Original Research Article

Role of HbA1C as an Indicator of Insulin Resistance in Non-Diabetic Syndrome X Patients of Rajasthan

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Abstract

The Syndrome X or metabolic syndrome, a cluster of metabolic and cardiovascular disorders, is typically characterized by abdominal obesity, insulin resistance, hyperglycemia, atherogenic dyslipidemia and hypertension. As the Syndrome X and diabetes mellitus has increased in the recent decades, the importance of early detection of insulin resistance is crucial. Therefore, the aim of this study was to elucidate the association of HbA1c with Syndrome X with insulin resistance using HbA1c as marker. This was a prospective, case control study and including 100 subjects. Out of which, 50 subjects were the patients of Syndrome X and 50 were normal control subjects. Venous whole blood specimen of case group was collected. Samples were also taken from healthy age and sex matched controls. All samples were analyzed for Glycated Haemoglobin (HbA1c) on HbA1c Analyzer. HbA1c level was significant (p<0.0026) in Syndrome X patients. Our results suggest that HbA1c may be a marker for metabolic syndrome and may identify in a certain degree insulin resistance in subjects.
Keywords: Syndrome X, Metabolic syndrome, Glycated haemoglobin, Insulin Resistance, Hyperglycemia, Diabetes mellitus, HbA1c analyzer.

INTRODUCTION

Metabolic Syndrome X is the name for a group of risk factors that raises the risk for heart disease and other health problems, such as diabetes and stroke. The most common factors for metabolic syndrome are hyperglycemia, dyslipidemia and hypertension [1]. It is estimated that around 20-25 per cent of the world's adult population have the metabolic syndrome and they are twice at risk of death from it and three times as likely to have a heart attack or stroke compared with healthy people without the syndrome. Additionally, people with Syndrome X have five-fold greater risk of developing type II diabetes [2].

The age-adjusted prevalence among adults population was estimated to be 24%–25% in the United States, was approximately 23% in European countries and estimated to be 20%–25% among South Asians. The prevalence in Asia has increased rapidly in the recent years due to rapid socioeconomic transitions to increasing affluence, urbanization, mechanization, auto-mobilization, and urban migration [3]. The prevalence of this chronic disease is still expected to increase, because the proportion of individuals above 65 years of age will almost double globally within the next years [4].

India is a major contributor to the global increase in cardiovascular disease through the increased mortality and prevalence of Syndrome X [5]. The incidence of this syndrome has been estimated to increase with age for individuals over 50 years of age. Syndrome X affects have reported prevalence varying from 13%-24.9% in northern India, 21 to 41% in southern India [6].

Around the world, diabetes diseases start to take an epidemic character, especially in developed countries. Diabetes mellitus affects 5% of the world's population and its prevalence is doubling [7]. Diabetes is associated with many cardiovascular risk factors, which may be present before the onset of hyperglycaemia or develop after the diagnosis of diabetes. In metabolic syndrome, insulin resistance plays a key pathogenic role, and it has been proposed that this syndrome is a powerful determinant of diabetes [8, 9].

Glycated haemoglobin (HbA1c) is widely accepted as a useful measure of mean blood glucose and therapeutic guideline of diabetes. HbA1c is a form of haemoglobin that is measured primarily to identify the average plasma glucose concentration over prolonged periods of time. HbA1c may also predict incident cardiovascular events, even in individuals without diabetes mellitus. Recent work suggests the utility of HbA1c as the predictor of future risk for diabetes mellitus in diverse ethnic groups [10-12]. Even though insulin resistance is one of the major aetiological factors in the development of Syndrome X, direct quantitative measurement of insulin sensitivity is not readily available and thus cannot be used as the diagnostic tool for the syndrome. Therefore, various diagnostic criteria for Syndrome X have been suggested [13]. It is shown that patients with high HbA1c significantly define the Syndrome X [14].

Further research needs to be performed in order to investigate the cut-offs of HbA1c in the diagnosis of Syndrome X. Therefore, we examined the association of HbA1c with the components of metabolic syndrome and tried to determine whether high HbA1c levels are significant in the diagnosis of Syndrome X, confirming its status as a possible indicator of Syndrome X in patient.

MATERIALS AND METHODS
Design of Study a Case-control analytical study setting

The present study was carried out in the Department of Biochemistry in collaboration with the Department of Medicine of Sardar Patel Medical College & PBM hospital, Bikaner. The study plan was approved by the Ethics Committee of the Institute. In this prospective, case control study in which 50 clinically confirmed or diagnosed patients of Syndrome X were enrolled. Valid consent was taken from all the patients before each sample collection.

Study Population

A total number of 100 participants of age between 30-80 years were chosen and they were divided into 2 groups:

Group-I: Clinically diagnosed cases of Syndrome X (n=50) and Group-II: Healthy controls (n=50).

Study Protocol: Following criterias were considered for selection of subjects in the study:

Inclusion Criteria

Patients who were medically fit to undergo medical examinations and laboratory investigations

were only selected. Normal healthy persons were considered as controls.

Exclusion Criteria

Patients suffering from diseases other than Syndrome X like Diabetes Mellitus, AIDS, carcinoma, autoimmune disease and other co-morbidities were excluded from study group. Pregnant women, serious ill patients or patients who have undergone any surgical intervention were also not included in the study.

