycated hemoglobin. We conclude that inflammatory biomarkers such as high-sensitivity C-reactive protein and ferritin are strongly and independently linked to type 2 diabetes mellitus and associated complications. Therefore, these inflammatory biomarkers such as high-sensitivity C-reactive protein (hs-CRP) and ferritin can be used to predict Type 2 DM and associated complications.

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