1. Introduction

Diabetes mellitus is one of the most prevalent endocrine disorders in the world [1]. Pre-diabetes (IFG and IGT) is often described as the 'gray area' between the normal blood sugar and diabetic levels. Pre-diabetic state of dyglycemia is often associated with insulin resistance (IR) and increased risk of cardiovascular pathology. There is a bi-directional association between Diabetes mellitus and iron metabolism. Systemic iron overload contributes to abnormal glucose homeostasis by: (i) insulin deficiency as a result of oxidative stress on the pancreatic beta cells leading to cell death and decreased secretion of insulin (ii) insulin resistance caused directly by iron overload [2-5]. Iron is a transitional metal and a potential catalyst in cellular reaction that produces reactive oxygen species [2]. The catalytic iron converts poorly reactive free radicals like H2O2 into highly reactive ones such as hydroxyl radical and superoxide anion that can initiate and propagate the cascades leading to oxidative damage [3,4]. Several studies have shown that there is increased oxidative stress in diabetic patients with iron overload [2]. Ferritin is a multi-subunit containing protein, molecular weight of 450kD with the capacity to sequester up to 4500 atoms of iron in a ferric form. It contains the enzyme ferroxidase that oxidizes ferrous form to ferric form. It serves to pack and isolate iron atoms thus preventing any toxic cellular damage by reactive oxygen species [7]. Ferritin is an index of body iron stores and also an inflammatory marker. The initial and the most common defect in patients with an earlier stage of damage induced by iron overload is liver-mediated insulin resistance [8]. A study has reported that hepatic iron overload syndrome is characterized by increased prevalence of glucose tolerance and diabetes, with hyperferritinemia and normal transferrin saturation [9]. Studies have shown that increased iron overload has an adverse effect on the endothelium that contributes to macro vascular complications and accelerates the development of atherosclerosis [10,11]. The pre-diabetic state of IGT is associated with IR and has an increased risk of development of cardiovascular complications. In this study we planned to investigate the serum ferritin levels in diabetic and pre-diabetic subjects.
**2. Material and methods**

This study was carried out in 120 male subjects with age group of 25 – 80 years. The subjects were divided into two groups. Group 1: 60 subjects of type 2 Diabetes mellitus on regular follow up. Group 2: 60 subjects of Pre-diabetics (IFG and IGT) were included in the study. (Exclusiv Critria includes) type 1 Diabetes mellitus, CKD stage 3 and above (by measuring creatinine values in each subject and calculate GFR using Cockcroft Gault formula), recent major surgery, infection, diabetic foot, recent history of blood loss, bleeding piles, iron therapy, history of cancer or chemotherapy.

**2.1 Study protocol**

The data was collected through standard questionnaire which included their personal data, drug usage, disease history and physical examination. Weight and height was measured and Body mass index was calculated based on weight / (height)^2 formula. Fasting blood sample was collected after 12 hours of fasting and 2 hours of post-glucose (75 g) blood sample was also collected subsequently. This study was approved by the institutional ethical committee and a written informed consent was obtained from all the subjects.

The blood glucose was measured by glucose oxidase and peroxidase method (Randox reagent) using the instrument Olympus AU 400. Serum iron by ferrozin method, TIBC by saturation precipitation method, creatinine by Jaffe’s method and ferritin by turbidimetric method with Beckman Coulter reagents in Olympus AU400.

**2.2 Statistics**

Statistical data analysis was done using SPSS programme. Arithmetic mean and standard deviation were worked out to assess the levels of various parameters in both groups under study. Student’s t-test was used for comparison of quantitative variables.

**3. Results**

A total number of 120 cases that includes 60 Diabetic and 60 Pre-diabetic were examined. The mean and standard deviation for BMI in diabetes was (25.5 ± 3.2) and in pre-diabetes (24.3 ± 2.1). Though, there was no significant difference between the two groups, high BMI in pre-diabetes is a risk factor to develop diabetes and its complications in future.

