ORIGINAL ARTICLE

Association of Serum Ferritin with Risk of Anemia in Non-Diabetic Adolescents with Family History of Type 2 Diabetes Mellitus

Maira Mahmood [1], Huma Ashraf [2], Anoosh Qayyum [3], Farwa Sijjeel [4], Naim A Nizami [5], Shazia Rashid [6]

Associate Professor Department of Biochemistry, FMH College of Medicine and Dentistry, Lahore [1]
Associate Professor Department of Biochemistry, CMH Lahore Medical College, Lahore [2]
Assistant Professor Department of Biochemistry, Ameer ud din Medical College, Lahore [3]
Assistant Professor, Blood Bank, Pakistan Institute of Medical Sciences, Islamabad [4]
Professor Department of Biochemistry, Rai Medical College, Sargodha[5]
Associate Professor, Institute of Molecular Biochemistry and Biotechnology, University of Lahore, Lahore[6]

Doi: doi.org/10.53685/jshmdc.v2i2.77

ABSTRACT

Background: Controversy occurs in the relationship between serum ferritin levels, insulin resistance and risk of developing anemia in adolescents with family history of diabetes.

Aims & Objectives: This study was designed to find out the association between serum ferritin levels with risk of developing anemia in non-diabetic adolescents with family history of type 2 diabetes mellitus (T2DM).

Materials & Methods: A descriptive cross-sectional was conducted in a local medical institute of Lahore. Study included 50 non-diabetic, non-obese male / female adolescent with family history of type 2 diabetes mellitus and 50 healthy male/female non-obese adolescents without family history of T2DM considered as controls. Level of serum ferritin and serum insulin was estimated by Enzyme Linked Immunosorbent Assay. Blood glucose was estimated by auto-analyzer. Insulin resistance was calculated by HOMA-IR index and beta cell function was assessed by HOMA- beta index.

Results: Levels of fasting blood sugar, insulin resistance were found to be increased with decreased level of serum ferritin and decrease beta cell function in both male as well as female cases as compared to controls. Negative correlation was found between serum ferritin and insulin resistance while a positive correlation was found between serum ferritin and beta cell function.

Conclusion: Low level of serum ferritin is associated with reduced beta cell function and increased insulin resistance. This may increase the risk of developing iron deficiency anemia that can affect both immune system as well as increase susceptibility to infections.

Key Words: Ferritin, Insulin Resistance, Type 2 Diabetes Mellitus

How to cite this article: Mahmood M, Ashraf H, Qayyum A, Sijjeel F, Nizami NA, Rashid S. Association of Serum Ferritin with Risk of Anemia in Non-Diabetic Adolescents with Family History of Type 2 Diabetes Mellitus. JSHMDC. 2021; 2(2): 77-84. doi: 10.53685/jshmdc.v2i2.77

Corresponding Author:
Dr Maira Mahmood
Associate Professor
Department of Biochemistry
FMH College of Medicine and Dentistry, Lahore
Email address: drmairamahmood@gmail.com
Received 22.09.2021, Revised 25.10.2021, Accepted 27.12.2021

INTRODUCTION

Adolescence is a serious era of growth, maturation, and development which needs proper nutrition. The lack of standard nutrition may result in different health problems. Nearly 85-90 % of adolescents who belong to developing countries are under-nourished. This may result in anemia and other health issues.[1]

Besides family history of T2DM, nutritional state both in the pre natal and post natal period, puberty, obesity, and inactive lifestyle may have an effect on insulin sensitivity in children and adolescents.[2]

It is known that levels of fasting blood glucose and HbA1c are increased in anemia and iron deficiency.[3] Iron metabolism may have a direct or indirect effect in developing T2DM, however, the correlation between iron metabolism and T2DM varies between races and gender.[4] The role of iron metabolism in pathogenesis of T2DM is mediated by failure of beta cell and insulin resistance.[5] Deficiency of iron can alter the homeostasis of glucose in humans and may negatively impact glycemic control which leads to development of T2DM and related complications.[6,7] It may also alter the function of mitochondrial respiratory chain thereby reducing the ability to perform physical exercise and hence may lead to increased insulin resistance.[8]

Ferritin is an important part of iron homeostasis, and is related with chronic ailments associated with inflammation like T2DM and hypertension.[6] More than 50 % the adolescents have deficiency of ferritin. Standard level of ferritin in healthy women is 18.0–115.0 μg/L and in healthy men it is 30.0–300.0 μg/L.[9] Levels of serum ferritin were more in diabetic women versus non diabetic women. Though, in Asian diabetic men the level of ferritin was low as compared to non-diabetic Asian men.[4]

