International Journal of Home Science 2020; 6(3): 527-531

International Journal of Home Science

ISSN: 2395-7476
IJHS 2020; 6(3): 527-531

www.homesciencejournal.com
Received: 10-09-2020
Accepted: 21-10-2020

Swati Suman
Research Scholar, University Department of Home Science, Ranchi University, Ranchi, Jharkhand, India

Seema Dey
Associate Professor, University Department of Home Science, Ranchi University, Ranchi, Jharkhand, India

Corresponding Author:
Seema Dey
Associate Professor, University Department of Home Science, Ranchi University, Ranchi, Jharkhand, India

HbA1c and its association with anthropometric parameters and renal profile in type 2 diabetes mellitus patients in Jharkhand

Swati Suman and Seema Dey

DOI: https://doi.org/10.22271/23957476.2020.v6.i3i.1093

Abstract
In terms of the worldwide burden, the WHO Global Burden of Disease estimated that around 177 million people in the world had diabetes in the year 2000 and estimates 194 million in the year 2003, and around two-thirds of these people live in developing countries. The projections for the future provide no comfort at all. If current trends prevail, the above figure may well more than double by the year 2025. The present study was conducted on a sample of 200 diabetic patients including both men and women in the age group of 30 – 70 years to assess the anthropometric measurements and HbA1c levels in the selected subjects. The study was an attempt to evaluate the diagnostic value of glycated haemoglobin (HbA1c) in predicting diabetes. Glycated haemoglobin (HbA1c) is routinely used marker for long term glycemic control. Each of the subjects was initially evaluated for Body Mass Index (BMI) and Waist Circumference (WC), and renal profile like Blood Urea Nitrogen (BUN) and serum creatinine (Cr). A detailed clinical evaluation including history and physical examination was done on each subject. The data obtained was collected and the occurrence and pattern of other complications was studied. It was analyzed that there are various factors that all together affects the glucose levels; no single factor shows the result alone. It was also observed that most of the subjects with HbA1c levels were overweight and obese and has the higher side of the Waist Hip ratio. Diet and exercise to some extent plays a role in the control of sugar level.

Keywords: HbA1c (Glycated Haemoglobin), BMI (Body Mass Index), WHR (Waist Hip Ratio), obesity

Introduction
Diabetes is now one of the most common non-communicable diseases globally. It is the fourth or fifth leading cause of death in most developed countries and there is substantial evidence that it is epidemic in many developing and newly industrialized nations. Complications from diabetes, such as coronary artery and peripheral vascular disease, stroke, diabetic neuropathy, amputations, renal failure and blindness are resulting in increasing disability, reduced life expectancy and enormous health costs for virtually every society. The prevalence of DM has increased dramatically around the globe, from an estimated 30 million cases in 1985 to 177 million in 2000. It is estimated that, more than 360 million individuals may develop diabetes by the year 2030 (Fauci, 2008) [5]. Diabetes is certain to be one of the most challenging health problems in the 21st century. Anthropometric parameters are commonly used as research tools to assess the non-communicable disease risk factors in the populations as they are inexpensive and easy to monitor at the community level (Elderman *et al.*, 2004) [4].
Type II diabetes is caused by a combination of decreased insulin secretion and decreased insulin sensitivity. Typically, the early stage of type 2 diabetes is characterized by insulin resistance and decreased ability for insulin secretion causing excessive post-prandial hyperglycaemia. This is followed by a gradually deteriorating first phase insulin response to increased blood glucose concentrations (Bruce *et al.*, 1988) [1]. Approximately 80-90% of T2DM patients are obese (>25 body mass index) and thus caloric restriction is usually the primary component utilized to improve glucose tolerance (Raskin *et al.*, 1994) [12]. The loss of as little as 5-10% of one's body weight can improve glucose uptake, reduce insulin secretion, and decrease hepatic glucose production. Furthermore, there are some indications that weight loss may be most effective in the early stage of T2DM when insulin secretion is greatest (Henry *et al.*, 1986) [6].

