

Association of Lifestyle Factors with Fetuin-A in Adolescents Having Familial Diabetic Background

Nazia Shahzadi,¹ Tariq Feroze Khawaja,² Imran Abdullah,³ Rakhshan Khurshid,⁴ Rehan Abdullah,⁵ Munazza Saduf⁶

Abstract

Objectives: A study was carried out to find the association of lifestyle factors with Fetuin-A in adolescents having familial diabetic background.

Methods: Study was conducted in the department of Biochemistry and department of Pathology from January 2019 to December 2019 at SIMS, SHL. Study included 35 self reported healthy male adolescents of ages 18-19 years having positive familial diabetic background (group A) whereas the subjects of same age and gender without familial diabetic background (relatives of type 2 diabetics) were placed in control group (group B). Type 2 diabetics and subjects having metabolic syndromes other than type 2 diabetes were excluded. Convenient sampling technique was used. A questionnaire based on demographic variables including lifestyle and eating habits was filled by study subjects after their informed consent. Serum levels of fasting blood glucose were estimated by autoanalyzer (HUMAN) and insulin and Fetuin-A by ELISA. Data was analyzed by SPSS 20.

Results: It was observed that 67% of total study subjects were having sedentary lifestyle and using energy dense diet and beverages in routine and found to have relatively higher levels of fasting blood sugar, serum insulin and serum Fetuin-A. However, when two groups were compared, statistically significant increase in levels of serum Fetuin-A was observed in group.

Conclusion: An association was observed between sedentary lifestyle, dietary pattern, and Fetuin-A in adolescents having familial diabetic background (group A).

Key Words: lifestyle factors, Fetuin-A, adolescents having familial diabetic background.

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Introduction

Type 2 diabetes mellitus is a complex, persistent metabolic problem. It displays a heterogeneous etiology with genetic predisposition and environmental factors which are important causes for expression of disease. It is diagnosed more frequently in children and adolescents.¹ Type 2 diabetes in adolescents is

termed as early onset adult type 2 diabetes mellitus. The incidence of early onset adult type 2 diabetes mellitus was 15 to 20 % globally.²

Concept of early-onset adult type 2 diabetes is supported by different factors like phenotype, unhealthy diet, sedentary lifestyle or increased duration of sitting may result in continued hyperglycemia with severe impact leading to overwhelming micro- and macrovascular complications.⁴ Although non-genetic factors create a direct link between type 2 diabetes and insulin resistance, the heritability also displays the arousal of type 2 diabetes mellitus from beta-cell dysfunction.⁵

Environmental and sedentary lifestyle are generally thought to increase the risk and incidence of early onset type 2 diabetes mellitus worldwide in current decades. Research based on physical inactivity with a concept that most of the time, individuals are sitting whether for their kind of job or watching television that

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| 1. Nazia Shahzadi | 2. Tariq Feroze Khawaja |
| 3. Imran Abdullah | 4. Rakhshan Khurshid |
| 5. Rehan Abdullah | 6. Munazza Saduf |

1,6. Department of Biochemistry, Services Institute of Medical Sciences (SIMS), Lahore

2. Sahara Medical College, Narowal.

3,5. INMOL (Institute of Nuclear Medicine and Oncology, Lahore)

4. Shalamar Medical and Dental College, Lahore

Correspondence:

Nazia Shahzadi, Senior Demonstrator, Department of Biochemistry, Services Institute of Medical Sciences (SIMS), Lahore. Email: nazia78y@gmail.com

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may affect the health with resultant poor metabolism of glucose & lipids leading to increased risk of diabetes mellitus, cardiovascular problems.⁶ Sedentary lifestyle not only affects above mentioned metabolic pathways but it may also increase the level of serum Fetuin-A and reduce the sensitivity of insulin.⁷

Fetuin-A is a glycoprotein mainly produced by liver and powerfully related to parameters associated with dysregulation of metabolic homeostasis like sensitivity of insulin, tolerance of glucose and levels of lipid profile. Fasting insulin level in non-diabetics must be < 25 mIU/L.