Serum ferritin levels were found to be directly related to fasting blood glucose and it is proposed that serum ferritin may be good predictor of insulin resistance.[10,11] High insulin resistance is related with low levels of iron stores (serum ferritin) and hemoglobin and people with high insulin resistance may also have iron deficiency without anemia.[12]

Though insulin resistance is related to high BMI, it is proposed that adolescents with normal BMI are also at risk of development of insulin resistance signifying that BMI is not its single determinant.[2]

Association of serum ferritin with risk of developing anemia is a worldwide health problem and related to economic and social development. It may occur in all age groups but is predominant in pregnancy and adolescents. Low levels of iron or ferritin are known to be related to diabetes as it may alter homeostasis of glycemic control. The present study was therefore designed to find the association of serum ferritin with risk of developing anemia in non-diabetic adolescents with family history of T2DM.

MATERIALS AND METHODS

A descriptive cross-sectional study was designed which included 50 non-diabetic, non-obese adolescents with family history of diabetes and 50 healthy age and gender matched controls without family history of diabetes.

Group A (1A, 1B) included 50 non diabetic male adolescent who had family history of T2DM whose diabetic parents were using oral hypoglycemic drugs or insulin. Their ages ranged from 18-20 years, and their BMI ranged from 20-25 kg/m2.

Group B (2A, 2B) with age range 18-20 years and their BMI ranged from 20-24 kg/m2 were considered as controls. They were non diabetic with no family history of diabetes or any other disease. Adolescents with thyroid disorders or

any other systemic or inflammatory diseases were excluded from the study.

The current study involved self-reported demographics that were noted on questionnaires. The study was planned to evaluate the level of serum ferritin and insulin resistance (IR) in both groups using ELISA. Fasting blood glucose level was estimated by standard kit using auto-analyzer. The minimum cut-off value of ferritin was considered to be 15.0 µg / L. Insulin resistance was calculated by HOMA-IR index using the formula based on fasting serum insulin (µU/ml) ×fasting blood glucose (mmol/l) / 22.50.[13] Study subjects having HOMA-IR value>1.64 were labelled as insulin resistant.[14]

The HOMA-beta cell function (HOMA-b) was calculated by using the following formula: 360 x fasting insulin (µU/mL) / (fasting glucose (mg/dL) - 63.[15]

Statistical Analysis

Data was analyzed by SPSS 20. Study variables were expressed as mean ± SD. Student't' test was used to compare the bio-chemical variables of study subjects and controls. P<0.05 was taken as statistically significant. Pearson coefficient correlation was used to find correlation between serum ferritin and insulin resistance as well as between serum ferritin and beta cell function. Pearson correlation is signified by 'r-values' and shows the true relationship between two variables. r-values between 0 and 0.3 or 0 and -0.3 specify a weak positive and negative relationship respectively. Furthermore, r- value between 0.3 and 0.7 or -0.3 and -0.7 specify a moderate positive and negative relationship respectively.[16]

RESULTS

Description of Table 1:

Demographic variables in male / female adolescents taken as cases showed mean BMI 23.09 and 25.14 Kg/m^2. In majority of both adolescents, the life style was sedentary with middle socioeconomic status. Both genders had a history of eating mixed diet including junk food. Majority, of the adolescents were living in hostels.

Description of Table 2:

Variations in the level of fasting blood sugar, serum insulin and serum ferritin in males and female adolescents with and without family history of T2DM was observed. Levels of fasting blood sugar and insulin resistance were increased in both genders in cases as compared to controls. On the other hand levels of serum ferritin and beta cell functions were decreased in both genders in cases.

Weak negative correlation was observed between serum ferritin and insulin resistance (Fig 1 and 2).

Description:

Correlation of serum ferritin with insulin resistance in male and female adolescents with family history of diabetes indicate weak linear negative relationship between serum ferritin and insulin resistance in both genders (p>0.05).

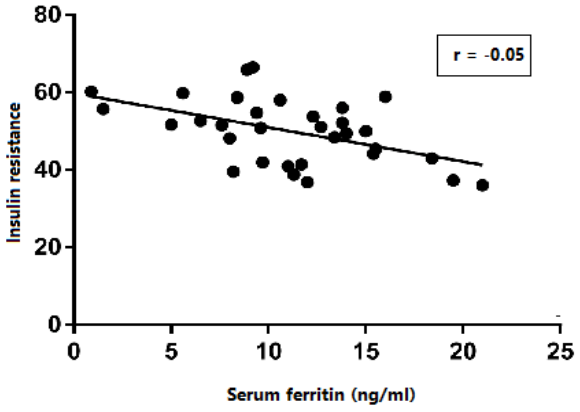

Figure 1: Correlation between insulin resistance and serum ferritin in male (r= -0.05)

