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RESEARCH ARTICLE

A STUDY OF SERUM FERRITIN LEVELS IN TYPE 2 DIABETES MELLITUSAND ITS CORRELATION WITH HBA1c LEVELS

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Abstract

Objectives: The etiopathology of type 2 DM is multifactorial. Recently, increased body iron levels have been associated with an increased risk of type 2 DM. Iron through oxidative injury leads to resistant hyperglycaemia and also microvascular diabetic complications. There are few studies which show an association between serum Ferritin and type 2 diabetes mellitus. The present study is conducted to know the association between S.ferritin and DM and correlate Diabetic nephropathyand retinopathy.

Methods:50 type 2 DM patients and 50 non-diabetic patients meeting the inclusion criteria were selected from Chalmeda Anand Rao Institute Of Medical Sciences, Karimnagar, Telangana were studied. Necessary Investigations like blood sugars, HbA1c, serum ferritin, urinary Protein and fundoscopy were done. Other relevant investigations were done to exclude patients falling under exclusion Criteria.

Results: This study included 50 patients with Type 2 Diabetic Mellitus and 50 controls. The mean Serum Ferritin level is 379.55 mcg/dl in diabetics compared to non-diabetics with mean serum Ferritin of 81.66 mcg/dl. About mean Serum ferritin levels with urinary proteinuria, serum ferritin was 317 mcg/l in diabetic patients with nil urinary protein, 421.43 mcg/l among 1+ urinary protein, 464.37 mcg/l among 2+ urinary protein, 569.02 mcg/l among 3+ urinary protein About Serum ferritin levels with diabetic retinopathy were 319.09 mcg/l in diabetic patients with no fundus changes, 410.02 mcg/l among grade 1 NPDR patients, 529 mcg/l among grade 2 NPDR patients, 543 mcg/l among grade 3 NPDR.

Interpretation And Conclusion: This study shows that the level of body iron measured in terms of Serum ferritin is higher in type 2 diabetic patients compared to Non-Diabetics. Diabetic Patients with MicroVascular Complications had higher levels of serum ferritin compared to those without any microvascular complications

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Introduction:-

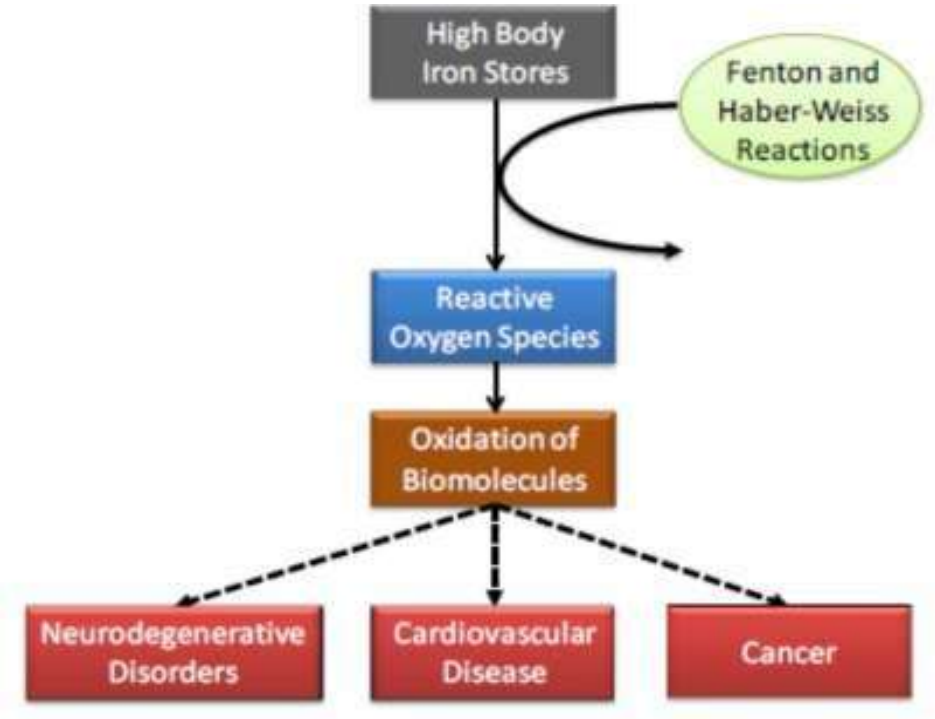
Diabetes mellitus is one of the most commonly seen metabolic disorders whichis characterized by hyperglycemia either due to insulin deficiency or insulin resistance.

It is associated with microvascular complications like diabetic nephropathy, Diabetic retinopathy, and Diabetic neuropathy and macro-vascular complications like coronary artery disease, peripheral vascular Disease etc. Because of these complications,it is associated with increased morbidity as well as increased mortality. It causes an economic burden to the family as well as to society[1].