Besides, Fetuin A directly increases the insulin resistance (0.5-1.4) via blocking the action of insulin, decreasing glucose transporter GLUT-4 sensitivity and inactivation of insulin receptor tyrosine kinase in liver and muscles. Additionally, it also interferes with the action of insulin in adipocytes.⁸ It is proposed by studies that regular exercise reduces Fetuin-A secretion from the liver and improves liver related insulin sensitivity in metabolic diseases including diabetes.⁹

Sedentary behaviour has appeared as a public health problem and increases the risk of non-communicable diseases. Globally, education, transport and relaxation time progressively shift many forms of physical activity into sedentary lifestyle. Now a days, individuals of every age group spend 50 % of their waking day in sitting that need small expenditure of energy. High levels of sedentary behaviour are related to high risk of non-communicable diseases including diabetes. It is therefore need of hour to find the parameters which may prove to be a link between sedentary lifestyle and risk of diabetes especially in adolescents who have a familial diabetic background.

Current study was aimed to determine the association of lifestyle factors with Fetuin-A in adolescents having familial diabetic background

Methods

A comparative cross-sectional study included 35 male adolescents of 18-19 years of age with risk factor as group A. Thirty-five subjects of same age and gender without risk factor were taken as group B. Both adolescents with and without familial diabetic background (Relatives of type 2 diabetics) were taken from diabetes management center of Services Hospital, Lahore. Study

duration was January 2019 to December 2019. A questionnaire based on demographic variables was filled by study subjects after their informed consent. Ethical approval of study was given by IRB committee of Services Hospital, Lahore.

About 5.0 cc blood was drawn from study subjects of both groups in fasting condition for estimation of blood glucose, serum insulin and serum Fetuin-A. Fasting blood glucose was estimated by glucose oxidase method using Auto analyzer (HUMAN). Level of serum insulin and Fetuin-A was analyzed by the technique of ELISA. Insulin resistance was calculated by formula: fasting insulin (micro-U/L) x fasting glucose (n mol/L)/ 22.5.10

Data of both groups was entered and analyzed by SPSS 20. Quantitative parameters age, BMI, biochemical parameters were expressed as mean ± SD. Independent student ‘t’ test was used to compare the age, BMI and biochemical parameters of group A and group B. p-value < 0.05 was considered as a statistically significant value.

Results

Demographic variables in male adolescents (first degree

Table 1: Demographic Variables in Study Subjects (Group A and B)

Variables	Male adolescents (n=70)
Age (years)	19.7±2.27
BMI (Kg/m ²)	24.94±1.66
Lifestyle	Sedentary(67 %) Active(33%)
Socioeconomic status	Upper class (65%) Middle class (35%)
Dietary Pattern	Balanced diet (30 %) Junk food (70%)
Current residence status	Day scholar (36 %) Hostellers(64 %)

Table 2: Variation in the Level of Fasting Blood Sugar, Serum Insulin and Serum Fetuin-A in group A and Group B. Values are Expressed as Mean ± SD

	Male adolescents With familial diabetic background (35)	Male adolescents without familial diabetic background (35)
Fasting blood sugar(mg/dl)	93.51±7.36	87.23±7.37
Serum Insulin(mIU/L)	5.99±2.3	5.85±3.61
Serum Fetuin-A(mg/l)	195.17±188.16*	157.26±138.82
Insulin resistance	0.99	0.76

*P < 0.05= Significant difference

relatives of diabetics) showed that mean age of adolescents was 19 years with a BMI 24.94 Kg/m². In 67% of study subjects, the lifestyle was sedentary while 33% were active. 65% belonged to upper socioeconomic class while 35% belonged to middle socioeconomic class. 30% were consuming balanced diet whereas 70% were consuming junk food as a major portion of their diet. 64% were living in hostels while 36% were day scholars. (Table 1). Variation in the level of fasting blood sugar, serum insulin and serum Fetuin-A in male adolescents with and without familial diabetic background was observed. Levels of fasting blood sugar, serum insulin and serum Fetuin-A were increased in group A as compared to group B. Values of insulin resistance were increased in male adolescents with familial diabetic background. Statistically significant difference was only observed in case of serum Fetuin-A. (Table 2).