The mean level of iron (99.2 ± 27.7 µg/dl), TIBC (308 ± 53.2 µg/dl) and Hb (14.3 ± 2.1 g%) did not show statistical difference as compared with the mean of iron (107.9 ± 30.1 µg/dl), TIBC (331.7 ± 49.2 µg/dl) and Hb (14.5 ± 2.4 g%) in pre-diabetic subjects (Table 1). The mean serum ferritin level in diabetic subjects was (224.8 ± 60.9 µg/dl) and in pre-diabetic subjects (175.6 ± 74.7 µg/dl). Statistical analysis showed that there was a significant increase in ferritin levels in diabetes as compared with the duration of diabetes (148.4 ± 54.6 months) (Figure 1).

**Table: 1 Mean & Standard Deviation (SD) of Parameters included in the study**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Diabetic Mean ±SD</th>
<th>Pre-Diabetic Mean ±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in Years)</td>
<td>54.15 ± 9.94</td>
<td>44.8 ± 12.49</td>
</tr>
<tr>
<td>BMI</td>
<td>25.52 ± 3.20</td>
<td>24.33 ± 2.17</td>
</tr>
<tr>
<td>Duration (in Months)</td>
<td>148.4 ± 54.61</td>
<td>5.42 ± 1.60</td>
</tr>
<tr>
<td>FBS (mg/dl)</td>
<td>147.08 ± 37.71</td>
<td>69.27 ± 19.72</td>
</tr>
<tr>
<td>PPBS (mg/dl)</td>
<td>268.90 ± 38.25</td>
<td>153.63 ± 12.43</td>
</tr>
<tr>
<td>Hb (g%)</td>
<td>14.33 ± 2.13</td>
<td>13.59 ± 2.41</td>
</tr>
<tr>
<td>Iron (µg/dl)</td>
<td>100.18 ± 28.53</td>
<td>102.44 ± 28.65</td>
</tr>
<tr>
<td>TIBC (µg/dl)</td>
<td>309.53 ± 53.98</td>
<td>322.04 ± 47.86</td>
</tr>
<tr>
<td>Ferritin (µg/L)</td>
<td>224.75 ± 60.99</td>
<td>175.57 ± 74.74</td>
</tr>
</tbody>
</table>

**Fig. 1 Comparison of Ferritin Levels in Diabetic and prediabetic subjects**

![Ferritin Levels Comparison](image)

**4. Discussion**

The result of this study showed that serum ferritin in diabetic patients is significantly higher and correlates with increased duration of diabetes.

Ferritin has been known as an index for body iron stores and also an inflammatory marker [12]. It releases iron in a controlled fashion and plays a central role in the maintenance of intracellular iron balance. Iron is a potent pro-oxidant that increases cellular oxidative stress causing inhibition of insulin internalization and action, resulting in hyperinsulinemia and IR [13]. Several studies have shown that IR is known to be closely related to the total body iron stores [14, 19]. We hypothesized that serum ferritin could be a marker of insulin resistance.

Type 2 Diabetes mellitus is associated with pancreatic beta-cell dysfunction and insulin resistance. The extracellular hyperglycemia targets the pancreatic beta-cells and causes oxidative stress. In addition, glycation of transferrin decreases its...
ability to bind ferrous ion and increases the pool of free iron which stimulates ferritin synthesis [15]. Thus, ferritin acts both as a source of iron which induces oxidative stress and as a mechanism that protects against iron toxicity [16]. Oxidative stress is increased in diabetics because of generation of oxygen free radicals and glucose auto-oxidation [20]. With increased duration of diabetes, the complex process of advanced glycation end product formation produces reactive oxygen species by metal catalyzed reaction. Another study showed that reactive oxygen species interfere with insulin signaling at various levels in the insulin receptor function and inhibits the translocation of GLUT4 in the plasma membrane [17]. Salonen et al presented a study where the level of serum ferritin predicts the risk of ischemic heart disease[18].

Hence, the investigation to study the status of iron overload in Diabetes and Pre-diabetes can assess oxidative stress resulting in insulin resistance and the risk of development of diabetes vascular complications.

5. Conclusion

Serum ferritin levels are higher in type 2 Diabetes mellitus which correlated well with the increased duration of diabetes. Ferritin is the marker of iron overload and has a role in insulin resistance. Thus, routine screening for serum ferritin concentration in pre-diabetes patients can be done to assess the body iron stores and the risk of development of diabetic vascular complications by reactive oxygen species.

6. References


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