HbA1c AS AN INDEX OF GLYCEMIC STATUS IN OBESE TYPE 2 DIABETICS

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ABSTRACT

Introduction: Type 2 diabetes has become a worldwide issue with the dramatic increase in incidence and prevalence over the past two decades. As the epidemiological burden of diabetes increases, the economic burden on individuals and nation is expected to rise. Obesity being one of the major risk factor for development of T2DM and its complication, glycemic control is crucial for management of diabetes. HbA1c is an index of long term glycemic status of diabetic subjects and has become the gold standard test around the world for initiation of treatment in diabetics. **Aims:** The aim of this study was to determine the association of obesity with T2DM and to correlate dysglycemia with obesity. **Material and Methods:** A total of 100 type 2 diabetics were enrolled for the study. The subjects were categorized based on the revised consensus guidelines for India for generalized obesity and abdominal obesity. **Results:** The results of the study showed that gender wise there was no significant difference of the various clinical and biochemical characteristics except for the duration of diabetes. Subjects of this study were mostly overweight and obese having abdominal obesity. A significant correlation was seen between the glycemic and metabolic status of the diabetic study population. **Conclusion:** Overall an increasing trend of dysglycemia in diabetic subjects with normal BMI, overweight to obese was observed. The prevalence of both central and peripheral obesity was increased in the diabetic subjects.

KEY WORDS: HbA1c, Obesity, Type 2 diabetes mellitus.

INTRODUCTION

Type 2 diabetes and obesity have become major health problems that have reached epidemic proportions. While the exact causes of diabetes are still not fully understood, it is known that several factors increase the risk of developing diabetes mellitus. There is a close association between obesity and type 2 diabetes. The global epidemic of obesity to a large extent explains the dramatic increase in the incidence and prevalence of type 2 diabetes over the past two decades [1].

Overweight and obese individuals are at a much higher risk of developing type 2 diabetes. In 2014, more than 1.9 billion adults, 18 years and older, were overweight. Of these over 600 million were obese. In 2014 among adults aged 18 years and over, 39% were overweight and 13% were obese [2]. There is a seven times greater risk of diabetes in obese people compared to those of healthy weight, with a threefold increase in risk for overweight people [3].

Obesity is thought to trigger changes to the body's metabolism. These changes cause fat tissue (adipose tissue) to release fat molecules into the blood, which can affect insulin responsive cells and lead to reduced insulin sensitivity. Both insulin secretion and insulin resistance develops early in obese persons who progress later on to diabetes.

Diet, nutrition and changing lifestyles are the major factors responsible for the increase incidence of diabetes in developing as well as developed countries. Despite having lower overweight and obesity rates, India has a higher prevalence of diabetes compared to western countries suggesting that diabetes may occur at a much lower body mass index (BMI) in Indians compared with Europeans [4].

DOI: 10.5455/ijcbr.2017.33.10

eISSN: 2395-0471
pISSN: 2521-0394

Aims and Objectives:

1. To establish a link between obesity and type 2 diabetes,
2. To define the role of abdominal obesity in type 2 diabetes,
3. To correlate the dysglycemia with obesity .

MATERIALS AND METHODS

Study design: This was an observational study

Ethical approval: Approval by the Institutional Ethics committee and informed consent from all the subjects

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enrolled in the study was obtained.

Study place: Outpatients from medicine department of Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation.

Sampling method: The subjects were selected by a systematic random sampling initially and divided into groups based on BMI.

Sample size: A total of 100 type 2 diabetes mellitus subjects of both sex were enrolled.

Inclusion criteria: Subjects in the age group of 30-70 years, obese [5] and type 2 diabetics of both sexes with more than one year duration of diabetes were included in the study.

Exclusion criteria: Subjects having cardiovascular or renal diseases and pregnant women, those who were on drugs (other than anti diabetics) that could alter the blood glucose and glycosylated haemoglobin levels like corticosteroids, oral contraceptives, thiazides diuretics, ascorbic acid, quinolones, beta blockers were excluded from the study.