Serum ferritin is an acute phase reactant and is a marker of iron stores in the Body. Increased accumulation of iron affects insulin synthesis and secretion in the pancreas and liver. Elevated iron stores may induce diabetes through a variety of mechanisms, including oxidative damage to pancreatic beta cells, impairment of hepatic insulin extraction by the liver, and interference with insulin's ability to suppress hepatic glucoseproduction [2,3].

HbA1c is currently the investigation of choice in monitoring the treatment of diabetes mellitus[7]. Measurement of HbA1c provides valuable information for the management of diabetes mellitus but HbA1c may be affected by a variety of genetic, haematologic and illness-related factors [8] like haemoglobinopathies (depending on the assay employed), certain types of anaemia, and disorders associated with accelerated red cell turnover such as malaria.[9,10]

Serum ferritin is an acute phase reactant and is a marker of iron stores in the body.[11] Iron is a transitional metal that can easily become oxidized and thus acts as an oxidant.[12] An important role of ferritin during the acute phase response is to restrict the availability of iron by sequestration into the cavity of the ferritin protein shell[13] High body iron stores that is serum ferritin have been linked to insulin resistance [14,15] metabolic syndrome,[14,16,17] and gestational diabetes.[18,19] Excess iron damages β-cells of the pancreas due to oxidative stress which can contribute to the pathogenesis of diabetes mellitus.[20]



Glycated Hemoglobin:

Haemoglobin A1c (HbA1c) is a glycated haemoglobin, formed by glycation of NH2- terminal valine residue of the b-chain of globin. Alternative names: Beta N-(1- deoxyfructos-1-yl) haemoglobin (IFCC approved nomenclature); haemoglobin A1c, HbA1c, glycated haemoglobin, glycohaemoglobin, GHb.[4]

Normal adult haemoglobin consists predominantly of HbA (α2β2), HbA2 (α2δ2) and HbF (α2γ2) (97, 2.5 and 0.5% respectively). About 6% of total HbA is termed HbA1, which in turn is made up of HbA1a1, HbA1a2, HbA1b and HbA1c. These fractions are defined by their electrophoretic and chromatographic properties, which differ slightly from those of the major component HbA0, despite the amino acid sequences of HbA1 and HbA0 being identical. HbA1c is the most abundant of these fractions and in health,comprises approximately 5% of the total HbA fraction. Structural and chemical investigations elucidated that the glucose, in the open chain format, binds to the N- terminal to form an aldimine (Schiff base) before undergoing an Amadori rearrangement to form a more stable keto-amine. This is a nonenzymatic process that occurs continuously in vivo.[5]

Formation OF HbA1c:
The normal lifespan of an erythrocyte is 120 days. In the presence of hyperglycaemia, as the erythrocyte circulates, the N-terminal valine residues of the βchain of haemoglobin gradually undergo nonenzymatic Glycation.6 The HbA1c thus formed, constitutes about 60% to 80% of the total glycated haemoglobin. The glycation of haemoglobin occurs over the entire 120-day lifespan of the erythrocyte.5

Due to the post-translational, post-secretory glycation, an unstable aldimine-Schiff base is formed, which is a reversible process. This slowly undergoes an Amadori rearrangement to form a stable irreversible ketamine linkage, which is an advanced glycation end-product.5 The reaction is essentially irreversible, meaning that once the haemoglobin molecule becomes glycated it remains so until the end of its lifespan. While the senescent erythrocytes lose their ability to metabolize glucose, they remain permeable to glucose. Thus, the intracellular glucose concentrations reflect the extracellular glucose concentrations. The clinical assay of HbA1c measures total glycation of haemoglobin: i.e., it measures glycation of haemoglobin in both less glycated young erythrocytes as well as more glycated senescent erythrocytes.

Materials And Methods:-

Source of Study:
Patients presenting to Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Telangana.

Method of collection of data Study design:
Case-control study

Sample size:
Cases: 50
Controls: 50

Inclusion Criteria:
Cases:
All patients of Type 2 Diabetes mellitus of more than 3-6 monthsduration. (annexure)

Controls:
People with FBS, PPBS and HBA1c levels less than that definingDiabetes mellitus. (annexure)

Exclusion Criteria:
For both case and controls :
1. Type 1 Diabetes mellitus.
2. Age <18 yrs.
3. Other states associated with altered serum ferritin and HBA1c levels like:
4. Hemochromatosis
5. Chronic alcoholics
6. Chronic inflammatory conditions
7. Hepatitis
8. Patients with repeated blood transfusions
9. Iron deficiency anaemia
10. Hypothyroidism/Hyperthyroidism.

