VOLUME - 12, ISSUE - 09, SEPTEMBER - 2023 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Biochemistry

THE RELATIONSHIP BETWEEN SERUM FERRITIN AND GLUCOSE TOLERANCE IN PREDIABETES PATIENTS.

Dr Huma Nasrat Assistant Professor, Department of Biochemistry, Gandhi medical college, Bhopal.

Dr Amit Singh Ray* Associate Professor, Department of Biochemistry, Gandhi medical college, Bhopal. *Corresponding Author

Dr Tripti Saxena Professor and Head, Department of Biochemistry, Gandhi medical college, Bhopal.

ABSTRACT The exact mechanism through which elevated serum ferritin promotes the development of type 2 diabetes is unknown. We examined the relationship between serum ferritin levels and impaired fasting glucose, a pre-diabetes stage associated with insulin resistance, in this study. Subjects & methods: including 100subjects with impaired fasting glucose (IFG) and 100 healthy people who were well matched for age and sex, were enrolled. Body mass index (BMI) and blood pressure of the participants were measured. Fasting blood glucose and ferritin were evaluated. All the data were analyzed by t-test, $\chi 2$ test and analysis of variance. Results The IFG group had higher serum ferritin concentrations (85.5+6.6 μg/L vs. 49.4+3.7 μg/L, p=0.001). A positive correlation was found between fasting plasma glucose and serum ferritin (r=0.29, p=0.001). Using multiple regression analysis, we found an association between serum ferritin and blood pressure (0.15, p=0.01), FPG (0.29, p=0.001). The odds ratio for the association of IFG in male subjects with a high serum ferritin level was 8.3 (95% CI: 1.2–11.9, p=0.01) and for females was 3.06 (95% CI: 0.58–15, p=0.1). Conclusion Based on the data from our study, an elevation in serum ferritin can be seen in pre-diabetes stage, before the occurrence of an overt diabetes mellitus.

KEYWORDS : diabetes mellitus, ferritin, impaired fasting glucose.

INTRODUCTION:

The prevalence of prediabetes is increasing which is an important risk factor for the development of overt diabetes and cardiovascular disease. Iron is an important mineral in normal physiological processes, and ferritin is a specialized iron storage protein, which reflects iron stores in the body [1]. Serum ferritin (SF) has been found to be a reliable tool, providing that confounding effects by inflammatory, hepatic, or neoplastic diseases are excluded [2]. Previous studies have demonstrated an association between increased SF levels and higher risks of diabetes [3, 4].

India is facing diabetes as the major public health problem and economic burden of potential diabetic patients. Thus, clarifying its etiology and looking for modifiable risk factors are of paramount importance for diabetes control and prevention. However, the exact mechanism through which elevated SF promotes the development of type 2 diabetes is unknown. Thus our study was designed to investigate the association between serum ferritin concentration and Impaired Fasting Glucose.

METHODS

Subjects: The study was conducted under the department of biochemistry, Gandhi medical college Bhopal after its approval by the institutional ethics committee. All the participants were informed about the aim and objectives of the study and informed consent was obtained from all of them before study initiation. The 100 cases with Fasting Plasma Glucose(FPG) were enrolled. Age and gender matched 100 control subjects with normal Body Mass Index, the definition of non-obese is BMI < 25 kg/m2, and it was identified by WHO criteria and normal fasting plasma glucose were included in the study. Each participant was asked predesigned questionnaire. The inclusion criteria included the following :(1) all subjects with FPG more than 110 mg/dL (6.105 mmol/L) and less than 126 mg/dL (6.993 mmol/L) for cases .AS per the Glucose metabolism classification using 2021 American diabetes association recommended standards. (2) clinically stable subjects with no previous medical history of diabetes, hypertension, dyslipidemia, coronary artery diseases, or cerebral stroke; (3)without clinical evidence of endocrinopathy; (4) not taking medications known to affect glucose and lipid metabolism, such as statins, glucocorticoids, thyroid hormones, and thiazide diuretics; (5) not having neoplasia and liver disease; (6) postmenopausal female subjects. The exclusion criteria included the following: (1) subjects with hepatic or renal dysfunction (2) subjects with anemia, blood transfusion, and the recent use of iron, who smokes, consuming alcohol, and having acute and chronic inflammation.

Measurements:

Anthropometric Measurements: Weight was measured by using a balanced-beam scale. Height was measured by the stadiometer and body mass index (BMI) was calculated based on weight in kilogram divided by the height in meter squared formula. Blood pressure was measured twice with a mercury sphygmomanometer after 10 min of rest while the subjects were seated, and the average of the two measurements was used for analysis. The mean reading was taken as the blood pressure of the subject. Mean systolic blood pressure (SBP) > 120 mmHg or diastolic blood pressure (DBP) > 90 mmHg or current and history of use of antihypertensive medications was defined as hypertension for the purposes of this study.