Methodology:

Anthropometric measurements, detailed history and biochemical indices were assessed for all the selected individuals. History regarding age, sex, duration of diabetes and family history of diabetes was recorded for all the subjects. Measurements were taken without the subjects wearing shoes or heavy clothing and according to the revised consensus guidelines. Body Mass Index (BMI) was calculated using the formula, weight in kilograms divided by height in meters squared (kg/m^2). The waist circumference (WC) was measured using non-stretchable flexible tape in horizontal position, just above the iliac crest, at the end of normal expiration, in fasting state, with the subject standing erect and looking straight forward and observer sitting in front of the subject. The currently recommended cut-offs of BMI and WC were based on the revised consensus guidelines for India [5] Normal BMI: 18.0-22.9 kg/m^2, Overweight: 23.0-24.9 kg/m^2, Obesity: >25 kg/m^2 and for WC are, Men: 90 cm, women: 80 cm, so grouping done accordingly as mentioned above. The subject was asked to fast overnight for a period of minimum eight hours. Venous blood sample was collected from the antecubital vein and analyzed for fasting plasma glucose (FPG) and glycosylated haemoglobin (HbA1c). Fasting plasma glucose was analyzed by glucose oxidase method [6] and HbA1c by Latex agglutination [7] inhibition assay on Randox Daytona automated analyzer.

Subjects were defined as having diabetes if there is documented evidence of diabetes or they were on oral hypoglycemics drugs or on insulin. Hypertension was diagnosed in subjects who were on antihypertensive medications or had a systolic BP**≥140** mmHg and/or a diastolic BP ≥90 mmHg.

Generalised obesity (GO) is obesity based on BMI, Abdominal obesity (AO) based on waist circumference (WC) and combined obesity (CO) when subjects have both GO and AO. Based on the gender and BMI the subjects were divided into three groups as those with normal BMI- Group I, overweight- Group II and obese Group III.

Statistical Analysis: Data was analyzed using SPSS software version 16. Non-parametric statistics were used for continuous variables that were non-normally distributed and parametric statistics was used for continuous variables that were normally distributed. Descriptive statistics were be used to identify the demographic and clinical details of the total sample. The statistical analysis was done by the unpaired two tailed 't' test, Pearson's correlation coefficient and kruskal wallis test. The statistical significance was kept as a p value of <0.05.

RESULTS

A total 100 type 2 diabetes mellitus subjects were enrolled out of which 57(57%) were females and 43(43%) were male diabetics. The mean age(in years), age of onset of diabetes (in years), duration of diabetes (in years), fasting plasma glucose (FPG in mg/dl), glycated haemoglobin (HbA1c%), body mass index (BMI in kg/m2) and waist circumference (WC in cm), systolic blood pressure (SBP in mm/Hg) and diastolic blood pressure (DBP in mm/Hg) of type 2 diabetics were 50±9.51, 43.9±7.39, 5.78±4.58, 157±51.5, 8.2±1.64, 27.7±5.03, 97±10.8, 129.6±15.94 and 80.2±10.44 respectively. Family history of diabetes was seen in 66 percent, hypertension in 36 percent and thyroid disorder in 6 percent of the total sample.

Gender wise the percentage of the diabetics who gave a positive family history of diabetes, history of hypertension and had thyroid disorder was more among the females than among the males, while smoking and alcohol drinking were predominantly seen in the males. A larger proportion of the diabetics of both sexes were on oral hypoglycaemic agents (OHA), from rural areas, had poorer glycemic control HbA1c >7%, higher BMI and waist circumference (WC). The most predominant occupation for female diabetics was housework while for males it was agriculture (Table 1).

Generalised obesity (GO), Abdominal obesity (AO) and combined obesity (CO) were seen in 72, 80 and 63 percent of the diabetic population respectively (Table 2).

The mean age, duration of diabetes, FPG, were higher in male than in female diabetics while the mean levels of BMI and HbA1c are higher in female than male diabetics but were not statistically significant. Duration of diabetes was longer in male as compared to female diabetics and statistically significant. Age of onset, systolic and diastolic blood pressure were found to be only marginally elevated in males as compared to female diabetics (Table 3).

