Journal of Rare Cardiovascular Diseases
ISSN: 2299-3711 (Print) | e-ISSN: 2300-5505 (Online)
www.jrcd.eu

ORIGINAL RESEARCH

To investigate the correlation of glycated hemoglobin and fasting blood sugar with serum angiopoietin like protein 6 levels in young adults with family history of type 2 diabetes mellitus

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Article History
Received: 08.10.2025
Revised: 22.10.2025
Accepted: 03.11.2025
Published: 17.11.2025

Abstract: ***Objective*** -the aim of the study was to evaluate the correlation between glycated hemoglobin and fasting blood sugar with serum angiopoietin like protein 6 levels in young adults with family history of type 2 diabetes mellitus. ***Materials and methods*** -It was a cross – sectional case control study. We have enrolled 100 subjects with family history of diabetes and 100 controls without any family history of diabetes. We have excluded the subjects already diagnosed with diabetes, age less than 18 years and more than 25 years.6 ml of blood sample was collected after overnight fasting from the individuals for the estimation of serum ANGPTL6, HbA1c and FBS. Fasting blood sugar levels, Hba1c levels and serum ANGPTL6 levels in healthy young adults with family history of diabetes and without family history of diabetes was compared by Mann- Whitney U test. Correlation between serum ANGPTL6 with fasting blood glucose levels and serum ANGPTL6 with HbA1c was established by using Pearsons's correlation coefficient. Statistically significance was established at p< 0.05. ***Results*** - Serum ANGPTL6 levels and HbA1c levels were significantly higher in young adults with family history of type 2 diabetes mellitus with the p value <0.001 and <0.05. While when FBS levels were compare in subjects with family history of T2DM and controls without family history of T2DM. There is no statistically significant exist (p 0.092). Table 2 shows a positive correlation between serum ANGPTL6 and HbA1c levels (r = 0.86, 95% confidence interval) while a weak positive correlation was observed between FBS & serum ANGPTL6 levels (r = 0.16, 95% confidence interval) ***Conclusions*** - Our study found out that the serum ANGPTL6 levels were significantly raised in young adults with family history of type 2 diabetes mellitus when compared with young adults without any family history of type 2 diabetes mellitus. A strong positive correlation exists between serum ANGPTL6 and HbA1c levels. Which suggest that a chronic mechanism maybe involved in increasing the serum ANGPTL6 levels.

Keywords: ANGPTL6, Type 2Diabetes Mellitus, FBS, HbA1c, β cell dysfunction.

INTRODUCTION

Diabetes Mellitus is a chronic multifactorial disorder whose characteristic feature is persistent hyperglycemia. The cause is either impaired insulin secretion or impaired peripheral actions of insulin. Among other complications of diabetes, the long-term specific effects include nephropathy, retinopathy and neuropathy[1]. About 1 in 11 adults world wide now have diabetes mellitus, 90% of whom have type 2 diabetes mellitus (T2DM). Asia is a major area of the rapidly emerging T2DM global epidemic. According to IDF the prevalence of diabetes is at increasing stake in India which was 7.1% in 2009 and increased by 8.9% in 2019 India ranks 2nd in global diabetes epidemic, 25.2 million adults are estimated to have impaired glucose tolerance the numbers are estimated to increase up to 35.7 million by the year 2045 [2].in Asian population β-cell dysfunction appears notably dominant as compared to European population. For survival insulin treatment may not be required but to regulate the blood glucose level and avert chronic complications it is necessary. The hyperglycemia is not severe enough to provoke visible or clinical symptoms of diabetes so, T2DM remains undiagnosed for a long time period and these people are at increased risk of developing macro and micro vascular complications[3]. ANGPTL6 is a liver derived hepatokinase which act in an endocrine manner and plays role in glucose homeostasis, lipid metabolism and insulin sensitivity [4]. The role of ANGPTL6 has been studied in animals which indicates improved insulin sensitivity and increased energy expenditure to counteract obesity [5]. ANGPTL6 knockout mice are more obese and develop hyperglycemia and insulin resistance while mice overexpressing ANGPTL6 are thinner than wild type mice and shows better insulin sensitivity [6].However, only a few studies on human are there whose results are in conflict with the findings of animal studies which suggest increased ANGPTL6 may be due to its protective role against obesity or obesity may induce ANGPTL6 resistance in human. The pathophysiology behind increased ANGPTL6 is not clear, though it was suggested that the raised ANGPTL6 levels are associated with improved metabolic profile or ANGPTL6 sensitivity is lost which ultimately cause ANGPTL6 resistance. ANGPTL6 counteracts insulin resistance before the development of T2DM and is associated with the low incidence of T2DM but not an effective antagonist after the manifestation of T2DM [7]. ANGPTL6 may act as a novel therapeutic target against obesity and T2DM as

well as a useful biomarker for the prediction of incident diabetes in humans.