Discussion

The incidence of type 2 diabetes in young male adults is noticeably increasing with risk factors of sedentary lifestyle independent of BMI.¹¹

We found that majority of male adolescents have sedentary lifestyle and raised values of Fetuin-A (marker of insulin resistance). Number of studies reported sedentary lifestyle in adolescents as well as other age groups and demonstrated that more sitting time seems to be related with diabetes independent of BMI. A study was carried out on 800 healthy individuals having sedentary lifestyle. Study observed that their sedentary time was indirectly related with sensitivity of insulin¹². Another study found that sedentary time was considerably associated with raised blood glucose, insulin secretion, insulin resistance, Fetuin A and lipid profile and may increase the risk of type 2 diabetes.¹³

It is proposed that skeletal muscle may have a role in homeostasis of glucose and insulin resistance. Study based on the role of exercise or physical activity in increasing the uptake of glucose on skeletal muscle gives insight on auxiliary materials that mimic the adaptations of skeletal muscle to exercise.¹⁶ Contrariwise a study found that insulin-secretory ability is reduced in first degree relatives of diabetics in comparison to their controls. However, the maximal glucose uptake rates are similar in both experimental and control groups who have regular exercise.¹⁴

Impaired expression of diabetes related gene is also observed with changing the phases of active lifestyle into inactive lifestyle. It is noticed that immobility motivates the expression of many genes and represses the expression of many genes and may affect metabolic pathways.¹⁵ We observed an inverse association between Fetuin-A and active lifestyle in adolescents having familial diabetic background. Some studies also found that Fetuin-A is a biomarker to evaluate the physiological reaction to physical inactivity. It is demonstrated that Fetuin-A is an early predictor of insulin resistance which have major role in progression of type 2 diabetes. Insulin resistance arises due to combined effect of genetic predisposition and lifestyle factors including lack of physical exercise and unbalanced nutritional habits. Exercise can stimulate molecular signaling pathways which can interfere with glucose uptake.¹⁶ Results of a recent study showed the quantity of Fetuin-A secreted by the liver may be a significant determinant of changes in insulin sensitivity of body. Study concluded that Fetuin-A may be a valuable marker of individual disparity due to lifestyle involvements.⁷

We agreed with a study who also found that western diet (junk food and beverages): an energy dense diet in conjunction with a sedentary lifestyle is the primary cause of type 2 diabetes. Study also found that there is a high risk of damage to β -cells in those individuals who have familial diabetic background. As loss of function of β -cells is the definitive reason of developing type 2 diabetes.¹⁷ Additionally beverages (sugar-sweetened) constantly seem to promote diabetes risk.¹⁸ We also found that most of the subjects were living in hostel. It is now common majority of subjects are living alone or living without family as they came from different cities. A study also stated that most of males not females are living solitary life which may be related to increased threat of type 2 diabetes.¹⁹

Conclusion

An association was observed between sedentary lifestyle, dietary pattern and Fetuin-A in adolescents with familial diabetic background. It is therefore a need of schemes for promotion of active lifestyle with activities based on aerobic fitness which may prevent the adolescents from prediabetic lifestyle and associated environmental factors. However, more research is needed on schemes used for the protection from type 2 diabetes mellitus.