A positive correlation was observed between the BMI and WC of both female and male diabetics (Figure 1) and (Figure 2), between BMI and HbA1c of both female and male diabetics (Figure 3 and Figure 4) and between WC and HbA1c of both female and male diabetics (Figure 5 and Figure 6). All the correlations showed a

Table 1. Clinical and biochemical characteristics in T2DM based on gender

Characteristics	Females	Males
Nos	57 (57)	43 (43)
Family history	40 (70.2)	26 (60.5)
Hypertension	20 (35.1)	16 (37.2)
Thyroid disorder	6 (10.5)	0 (0)
Alcohol	1 (1.8)	24 (55.8)
Smoking	1 (1.8)	21 (48.8)
Anti-diabetics		
OHA	44 (77.2)	41 (95.3)
OHA & Insulin	13 (22.8)	2 (4.7)
Diet		
Vegetarian	1 (1.8)	1 (2.3)
Mixed	56 (98.2)	42 (97.7)
Habitation		
Rural	34 (59.6)	26 (60.5)
Urban	23 (40.4)	17 (39.5)
Occupation		
Housework	34 (59.6)	0 (0)
Daily Wage	15 (26.3)	7 (16.3)
Agriculturer	7 (12.3)	12 (27.9)
Teacher	1 (1.8)	4 (9.3)
office/disability	0 (0)	6 (13.9)
Shop owner	0 (0)	5 (11.6)
driver	0 (0)	3 (7.0)
carpenter/painter	0 (0)	6 (13.9)
HbA1c		
<7%	18 (31.6)	15 (34.9)
>7%	39 (68.4)	28(65.1)
WC		
F <80 cm	1 (1.8)	----
F >80 cm	56 (98.2)	----
M <90 cm	-----	19 (44.2)
M >90 cm	-----	24 (55.8)
BMI		
18.0-22.9 kg/m^2	3 (5.3)	11 (25.6)
23.0-24.9 kg/ m^2	12 (21)	2 (4.6)
>25 kg/m^2	42 (73.7)	30 (69.8)
Data presented as number of patients with percentages in parentheses		

Table 2. Characteristics of types of obesity in T2DM

Types of obesity	Female (57)	Males (n=43)	Total (n=100)
Generalised Obesity	42(73.7)	30(69.8)	72(72)
Abdominal Obesity	56(98.2)	24(55.8)	80(80)
Combined Obesity	42(73.7)	23(53.5))	63(63)
Data presented as number of patients with percentages in parentheses			

Table 3. Clinical and biochemical characteristics in female and male diabetics

Characteristics	Females (n=57)	Males (n=43)	p value
Age (yrs)	48.49±9.47	52.04±9.29	0.0643
Age of onset (yrs)	43.63±7.23	44.23±7.67	0.6899
Duration of DM (yrs)	4.84±3.7	7.02±5.33	0.017*
SBP(mm/Hg)	127.89±14.73	131.86±17.4	0.2202
DBP(mm/Hg)	79.65±10.17	80.93±4.87	0.4482
WC(cm)	98.63±10.25	94.93±11.27	0.09
BM I(kg/m^2)	28.58±5.02	26.64±4.87	0.0531
FPG (mg%)	151.02±52.2	164.95±50.1	0.183
HbA1c (%)	8.31±1.68	8.1±1.6	0.4528
Data presented as Mean ± SD, *P<0.05			

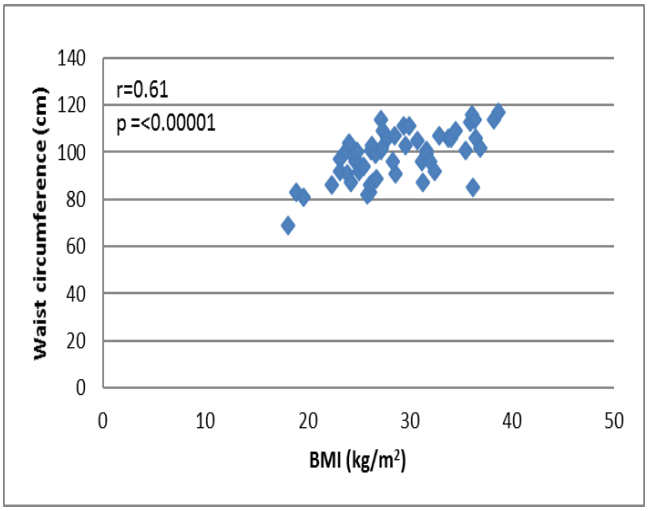

Figure 1. Correlation between BMI and WC in female diabetics

significant p value.