Laboratory Examinations:

After an overnight fast of 8 h, blood samples were drawn under aseptic precaution from an antecubital vein in each subject into plain and fluoride vacutainer tubes. Laboratory measurements were performed at the clinical biochemistry laboratory of Gandhi medical college, Bhopal. Fasting Plasma glucose and serum ferritin was analyzed on BA-400 (bio system) fully automated analyzer. Fasting Plasma glucose was measured by the glucose-peroxidase enzymatic method, with a detection limit of 3.6mg/dL along with the linearity of 500mg/dL. Repeatability coefficients of variation (CV) 1.0% for lower limit and 0.4% for upper limit concentrations. Within-laboratory coefficients of variation (CV) was 1.7% for lower limit and 1.1 % for upper limit concentrations. Serum ferritin was measured by latex agglutination method, with a detection limit of 5.4 μg/L along with the linearity of 500 μg/DL.Repeatability coefficients of variation (CV) 3.0% for lower limit and 1.6% for upper limit concentrations. Within-laboratory coefficients of variation

(CV) was 3.9% for lower limit and 2.6 % for upper limit concentrations.

Statistical Analyses

All analyses were performed using the SPSS 14.0 statistical software. Data was expressed as the means ±SD. Count data was expressed as percentage. Student's t-tests or 2 tests were used to compare clinical and laboratory data. Pearson regression and analysis of variance was used and the odds ratio was calculated for detection of a glucose-impaired condition in the presence of high serum ferritin concentration. Significance was considered at a level of p=0.001.

RESULT

In our study, 200 people were studied, including 100 cases with IFG and 100 control with normal plasma glucose concentration. Table 1 shows the anthropometric and laboratory characteristics of the case and control subjects in this study. Serum ferritin was higher in the IFG cohort (85.5±6.6 μg/L vs. 49.4±3.7 μg/L, p=0.001). Levels of fasting plasma glucose in the cases group were much higher than in the healthy control subjects. On comparing laboratory findings for cases and control subjects, a significant difference was found in their serum ferritin concentrations; Positive correlation was found between FPG and serum ferritin in this study (r=0.29; p=0.001). Using multiple regression analysis, we found a significant correlation between serum ferritin and blood pressure, FPG but not with BMI depicted by table2. The odds ratio for the association of IFG with high serum ferritin concentration was 3.3 (95% CI 1.3–8.3, p=0.01). The odds ratio for the association of IFG in male subjects with high serum ferritin level was 8.3 (95% CI 1.2–11.9, p=0.01) and for females was 3.06 (95% CI 0.58–15, p=0.1).

Table 1: Clinical And Laboratory Characteristics Of The Cases And Controls.

Variable	Control(NPG) N=100	Cases(IFG) N=100	p-value
Age	47.7±16	47.7±16	0.9
BMI (kg/m2)	22.7 ± 1.2	23.1 ± 1.1	0.232
SBP (mmhg)	110.2 ± 10.4	124.9 ± 18.2	0.004
DBP (mmhg)	86.4 ± 8.4	90.4 ± 9.4	0.000
FPG (mg/dL)	92±8.7	115±4.7	0.001
Ferritin (μg/L)	49.4±3.7	85.5±6.6	0.0001

- Key: NPG=normal plasma glucose;FPG = fasting plasma glucose; BMI = body mass index; For continuous variables, data shown are mean ± SD
- *p values calculated from the comparisons between the normal and IFG groups. Significance was considered at a level of p=0.001.

Table 2. Correlations (r) Between Serum Ferritin And Other Variables In Cases And Controls.

Variable	Ferritin concentration (μg/L)	p value
BMI (kg/m2)	0.06	0.4
SBP (mmhg)	0.023	0.863
DBP (mmhg)	0.099	0.454
FPG (mg/dL)	0.29	0.001

DISCUSSION

In the present study, we found that the Serum Ferritin levels significantly increased when the glucose metabolic disorder was deteriorated. Our findings provided us with new evidence of SF being regarded as a biomarker for insulin resistance but not relevant with beta cell function. Several studies showed the association between SF and diabetes [5-7]. However, few studies conclude that Serum Ferritin may not be a strong risk factor in the pathogenesis of obesity and diabetes [8]. Although the exact mechanism of the association between Serum Ferritin and diabetic disorder remains to be clarified. So far, several possible biological pathways might be proposed to explain the observed findings. Firstly, Serum Ferritin is regarded as a biomarker of body iron store, whose catalytic effects could induce lipid peroxidation [9]. Lipid peroxidation might be involved in the development of insulin resistance [10]. Secondly, excess body iron may be directly involved in insulin signaling [11] and is able to form highly reactive free radicals, which can lead to disturbed glucose metabolism and subsequent hyperglycemia [12]. Finally, there are some evidences of a relevant relationship between Serum Ferritin levels and inflammation [13]. Thus concluded that SF may not be a strong risk factor in the pathogenesis of obesity and diabetes.