Table 1: Anthropometric profile in adolescents with family history of T2DM

Variables	Male (n=25) mean±SD	Female (n=25) mean±SD
Age (years)	19.0±1.24	19.2±1.13
BMI (Kg/m^2)	24.40±4.5	23.80±2.6
Life style		
Active	08	07
Sedentary	17	18
Socioeconomic Status		
Class A(Monthly income<30000)	09	08
Class B(Monthly income >30000)	16	17
Blood pressure (mm/Hg)	120 ± 25.6	118.±24.5
Diet	Mix diet / Junk food	Mix diet / Junk food

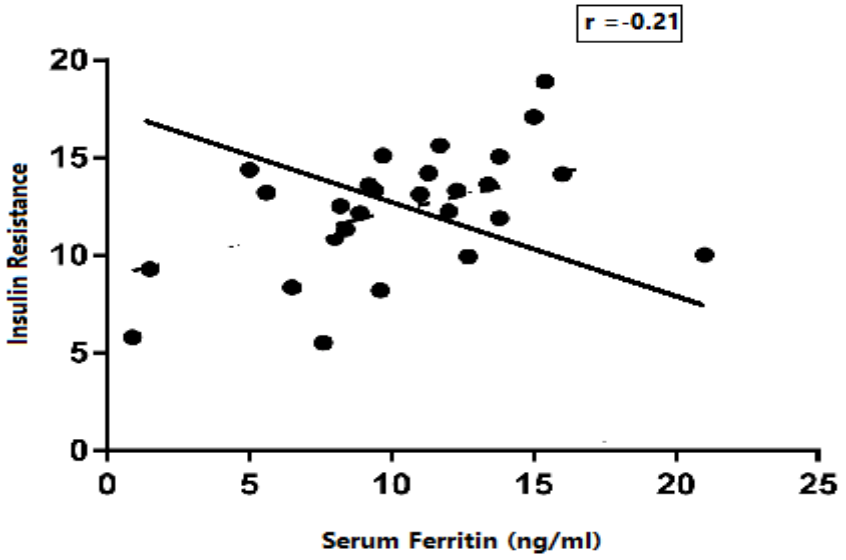

Figure 2: Correlation of insulin resistance with serum ferritin in female (r= -0.21)

Table 2: Variation in the level of biochemical parameters in male and female adolescents with or without family history of T2DM.

Variables	Group 1A Male adolescents with family history (n=25)	Group 2A Male adolescents without familial diabetic background (n=25)	Group 1B Female adolescents with family history (n=25)	Group 2B Female adolescents without familial diabetic background (n=25)	p-value
FBS (mg/dl)	93.51±7.36	87.23±7.37	95.31±6.98	94.32± 7.83	>0.05
S I (mIU/L)	5.99±2.3	5.85±3.61	7.21±3.31	7.22±4.5	>0.05
S F (ng/ml)	14.35 ± 3.5	20.75± 4.1	12.38 ±3.41	18.25± 3.1	>0.05
IR	0.99±0.03	0.86±0.021	0.97±0.02	0.96±0.011	>0.05
β cell function	74.88±4.09	84.4±32.84	78.8±4.09	83.3±33.84	>0.05

FBS= fasting blood sugar; SI= Serum Insulin;; SF= Serum ferritin; IR= Insulin resistance. *p-value ≤ 0.05 taken as significant

DISCUSSION

The speedy growth during adolescence, menarche, and the intake of non-standard diet with low content of iron, results in depletion of iron stores and increases the vulnerability of adolescents to development of iron deficiency anemia.[17]

According to our study majority of study subjects had a sedentary style and belonged to middle socioeconomic status. Majority, of the adolescents were living in hostels, where diet doesnot fulfill the criteria of standard diet. A study demonstrated that sedentary life style is the main reason for various health problems. As most people have an inactive life style, this predisposes them to the risk of developing metabolic diseases including dyslipidemia and impaired glucose metabolism resulting in development of T2DM and hypertension. It is noted that 95 to 100 % adolescents are at risk of developing diabetes due to their inactive life style. This study proposed that poor nutritional state and physical inactivity may lead to reduced serum ferritin stores and hence increase the risk of developing anemia.[2,18]

According to our study both genders used mixed diet (vegetable with chicken/meat) along with junk food. It is proposed that diet with high protein and low carbohydrate may be a reason of high values of blood iron and associated with insulin resistance in the peripheral tissues and liver.[19] however a study found that altered status of iron is enough to impair homeostasis of glucose.[20]