An increasing trend in WC and BMI and HbA1c is seen from Group I to Group III with a statistical significant difference. A statistical significant difference was noted also for age of the diabetics, and age of onset of diabetes on comparison of the three groups- Group I, II and III (Table 4).

DISCUSSION

Several large randomized prospective trials have demonstrated that an HbA1c target of 7% or below was associated with significantly lower risk of diabetes-related microvascular complications. [8,9].

Diabetes mellitus is rapidly reaching potentially epidemic proportions in India and the level of morbidity and mortality due to diabetes and its potential complications are enormous. Diabetes imposes a large economic burden on individuals, family, society and on the national healthcare system as a whole.

The prevalence of T2DM parallels the increasing preva-

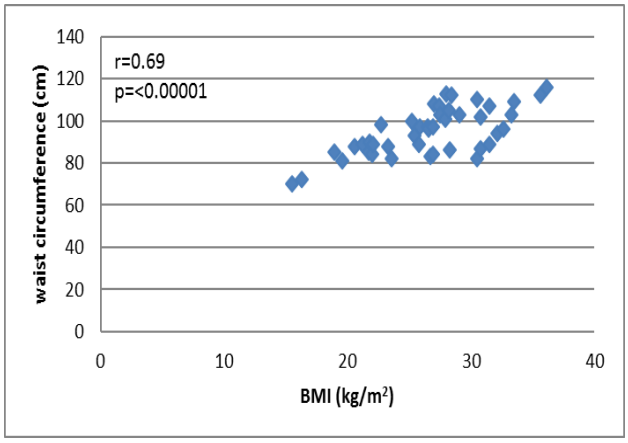

Figure 2. Correlation between BMI and WC in male diabetes

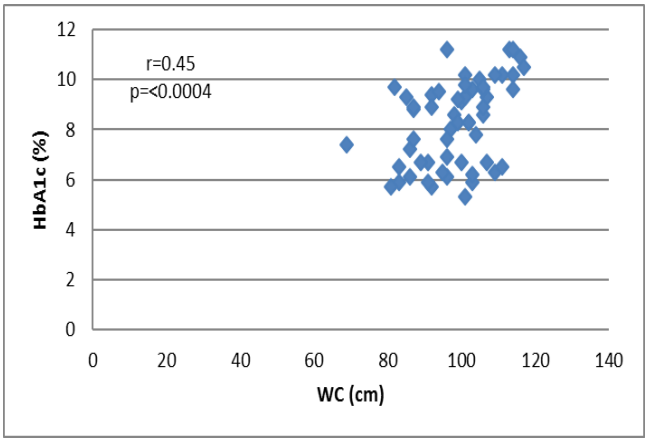

Figure 5. Correlation between WC and HbA1c in female diabetics

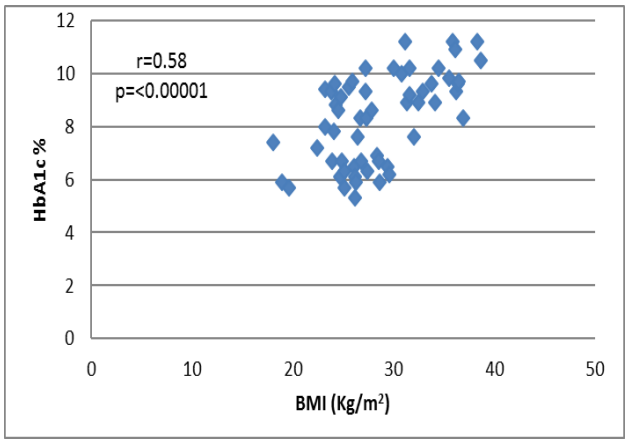

Figure 3. Correlation between BMI and HbA1c in female diabetics

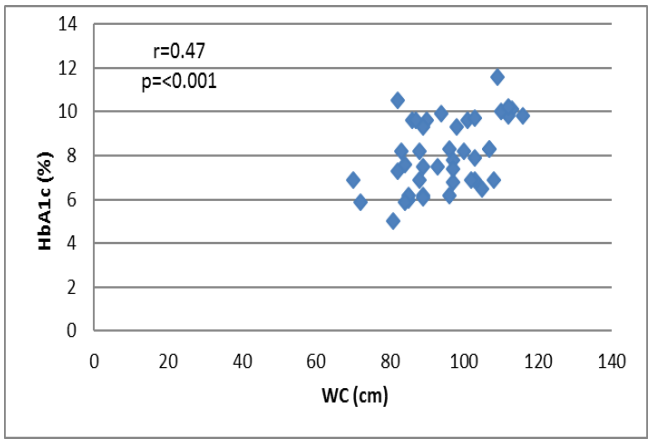

Figure 6. Correlation between WC and HbA1c in male diabetics

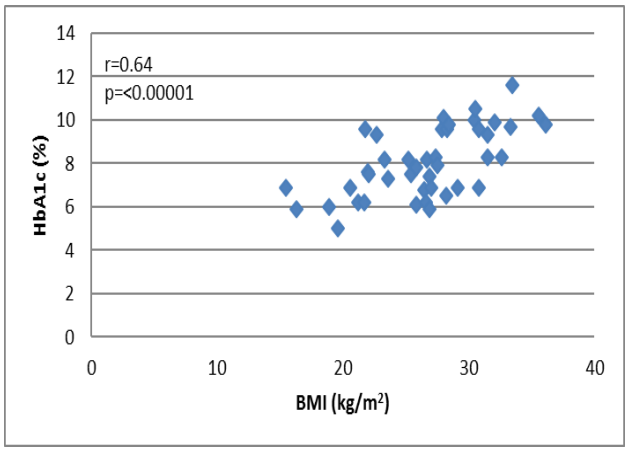

Figure 4. Correlation between BMI and HbA1c in male diabetics