Conflict of Interest: None

References

1. Temneanu OR, Trandafir LM, Purcarea MR. Type 2 diabetes mellitus in children and adolescents: a relatively new clinical problem within pediatric practice. *J of Med and Life*. 2016;9(3):235-239.
2. Lascar N, Brown J, Pattison H, Barnett AH, Bailey CJ, Bellary S. Type 2 diabetes in adolescents and young adults. *Lancet Diab Endocrinol*. 2018;6(1): 69–80. [https://doi.org/10.1016/S2213-8587\(17\)30186-92](https://doi.org/10.1016/S2213-8587(17)30186-92).
3. Chawla A, Chawla R, Jaggi S. Microvascular and macrovascular complications in diabetes mellitus: Distinct or continuum?. *Indi J Endocrinol Metab*. 2016; 20(4): 546-551. doi:10.4103/2230-8210.183480.
4. Asamoah A, Obirikorang C, Emmanuel Acheampong, Max Efui Annani-Akollor, Edwin Ferguson Laing, Eddie-Williams Owiredo, and Enoch OdameAnto Heritability and Genetics of Type 2 Diabetes Mellitus in SubSaharan Africa: A Systematic Review and Meta-Analysis Evans. *J of Diab Res Vol2020, Article ID 3198671, 11 pages* <https://doi.org/10.1155/2020/3198671>.
5. Hamilton MT, Hamilton DG, Zderic TW. Sedentary behavior as a mediator of type 2 diabetes. *Med Sport Sci*. 2014;60(1):11-26. doi:10.1159/000357332.
6. Ward K, Mulder E, Frings-Meuthen PF, O’Gorman SJ, Cooprt D. Fetuin-A as a Potential Biomarker of Metabolic Variability Following 60 Days of Bed Rest. *Front. Physiol*. 19 October 2020 <https://doi.org/10.3389/fphys.2020.573581>.
7. Bourebaba L, Marycz K. Pathophysiological Implication of Fetuin-A Glycoprotein in the Development of Metabolic Disorders: A Concise Review. *J Clin Med*. 2019;8(12):2033-2033. Published 2019 Nov 21. doi:10.3390/jcm8122033.
8. Lee, S., Norheim, F., Gulseth, H. L., Langleite, T. M., Kolnes, K. J., Tangen, D. S., et al. Interaction between plasma fetuin-A and free fatty acids predicts changes in insulin sensitivity in response to long-term exercise. *Phys. Rep*. 2017; 5(1):13183-13183. doi: 10.14814/phy2.13183.
9. Ennequin G, Sirvent P, Whitham M. (2019). Role of exercise-induced hepatokines in metabolic disorders. *Am. J. Physiol. Endocrinol. Metab*. 2019; 317(1): 11–24. doi: 10.1152/ajpendo.00433.2018
10. NDC Risk Factor Collaboration. Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4.4 million participants. *Lancet*. 2016;387(1):1513-1513.
11. Lahjibi E, Heude B, Dekker JM, Højlund K, Laville M, Nolan J, Oppert JM, Balkau B RISC Study Group. Impact of objectively measured sedentary behaviour on changes in insulin resistance and secretion over 3 years in the RISC study: interaction with weight gain. *Diab Metab*. 2013;39(3):217–25.
12. Khadir A, Kavalakatt S, Madhu H, Devarajan S, Tuomilehto J. Fetuin-A levels are increased in the adipose tissue of diabetic obese humans but not in circulation. *Lipids in Health and Disease*. 2018; 17(1):291-291.
13. Yang J. Enhanced skeletal muscle for effective glucose homeostasis. *Prog Mol Biol Transl Sci*. 2014; 121(1): 133-63. doi: 10.1016/B978-0-12-800101-1.00005-3.
14. Dela F, Stallknecht B. Effect of physical training on insulin secretion and action in skeletal muscle and adipose tissue of first-degree relatives of type 2 diabetic patients. *Am J Physiol Endocrinol Metab*. 2010; 299(1): 80-91. doi: 10.1152/ajpendo.00765.2009.
15. Zelezniak A, Pers TH, Soares S, Patti ME, Patil KR (2010) Metabolic Network Topology Reveals Transcriptional Regulatory Signatures of Type 2 Diabetes. *PLoS Comput Biol* 6(4): e1000729. <https://doi.org/10.1371/journal.pcbi.1000729>
16. Kolb H, Martin S. Environmental/lifestyle factors in the pathogenesis and prevention of type 2 diabetes. *BMC Med*. 15, 131 (2017). <https://doi.org/10.1186/s12916-017-0901-x>
17. Chatterjee S, Khunti K, Davies MJ. Type 2 diabetes. *Lancet*. 2017;389(10085):2239–51. doi:10.1016/S0140-6736(17)30058-2
18. Jannasch F, Kroger J, Schulze MB. Dietary patterns and type 2 diabetes: a systematic literature review and meta-analysis of prospective studies. *J Nutr*. 2017; 147(6): 1174–82.
19. Brinkhues S, Dukers-Muijers NHTM, Hoebe CJPA, van der Kallen CJH, Dagnelie PC, Koster A, et al. Socially isolated individuals are more prone to have newly diagnosed and prevalent type 2 diabetes mellitus—the Maastricht study. *BMC Pub Hlth*. 2017; 17(1): 955-955. Published 2017 Dec 19. doi:10.1186/s12889-017-4948-6.

Authors Contribution

N.S, T.F.K, R.K.: Conceptualization of Project

N.S: Data Collection

N.S, M.S, R.K: Literature Search

R.A, I.A, M.S: Statistical Analysis

T.F.K, I.A, R.A: Drafting, Revision

N.S: Writing of Manuscript