Diet and physical activity are not only aimed for weight reduction but also have a role in boosting immunity including (immune activation and immune-senescence) and metabolism (obesity, diabetes, and metabolic syndrome).[21]

Consumption of fresh foods, eggs and consuming meals 3 times / day were also related to lower risk of anemia. Besides lack of knowledge, low financial status, female gender and limited usage of eggs, flesh food and milk products as well consumption of meal 1-2 times /day may increase the risk of development of anemia.[22] One of the study reported that Indian girls in their adolescent age have a habit to use food rich in vitamin with less amounts of protein in comparison with boys.[23]

Levels of fasting blood sugar and insulin resistance were increased in cases as compared to controls. On the other hand levels of serum ferritin and beta cell functions were decreased in cases as compared to controls. However, a study found that impaired fasting blood glucose is predominant in men than women and therefore males have a high risk of developing diabetes.[24,25,26] A study also demonstrated that beta cell dysfunction is related with high levels of insulin resistance after the continuous ingestion of full carbohydrate rich meals and more common in Asians as compared to Caucasians.[27] Another study stated that T2DM may progress more with increasing insulin resistance and ultimately results in diabetes due to collapse of β cells.[28]

We disagreed with a study who reported that low BMI is related with low values of serum ferritin and insulin level. And there is low risk of diabetes with low values of serum ferritin.[29]

Results of another study were found to be in support our findings whereby decreased values of serum ferritin were associated with iron deficiency anemia and reduced insulin sensitvity.[24] Early identification and treatment of iron deficiency leads to early recovery of glycemic control and may help in avoiding complications.[6] It is suggested that stored form of iron; serum ferritin reflects glycemic status in people with incidence of iron deficiency or anemia.[25]

Limitations

Oral glucose tolerance test and HbA1c of study subjects should also have been performed as it is a standard test for estimation of glycemic control. Secondly, data of older adolescents should be available which may help to compare the differences in the incidence of anemia between early stages of adolescence and older stages of adolescence. Third, we concentrated on high carbohydrate and protein based foods, but some studies found that regular use of fruits and vegetables (green leafy) also helped to reduce the risk of anemia in adolescents.[16]

CONCLUSION

It is concluded that though low levels of serum ferritin may reduce beta cell functions and accounts for increased levels of insulin resistance. Furthermore, this low value of serum ferritin in adolescents with family history of diabetes may increase the risk of developing iron deficiency anemia. There is a need for screening of anemia especially in adolescents who have positive family history of diabetes and so they may take proper preventive meausures to decrease the risk of developing anemia.

Source of funding

None

Conflicts of interest

Authors declared that there is no conflict of interest.

Contributors

MM: Contributed to the conception and design of the work.
HA: collected data and critically revised the work.
AQ and FS: contributed to literature review and writing

NA: participated in data entry, statistical analysis and interpretation

SR: was responsible for drafting the cover, proof reading and approving the final version of this work.

All authors signed the agreement to be accountable for all aspects of work.

REFERENCES

1. Christian P, Smith ER. Adolescent undernutrition: global burden, physiology, and nutritional risks. Ann Nutr Metab. 2018; 72(4): 316–328.

2. Levy-Marchal C, Arslanian S, Cutfield W, Sinaiko A, Druet C, Marcovecchio ML et al. Insulin resistance in children: consensus, perspective, and future directions. Insulin Resistance in Children Consensus Conference Group. J Clin Endocrinal Metab. 2010; 95(12): 5189-5198.

3. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2013; 36: S67–S74.

4. Liu J, Li Q, Yang Y, Ma L. Iron metabolism and type 2 diabetes mellitus: A meta-analysis and systematic review. JDI 2020 11(4): 946-955

5. Simcox JA, McClain SA. Iron and Diabetes Risk. Cell Metabolism. 2013; 17(3): 329-341.

6. Soliman AT, De Sanctis V, Yassin M, Soliman N. Iron deficiency anemia and glucose metabolism. Acta Biomed. 2017; 88(1): 112-118.

7. Fasil A, Biadgo B, Abebe M. Glycemic control and diabetes complications among diabetes mellitus patients attending at University of Gondar Hospital, Northwest Ethiopia. Diabetes. Metab Syndr Obes. 2019; 12: 75-83.

8. Manios Y, Moschonis G, Chrousos GP, Lionis C, Mougios V, Kantilafti M et al. The double burden of obesity and iron deficiency on children and adolescents in Greece: the Healthy Growth Study. J Hum Nutr Diet. 2013; 26(5): 470-478.