Glycated hemoglobin (HbA1c) is a routinely used marker for long-term glycemic control. In accordance with its function as an indicator for the mean blood glucose level, HbA1c predicts the risk for the development of diabetic complications in diabetes patients. Apart from classical risk factors like dyslipidemia, elevated HbA1c has now been regarded as an independent risk factor for cardiovascular disease in subjects with or without diabetes (Khaw *et al.*, 2004) [8]. HbA1c was introduced into clinical use in the 1980s and subsequently has become a cornerstone of clinical practice (Massi-Benedetti, 2006) [10]. HbA1c reflects average plasma glucose over the previous eight to 12 weeks (Nathan *et al.*, 2007) [11]. It can be performed at any time of the day and does not require any special preparation such as fasting. These properties have made it the preferred test for assessing glycaemiccontrol in people with diabetes. More recently, there has been substantial interest in using it as a diagnostic test for diabetes and as a screening test for persons at high risk of diabetes (International Expert Committee Report, 2009) [7].

Various studies have shown that anthropometric parameters such as BMI, waist circumference (WC), waist hip ratio (WHR), and waist height ratio (WHTR) are useful indicators for predicting incidence of type 2 diabetes in populations (Stevens *et al.*, 2001; Lincoln *et al.*, 2002) [13, 9]. Abdominal obesity is increasingly being recognized as a major risk factor for cardiovascular disease. Compared with body mass index, waist circumference (Waist circumference is the measure of the waist specifically at the upper hip bone with a tape measure) and waist-to-hip ratio (This ratio is calculated by dividing the hip circumference by waist circumference at its narrowest point) appear to be more strongly associated with metabolic risk factors, incident CVD events, and death. A considerably high percentage of body fat especially when concentrated at the visceral section of the body predisposes one to cardiac disorders, type II diabetes and hypertension. Unfortunately, people cannot tell by simply weighing themselves and looking at BMI chart what their percentage body fat is or if they are over fat or under fat. This is because the chart makes no allowance for muscle development, and most people don't really know what their frame size is (Donoghue, 1985) [3].

Objective: To study the physical parameters and renal profile in Diabetic patients.

Assumption: There will be a positive relation between HbA1c and BMI, WHR.

Methodology

A cross sectional study of 200 Type 2 diabetic patients was done. The participants were already diagnosed as type 2 diabetics and undergoing treatment. A total of 200 type 2 diabetic patients attending the diabetic clinic at the Diabetes Care Centre (OPD), were randomly selected for the study. The participants were already diagnosed as having Type 2 diabetes and were under treatment at the diabetic clinic. BMI was calculated as weight kg/height squared (kg/m²) and subjects were considered as normal weight if their BMI was < 23 kg/m², overweight if their BMI was from 23 to 29 kg/m² and obese if their BMI was ≥ 30 kg/m².

Hemoglobin A1C (HbA1c) test measures the amount of blood sugar (glucose) attached to hemoglobin. Hemoglobin is the part of red blood cells that carries oxygen from lungs to the rest of your body. An HbA1c test shows that average amount of glucose attached to hemoglobin over the past three months. It's a three-month average because that's typically how long a red blood cell lives. Four basic types of methods are used most commonly to measure HbA1c: immunoassay, ion-exchange high-performance liquid chromatography (HPLC), boronate affinity HPLC, and enzymatic assays. Most immunoassays measure HbA1c specifically; antibodies recognize the structure of the N-terminal glycated amino acids (usually the first 4–10 amino acids) of the Hb β chain. Ion-exchange HPLC separates Hb species based on charge differences between HbA1c and other hemoglobins. With boronate affinity methods, *m*-aminophenylboronic acid reacts specifically with the *cis*-diol groups of glucose bound to Hb. This method measures total glycated GHB, including HbA1c and Hb glycated at other sites, and tends to demonstrate the least interference from the presence of Hb variants andderivatives. The enzymatic method currently available measures HbA1c by using an enzyme that specifically cleaves the N-terminal valine.In our study Fully Automated H.P.L.C. using Biorad Variant II Turbo, NGSP Certified method was used.

Reference Range

Below 6.0% -Normal Value
6.0% - 7.0% -Good Control
7.0% - 8.0% -Fair Control
8.0% - 10% -Unsatisfactory Control
Above 10% -Poor Control

Results and discussion

Type 2 diabetes constitutes about 85% to 95% of all diabetes in developed countries, and accounts for an even higher percentage in developing countries. It is now a serious global health problem, which, for most countries, has evolved in association with rapid cultural and social changes, ageing populations, increasing urbanization, dietary changes, reduced physical activity, and other unhealthy lifestyle and behavioral patterns. The change in lifestyle is a worldwide phenomenon, occurring in both developed and emerging nations, where it is most prevalent in urban areas.