Limitations

First, our study was that this research is a cross-sectional study. Experimental and prospective studies are warranted to elucidate the role of Serum Ferritin in glucose metabolism. Second, Serum Ferritin levels differ significantly according to sex. Many of the research conclusion showed that gender might modify the effects of SF on diabetes and insulin resistance [13–14]. This might be merely statistical interaction, which does not mean biological interaction between gender and ferritin. Therefore, the longitudinal relationship study between SF levels and glucose metabolism in nonobese adults needs to confirmed.

CONCLUSION

Reduced dietary iron intake, especially in men and postmenopausal women with additional risk factors for type 2 diabetes, may be advisable. Actively lowering body iron stores may be effective in preventing type 2 diabetes in selected subjects with impaired glucose metabolism.

Conflict Of Interest Statement

None declared

REFERENCES

[1] C. Zafon, A. Lecube, and R. Simo, "Iron in obesity. An ancient ´ micronutrient for a modern disease," Obesity Reviews, vol. 11, no. 4, pp. 322–328, 2010.

[2] H.-T. Kang, J. A. Linton, and J.-Y. Shim, "Serum ferritin level is associated with the prevalence of metabolic syndrome in Korean adults: the 2007-2008 Korean National Health and Nutrition Examination Survey," Clinica Chimica Acta, vol. 413, no. 5-6, pp. 636–641, 2012.

[3] L. H. Dekker, M. Nicolaou, D. L. Van Der A et al., "Sex differences in the association between serum ferritin and fasting glucose in type 2 diabetes among South Asian Surinamese, African Surinamese, and ethnic Dutch: the population-based SUNSET study," Diabetes Care, vol. 36, no. 4, pp. 965–971, 2013.

[4] L. Sun, G. Zong, A. Pan et al., "Elevated plasma ferritin is associated with increased incidence of type 2 diabetes in middleaged and elderly Chinese adults," Journal of Nutrition, vol. 143, no. 9, pp. 1459–1465, 2013.

[5] N. G. Forouhi, A. H. Harding, M. Allison et al., "Elevated serum ferritin levels predict new-onset type 2 diabetes: results from the EPIC-Norfolk prospective study," Diabetologia, vol. 50, no. 5, pp. 949–956, 2007.

[6] S. K. Kunutsor, T. A. Apekey, J. Walley, and K. Kain, "Ferritin levels and risk of type 2 diabetes mellitus: an updated systematic review and meta-analysis of prospective evidence," Diabetes/Metabolism Research and Reviews, vol. 29, no. 4, pp. 308–318, 2013.

[7] M. L. Jehn, E. Guallar, J. M. Clark et al., "A prospective study of plasma ferritin level and incident diabetes: the Atherosclerosis Risk in Communities (ARIC) study," American Journal of Epidemiology, vol. 165, no. 9, pp. 1047–1054, 2007

[8] M. Gupta, A. Palta, R. Singh, and S. Lehl, "Body iron stores in middle-aged North Indian patients with type 2 diabetes and obesity," Journal of Mid-life Health, vol. 5, no. 2, p. 72, 2014.

[9] G. Deray, A. Heurtier, A. Grimaldi, V. L. Vacher, and C. I. Bagnis, "Anemia and diabetes," American Journal of Nephrology , vol. 24, no. 5, pp. 522–526, 2004

[10] J. Emerit, C. Beaumont, and F. Trivin, "Iron metabolism, free radicals, and oxidative injury," Biomedicine and Pharmacotherapy, vol. 55, no. 6, pp. 333–339, 2001.

[11] A. S. Soto Gonzalez, D. B. Guerrero, M. B. Soto, S. P. D ´ ´ıaz, M. Martinez-Olmos, and O. Vidal, "Metabolic syndrome, insulin resistance and the inflammation markers C-reactive protein and ferritin," European Journal of Clinical Nutrition, vol. 60, no. 6, pp. 802–809, 2006.

[12] N. M. Pham, A. Nanri, S. Yi et al., "Serum ferritin is associated with markers of insulin resistance in Japanese men but not in women," Metabolism: Clinical and Experimental, vol. 62, no. 4, pp. 561–567, 2013.

[13] C.-H. Kim, H.-K. Kim, S. J. Bae, J.-Y. Park, and K.-U. Lee, "Association of elevated serum ferritin concentration with insulin resistance and impaired glucose metabolism in Korean men and women," Metabolism: Clinical and Experimental, vol. 60, no. 3, pp. 414–420, 2011.