9. Shattnawi, KK, Alomari MA, Al-Sheyab, Salameh AB. The relationship between plasma ferritin levels and body mass index among adolescents. Sci Rep 2018; 8: 15307.

10. Kim MK, Chon SJ, Jung YS, Kim BO, Noe EB, Yun BH, et al. The Relationship between Serum Ferritin Levels and Insulin Resistance in Pre- and Postmenopausal Korean Women: KNHANES 2007–2010. PLoS ONE 2016; 11(6): e0157934.

11. Vaquero MP,Martinez- Mauedo D, Zapatera B, Gallego-Narbon A, Saura-Calixto FF, Perez-Jimenz J. Serum Ferritin, a predictor of insulin resistnace? Clin Nutr 2018; 37(Supp 1): S260

12. Altunoğlu E, Müderrisoğlu C, Erdenen F, Ulgen E, Ar MC. The impact of obesity and insulin resistance on iron and red blood cell parameters: a single center, cross-sectional study. Turk J Haematol. 2014; 31(1): 61-67

13. Strage EM, Ley CJ, Forkman, J. Ohuland M, Stadig S, Bergh A et al. Homeostasis model assessment, serum insulin and their relation to body fat in cats. BMC Vet Res. 2021; 17:34

14. Einhorn D. American College of Endocrinology position statement on the insulin resistance syndrome. Endocrine practice. 2003; 9(3): 237-252

15. Cersosimo E, Solis-Herrera C, Trautmann ME, Malloy J, Triplitt CL. Assessment of pancreatic β-cell function: review of methods and clinical applications. Curr Diabetes Rev. 2014; 10(1): 2-42.

16. Ratner B. The correlation coefficient: Its values range between +1and−1, or do they? J Target Meas Anal Mark 2009; 17: 139–142.

17. Seyoum Y, Humblot C, Nicolas G, Thomas M, Baye K. Iron deficiency and anemia in adolescent girls consuming predominantly plant-based diets in rural Ethiopia. Sci Rep 2019; 9:17244.

18. Hamilton MT, Hamilton DG, Zderic TW. Sedentary behavior as a mediator of type 2 diabetes. Med Sport Sci. 2014; 60: 11-26.

19. Bugianesi E, Manzini P, D'Antico S, Vanni E, Longo F, Leone N, Massarenti P, Piga A, Marchesini G, Rizzetto M. Relative contribution of iron burden, HFE mutations, and insulin resistance to fibrosis in nonalcoholic fatty liver. Hepatology. 2004. 39(1): 179-187.

20. Davis, M.R., Hester, K.K., Shawron, K.M. Lucas EA, Smith BJ, Clarke SL. Comparisons of the iron deficient metabolic response in rats fed either an AIN-76 or AIN-93 based diet. Nutr Metab (Lond) 2012; 9: 95

21. Luzi L, Radaelli MG. Influenza and obesity: its odd relationship and the lessons for COVID-19 pandemic. Acta Diabetol. 2020; 57: 759-764.

22. Zhu Z, Sudfeld CR, Cheng Y. Qi Qi, Shaoru Li, Mohamed E et al. Anemia and associated factors among adolescent girls and boys at 10–14 years in rural western China. BMC Public Health 2021; 21: 218

23. Aurino E. Do boys eat better than girls in India? Longitudinal evidence on dietary diversity and food consumption disparities among children and adolescents. Econ Hum Biol. 2017; 25: 99–111

24. Attard S, Herring A, Wang H, Howard AG, Thompson AL, Adair LS et al. Implications of iron deficiency/anemia on the classification of diabetes using HbA1c. Nutr & Diabetes 2015; 5:e166

25. Mauvais-Jarvis F. Gender differences in glucose homeostasis and diabetes. Physiol Behav. 2018; 187: 20-23

26. Ali A, Taj A, Ahmed MU, Tabrez E. Frequency of impaired fasting glucose in first degree relatives of Type-II diabetic patients and its association with Body Mass Index. Pak J Med Sci. 2020; 36(3): 407-411

27. Yabe D, Seino Y, Fukushima M, Seino S. β Cell Dysfunction Versus Insulin Resistance in the Pathogenesis of Type 2 Diabetes in East Asians. Curr Diab Rep 2015; 15: 36

28. Ogihara T, Mirmira RG. An islet in distress: beta cell failure in type 2 diabetes. J Diabetes Investig. 2010; 1: 123–33.

29. Hughes EA, Patel JV, Bredow Z, Gill PS, Chackathayil J, Agaoglu ES, Flinders P, Mirrielees R. Ferritin as a risk factor for glucose intolerance amongst men and women originating from the Indian subcontinent. Int J Endocrinol. 2015: 6