Procedural Steps

Overnight fasting blood samples (5-7 ml) were collected by venepuncture under aseptic conditions from cases and controls. For HbA1c, venous whole blood specimen is collected in EDTA (or heparin or potassium oxalate or sodium fluoride) containing tube. Whole blood specimens are stable up to 14 days stored at 2-8°C or up to 8 hours at room temperature before analysis. Haemolysed samples were discarded. All samples were analyzed for HbA1c on HbA1c analyzer which uses chromatography technique.

STATISTICAL METHODS

Quantitative data expressed in the form of Mean ± SD was recorded in Microsoft Excel. Graph Pad software was used to analyze statistical significance of data. Inference drawn with the use of appropriate test of significance. The level of significance was determined by employing t-test. Only when p-value was less than 0.05 was the difference between two groups considered as statistically significant.

RESULTS

Both cases and age matched controls were compared for baseline level of HbA1c (Table-1). The mean HbA1c level was found to be 5.84±0.65% [mean ± standard deviation (SD)] in normal control subjects.

The mean HbA1c level was found to be 6.76±2.0% in the patients of Syndrome X. The increase in HbA1c level was statically significant as evident by P value (p<0.0026) as indicated by Figure-1.

Table-1: Comparison of HbA1c level in patients and controls.

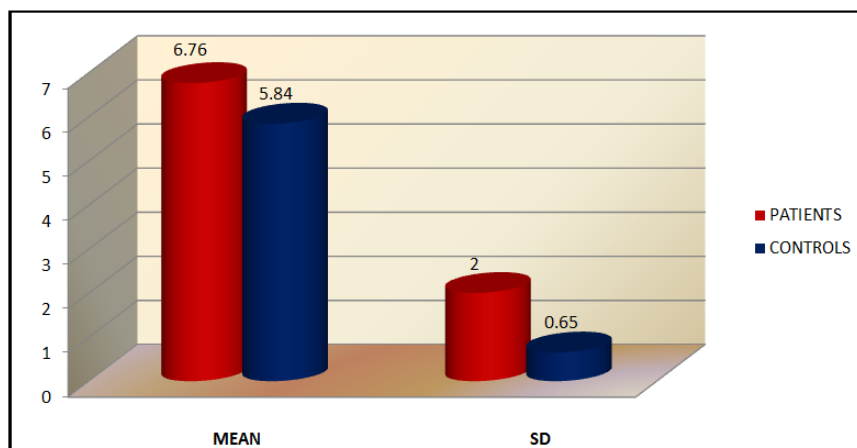|	Patients	Controls
MEAN	6.76	5.84
SD±	2.0	0.65
SEM	0.28	0.09
T		3.093
Df		98
SE		0.297
P-VALUE		0.0026** (S)

** Significant (S)

Fig-1: Mean ± SD HbA1c level in patients and controls

DISCUSSION

Our results show statistically significant increase in HbA1c level in the patients suffering from Metabolic Syndrome X. This might be due to abnormally high blood glucose levels over past 6-8 weeks since; HbA1c is a form of haemoglobin that is measured primarily to identify the average plasma glucose concentration over prolonged periods of time. Because the rate of formation of HbA1c is directly proportionally to ambient glucose concentration, our result would indicate higher glucose levels in study cases compared to controls.

HbA1c may also predict incident cardiovascular events, even in individuals without diabetes mellitus. Recent work suggests the utility of HbA1c as the predictor of future risk for diabetes mellitus in diverse ethnic groups [10-12]. Even though insulin resistance is one of the major aetiological factors in the development of Syndrome X, direct quantitative measurement of insulin sensitivity is not readily available and thus cannot be used as the diagnostic tool for the syndrome. Therefore, various diagnostic criteria for Syndrome X have been suggested [13]. It is shown that patients with high HbA1c significantly define the Syndrome X [14].

This is also favored by the studies done by Kim HK [15] who concluded that employment of the HbA1c criterion may be useful to define Syndrome X in subjects at increased risk for cardiovascular disease and insulin resistance.

In the study done by Sang Hyun Park *et al.*, [16], the usefulness of HbA1c as a diagnostic tool for Syndrome X was established to determine the cut-off value of HbA1c as a criterion for Syndrome X, in non-diabetic subjects. The mean HbA1c was 5.54% in all subjects and showed no significant difference between genders. This supports our present study.

According to Parco M Siu and Queenie S Yuen [17], significant correlation relationships existed between FPG (fasting plasma glucose) and HbA1c in both subject pools diagnosed with and without Syndrome X & findings suggest that HbA1c enhances the detection of hyperglycemia for the diagnosis of Syndrome X.

Gabriela Saravia *et al.*, [18] in their study on non-diabetic male subjects concluded that HbA1c and specially insulin levels were associated with metabolic Syndrome criteria, their clustering, and insulin resistance. Thus, HbA1c may be a useful diagnostic criterion for Syndrome X.

CONCLUSION

We conclude that HbA1c level in Syndrome X patients is significantly higher as compared to healthy subjects. This shows that HbA1c can be used as a marker to detect insulin resistance in such patients, which may predict the risk and chance of developing diabetes mellitus in future in Syndrome X patients.

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