MATERIAL AND METHODS

This study was undertaken in the Department of Biochemistry, MMMC & H, Kumarhatti, Solan (HP) after getting the clearance from the institutional ethics committee for human research. The subjects were apparently healthy young adults with and without family history of type 2 DM, within the age group 18-25 years, visiting MMMC & H, Solan was screened for the eligibility criteria. It was a cross – sectional case control study. We have enrolled 100 subjects with family history of diabetes (family history was verified according to American diabetes association definition for diagnosis of diabetes) and 100 controls without any family history of diabetes. We have excluded the subjects already diagnosed with diabetes, age less than 18 years and more than 25 years.

From the subjects, 6ml of blood sample was collected after overnight fasting from the individuals who fall under the inclusion criteria through venipuncture from the antecubital vein in a disposable syringe under aseptic conditions. Out of which 2ml was transferred in an EDTA vacutainer for HbA1c estimation, 2ml in fluoride vacutainer for fasting blood sugar estimation and remaining 2ml was transferred in the plain vacutainer for ANGPTL6 estimation. The sample was collected after informed consent from the subjects. FBS and HbA1c estimated routinely while for the estimation of ANGPTL6 all the samples were centrifuged, serum was separated and stored at -20 ºC to avoid the freeze and thaw cycle. Serum samples for the analysis of ANGPTL6 were batch analyzed using human ANGPTL6 ELISA kit (Shanghai Coon Koon Biotech Co Ltd). HbA1c levels were estimated by the Tina-quant HbA1c Gen.3 assay oncobas c systems. FBS was estimated by hexokinase method oncobas c system. Potential source of confounding factor was adjusted by randomization and selecting apparently healthy young adults who are not on any kind of medication and living healthy life after verifying their parental history of diabetes. However other factors like metabolic disorders, PCOD, Thyroid abnormalities etc affecting the ANGPTL6 levels were not adjusted. Any biochemical analysis biasness was adjusted by randomly numbering the sample and not being specified the status of subject or controls.

For statistical analysis Microsoft Excel and IBM SPSS, version 20 is used. Fasting blood sugar levels, Hba1c levels and serum ANGPTL6 levels in healthy young adults with family history of diabetes and without family history of diabetes was compared by Mann-Whitney U test. Correlation between serum ANGPTL6 with fasting blood glucose levels and serum ANGPTL6 with HbA1c was established by using Pearsons's correlation coefficient. Statistically significance was established at $p< 0.05$.

RESULTS AND OBSERVATIONS:

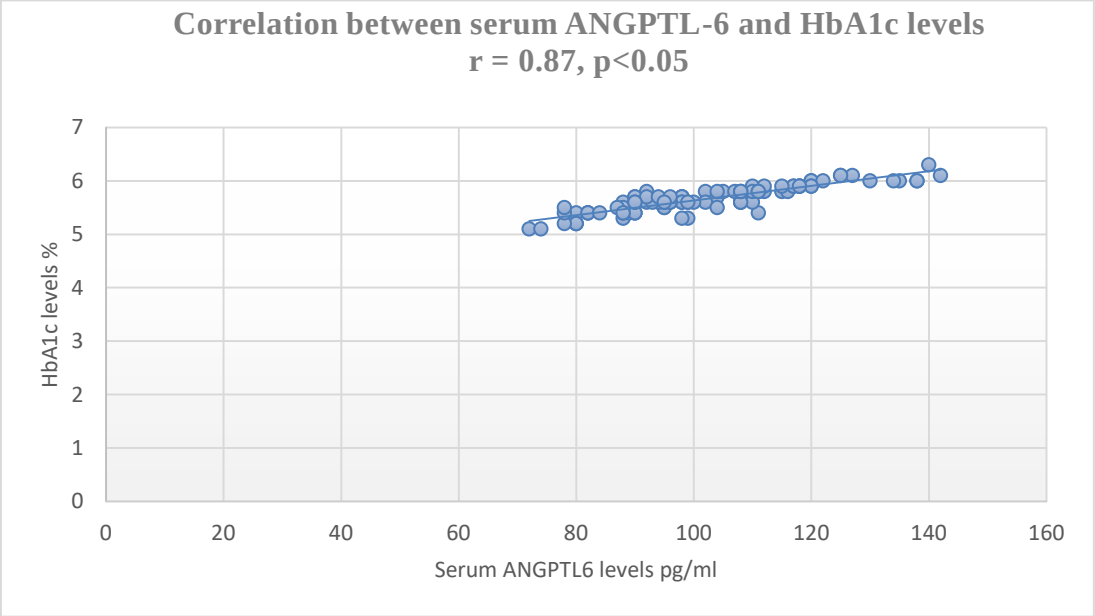
TABLE 1. Comparison of serum ANGPTL 6, Hba1c and FBS levels in subjects with family history of T2DM and controls without family history of T2DM

Parameters	With Family History of Diabetes; (n=100)	Without Family History of Diabetes; (n=100)	P Value
	Mean ± SD	Mean ± SD	
Serum ANGPTL 6	100.608 ± 16.42	42.23 ± 5.85	<0.05*
Hba1c	5.62 ± 0.25	5.43 ± 0.18	<0.05*
FBS	91.00 ± 9.42	88.93 ± 6.09	0.092