Results:-

Table 1:- Age wise distribution:

Age group(years)	Diabetics(Cases)	Non-diabetics (Controls)
41-45	7	17
46-50	5	8
51-55	9	10
56-60	6	8
>60	23	7

In this study among diabetic patients, 14% are in the 41-45 year age group, 10% in the 46- 50 year age group, 18% in the 51-55 year group, 12% in the 56-60 year group and 46%in more than 60 year age group.

Among non-diabetics, 34% are in the 41-45 year age group, 16% in the 46-50 year age group, 20% in the 51-55 year age group, 16% in the 56-60 year group and 14% inmore than 60-year aged group

Table 2:- Sex wise Distribution.

Group	Male	Female	Total
Diabetics	36	14	50
Non-diabetics	33	17	50
Total	59	31	100

In this study among diabetics 36(72%) were male, 14(28%) were female and among the non-diabetic population 33(66%) were male patients,17(34%) were female patients.

Table 3:- Correlation of HbA1c and Serum Ferritin.

HbA1c%	Diabetics	Mean S.ferritin±SD in diabetics (mcg/l)
<6.5	0	
6.5-7.5	9	209+73
7.6-9	33	270+106.3
>9	18	355.1+117

Table 4:- Corelation of Serum Ferritin and urine proteinuria.

Grade of proteinuria	Diabetics	Mean S.ferritin±SD in diabetics (mcg/l)
0	35	317+65
1+	13	421.43+127
2+	8	464.37+76
3+	4	569.02+128

Table 5:- Correlation of Serum Ferritin and Diabetic Retinopathy:

Grade of diabeticretinopathy	Diabetics	Mean S.ferritin±SD in diabetics (mcg/l)
No retinopathy	32	319.09+59
Mild NPDR	18	410.02+80
Moderate NPDR	9	529+148
Severe NPDR	1	543.09
PDR	0	0

Discussion:-

In the present era, there are many parameters to diagnose and prognosticate the diabetic status of an individual. Here in this study, we are trying to compare levels of Serum Ferritin with diabetic status and long-term complications like Diabetic Nephropathy and Diabetic Retinopathy.

In the present study, the Mean serum ferritin levels of diabetics are 379.55+118 µg/dl which is significantly high compared to non-diabetics whose mean serum ferritin is 81.66+26 µg/l with a p-value being <0.05 which is statistically significant.

Table 6:- Comparison of the present study with other studies about cases andcontrols.

	Cases(Diabetics)			Controls(Non-Diabetics)		
	Present study	Mahalaxmi et al.	Maheswari et al.	Present study	Maheswari et al.	Mahalaxmi et al.
No.of populalation	60	56	50	60	31	50
Serum ferittin(min µg/l)	379.55	457	319	81.66	84	67

Conclusions:-

High serum ferritin levels are associated with type 2 diabetes mellitus and its long‐term microvascular complications.

Higher levels of Serum ferritin are associated with high HbA1c levels.

High serum ferritin levels are suggestive of poor glycaemic control.

Summary

The present study included 50 type 2 diabetic patients and 50 non-diabetic patients from Hospitals attached to Bangalore Medical College and Research Institute.

Out of 50 Diabetic Patients, 36 were Male, 14 were Female and out of 50 non-diabetics 33 were male and 1 was female.

About mean serum ferritin levels with diabetic status, diabetics have a mean serum ferritin level of 379.55 mcg/l, which is greater than that of non-diabetics (81.66 mcg/l).

About serum ferritin and HbA1c, Serum ferritin levels were 209 mcg/l in diabetic patients with HbA1c less than 7.5%, 270 mcg/l between 7.5 and 9%, and 355.1 mcg/l in patients with HbA1c more than 9%.

About mean Serum Ferritin levels with Duration of Diabetes, Serum Ferritin levels have a positive correlation, where ferritin levels were 312.3 mcg/dl among patients with duration 0-3 yrs, 380.2 mcg/dl for patients with duration 4-6 years, 384.52 mcg/dl for patients with duration >6yrs.

About mean Serum ferritin levels with urinary proteinuria, serum ferritin was 317 mcg/l in diabetic patients with nil urinary protein 421.43 mcg/l among 1+ urinary protein, 464.37 mcg/l among 2+ urinary protein, 569.02 mcg/l among 3+ urinary protein

Serum ferritin levels with diabetic retinopathy were 319.09 mcg/l in diabetic patients with no fundus changes, 410.02 mcg/l among grade 1 NPDR patients, 529 mcg/l among grade 2 NPDR patients, 543 mcg/l among grade 3 NPDR.

Conflict Of Interest

None.

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