lence of obesity. The increase in the incidence and prevalence of type 2 diabetes over the past few decades is due to obesity reaching to epidemic proportions [1]. Over the years an increase prevalence of obesity in both urban and rural India has been observed [10]. Obesity is one of the major risk factor for type 2 diabetes, yet there has been little research focusing on this risk factor across India.

Both type 2 diabetes and obesity are associated with insulin resistance due to β cell dysfunction resulting in increased release of NEFAs [11]. Another important factor that determines insulin sensitivity is body fat distribution. Insulin resistance is associated with body mass index at any degree of weight gain. Individuals whose fat distribution is more peripheral have more insulin sensitivity than do individuals whose fat distribution is more central [12].

The mean BMI and WC of the subjects in this study was 27.7 kg/m^2 and 97cm, indicating that on average, subjects were obese. Diabetes prevalence and body mass index differ by ethnicity. Studies have shown that the mean BMI of the Asian subjects was lower compared to that of patients from other ethnic backgrounds and the risk of type 2 diabetes starts at a lower BMI for Asians than other ethnicities. The mean BMI of the subjects in other studies was 26 kg/m^2 [13] and in another study BMI in female diabetics was 28.60 ± 4.91 and 26.47 ± 4.68 in male diabetics [14]. Our study is in agreement with this study with BMI being 28.58±5.02 and 26.64±4.87 in female and male diabetics.

Yousefzadeh G et al [14] observed mean BMI and WC were significantly more prevalent in women than men but in our study, though mean BMI and WC were significantly more prevalent in women than men, it was not statistically significant.