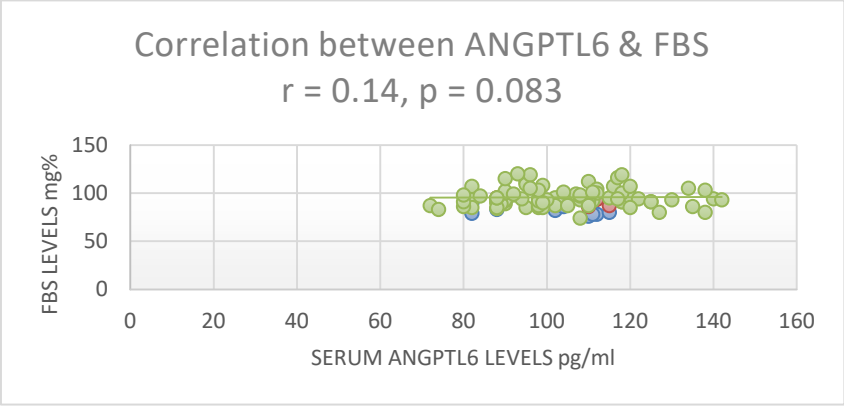
Table 1 shows comparison of biochemical parameters in subjects with family history of T2DM and controls without family history of T2DM.Serum ANGPTL6 levels and HbA1clevels were significantly higher in young adults with family history of type 2 diabetes mellitus with the p value<0.001 and <0.05. While when FBS levels were compare in subjects with family history of T2DM and controls without family history of T2DM. There is no statistically significant exist (p 0.092). Table 2 shows a positive correlation between serum ANGPTL6 and HbA1c levels (r = 0.86, 95% confidence interval) while a weak positive correlation was observed between FBS & serum ANGPTL6 levels (r = 0.16, 95% confidence interval)

TABLE 2. Correlation of ANGPTL6 with HbA1c and FBS among the subjects.

Parameters	Mean ± SD	Karl Pearson's coefficient of Correlation (r)	P Value
ANGPTL 6	100.608 ± 16.42	0.86	<0.05*
HbA1c	5.62 ± 0.25		
ANGPTL 6	100.608 ± 16.42	0.16	0.083
FBS	91.00 ± 9.42		



A strong positive correlation was observed between serum ANGPTL-6 and HbA1c levels with r = 0.87, p<0.05.



A weak non- significant correlation was observed between serum ANGPTL-6 andFBS level With r = 0.14, p = 0.083.

DISCUSSION

This study aimed to investigate the association of glycated hemoglobin and fasting blood sugar with serum ANGPTL6levels in young adults having family history of type 2 diabetes mellitus. It was observed that ANGPTL6 levels were higher in young adults with family history of type 2 diabetes mellitus when compare with controls without any history of type 2 diabetes mellitus. A previous study by Shimomura et al. had suggested ANGPTL6 might be associated with counteracting insulin resistance and obesity [8]. Kang et al. showed that serum ANGPTL6 levels was higher in participants with prediabetes. RaisedANGPTL6 levels may have a protective role against diabetes[4]. Further our study shows positive correlation between HbA1c and FBS with serum ANGPTL6 levels. The correlation between HbA1c and serum ANGPTL6 levels is a strong positive correlation which is statistically significant while the correlation between FBS with serum ANGPTL6 levels is a weak positive correlation which is not statistically significant. Our results are in accordance with a study conducted by Vikaas et al. Which suggest that a chronic mechanism may be involved in increasing the serum ANGPTL6 levels [9].
Our study supports the earlier study by Shimomura et al suggesting raised levels of serum ANGPTL6 might be counteracting obesity and insulin resistance before the onset of the disease [8]. Kitazawa et al. studied an animal model and found that ANGPTL6 gene deleted mice were obese and developed glucose intolerance and hyper insulinemia [10]. Our study cannot explain the strong positive correlation between serum ANGPTL6 levels and HbA1c is because of pathophysiological events or a beneficial phenomenon to resist the development of the disease. While a study by Kadomastu et al. suggest that circulating levels of ANGPTL6 are increased in diabetes or obesity and cannot alter the obesity [11].

The functions of human ANGPTL6 are not yet fully discovered and understood, as such so far to understand the functions and underlying mechanism we need further studies. Taking our results into consideration, we can suggest that the raised levels of ANGPTL6 in young adults with family history of type 2 diabetes mellitus when compared with controls might be to counteract the onset of the disease. Early detection before the onset of the disease is need of the time as the cases of the T2DM are alarmingly high and increasing every year worldwide. ANGPTL6 levels were found raised before the onset of the disease this can act as a marker of a therapeutic target against the disease. But our study is limited to the cross-sectional data only and the sample size is small (n=100) further cohort studies are need to identify the role of ANGPTL6 as biomarker.

CONCLUSION

Our study found out that the serum ANGPTL6 levels were significantly raised in young adults with family history of type 2 diabetes mellitus when compared with young adults without any family history of type 2 diabetes mellitus. These raise levels were found before the onset of the disease and are positively correlated with glycated hemoglobin levels. ANGPTL6 maybe act as a useful biomarker to identify the disease before its onset.

Financial support
Nil
Conflicts of interest
None

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