Table 4. Clinical and biochemical characteristics in female and male diabetics based on BMI

Characteristics	Group I (n=14)	Group II (n=14)	Group III (n=72)	p value
Age (yrs)	57.4±8.66	44.1±8.25	49.8±9.07	0.0007*
Age of onset(yrs)	49.1±8.06	39.4±5.43	43.8±7.03	0.004*
Duration of DM(yrs)	8.2±5.31	4.71±3.63	5.51±4.5	0.118
SBP(mm/Hg)	132.9±19.39	127.9±18.1	129.3±14.95	0.651
DBP(mm/Hg)	80.7±11.4	81.4±13.51	79.9±9.71	0.926
WC(cm)	83.1±8.20	94.6±6.97	100.2±9.60	< 0.001*
BMI (kg/m^2)	19.9±2.21	23.92±0.72	30±3.75	< 0.001*
FPG (mg%)	143±61.49	142.3±29.61	162.6±52.3	0.23
HbA1c (%)	6.86±1.33	8.06±1.13	8.5±1.66	0.0027*
Data presented as Mean ± SD Group I- Normal BMI, Group II- Overweight, Group III- Obese, *P<0.05,				

In a study by Sheth et al the prevalence of central obesity was found to be higher (75 %) compared to peripheral obesity (59.83 %) in overall study population [15]. Pradeepa R et al observed an increasing trend in all three types of obesity- generalized obesity (GO), abdominal obesity (AO) and combined obesity (CO) with glucose intolerance. They observed GO, AO and CO in 48.5 %, 57.9% and 44.6% of the diabetics respectively [10]. Our study reports a higher prevalence of all the three types of obesity viz; 72%, 80% and 63% in GO, AO, and CO respectively.

Anjana RM et al (2014) found males to be significantly more active than females [16] while Pradeepa R et al observed that the female gender, hypertension, diabetes, higher socio-economic status, physical inactivity and urban residence were significantly associated with generalized, abdominal and combined obesity [10].

Our study shows a higher percentage of the female diabetics associated with housework and males with agriculture. This can also explain the higher incidence of obesity in female diabetics in our study.

Good glycaemic control (HbA1c < 7%) was observed in approximately one-thirds of the diabetic rural and urban population in our study which is in accordance with the study by Unnikrishnan R [17].

Another study [14]reported the mean level of HbA1c in total subjects as 8.56 ± 4.72% (mean 7.80%) in which only 31.66% of men and 26% of women had controlled level of HbA1c (<7%). Our study showed a lower mean HbA1c of 8.2±1.64, and a higher percentage 34.9% of males and 31.6% of the female diabetics having an HbA1c <7%.

In a study by Bhansali A et al, hypertension (both known and newly diagnosed) has been observed in approximately one-fourth of the studied population [18] whereas our study shows more than one-third of the diabetic population as hypertensive.

Firouzi S et al reported that there were no statistically significant differences between men and women in terms of glycemic and metabolic status. However, women had a significantly higher mean BMI and lower mean waist circumference compared to men [13]. Although our study shows higher BMI and WC in women, no statistically significant differences between men and women in terms of glycemic and metabolic status.

While no correlation was found between obesity and HbA1c control in a study by Anari R [19] Sheth et al observed significant linear association of HbA1c in T2DM subjects with central- and peripheral obesity [15]. Our study shows a significant linear correlation between BMI, WC and HbA1c in T2DM subjects.

CONCLUSION

As prevalence of both central and peripheral obesity was observed in more in approximately half of the male diabetics and three fourths of the female diabetic subjects, with an increasing trend of dysglycemia in obese diabetic subjects , obesity is significantly associated with poorer glycemic control overall in male and female diabetic subjects.

Acknowledgement: We are grateful to the principal Dr. PSN Murthy and the Director General Dr. C Nageswara Rao for the support given to conduct the study .

Financial Support : Institutional.

Conflicts of Interest: There are no conflicts of interest.

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How to Cite this article: Shabana S, Ramya K, Sasisekhar T.V.D, Santosh Kumar A. HbA1c as an Index of Glycemic Status in Obese Type 2 Diabetics. *Int. j. clin. biomed. res.* 2017;3(3): 34-39.