Age wise distribution

Total 200 respondents were included of different age group between 30 to 70 years. A major portion contributing to this disease comes under the age group of 40 to 60 years. Only 19 subjects were in age 30 – 40 who suffered from this disorder. Person above 40 years are at more risk than the younger ones. Maximum males were suffering from diabetes than the females. Maximum patients were of age group 50 - 60. A total of 62 patients were in this group and a total of 60 patients were there in age group 60 -70 (Fig 1).

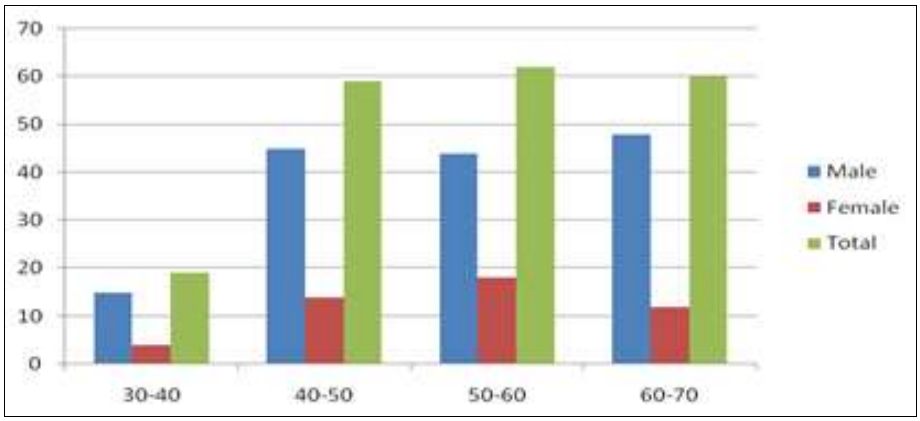

Fig 1: Age wise distribution

Association of HbA1c with physical activity

Exercise has been purported as significant aid in reducing one's weight, a problem with which most T2DM patients must contend. This is important because a reduction in weight can increase insulin action and decrease insulin resistance. Furthermore, a consistent regimen of exercise has also been shown to reduce risk factors associated with cardiovascular disease. The subjects not performing any kind of physical activity in whole week had an average HbA1c of 9.0% which is very high. Whereas, the subjects who performed physical activity regularly 3-4 times in a week had an average HbA1c of 7.38. The average HbA1c of the subjects having physical activity more than 5 times a week had 8.45 which means physical activity is not a single factor for controlling the HbA1c level (Table 1).

Table 1: Association of HbA1c with physical activity

	Average HBA1C	Frequency
No regular activity	9.00	82
< 3Times/ Week	8.39	20
3-4 Times/ week	7.38	10
5 Times/ Week	6.90	2
> 5 times/ Week	8.45	86

Association of diet with HbA1c

Approximately 80-90% of T2DM patients are obese (>25 body mass index) and thus caloric restriction is usually the primary component utilized to improve glucose tolerance (Raskin *et al.*, 1994) [12]. The loss of as little as 5-10% of one's body weight can improve glucose uptake, reduce insulin secretion, and decrease hepatic glucose production. Furthermore, there are some indications that weight loss may be most effective in the early stage of T2DM when insulin secretion is greatest (Henry *et al.*, 1986) [6]. For individuals using insulin therapy as well, the timing of food consumption is as important as the amount and types of food consumed (Cox *et al.*, 1992) [2].

In the present study when association of HbA1c was studied in comparison with adherence to the diabetic diet, it was observed the subjects who followed strict diet had an average HbA1c 8.02% and those who doesn't followed had 9.05% of HbA1c. The subjects who followed the diet occasionally had an average HbA1c 8.4% and those who never followed the diet had 9.79% of HbA1c. So, from the above data we can conclude that diet plays an important role in maintenance of HbA1c level. (Table 2)

Table 2: Association ofHbA1c with Diet

	Average HBA1C	Frequency
Yes Adherence to Diet	8.02	38
No	9.05	40
Occasional	8.40	102
Never	9.79	20

t Stat 48.275**

Glycated haemoglobin (HbA1c)

Glycated hemoglobin (HbA1c) is a routinely used marker for long-term glycemic control. In accordance with its function as an indicator for the mean blood glucose level, HbA1c predicts the risk for the development of diabetic complications in diabetes patients. Majority of subjects had HbA1c in the range of 8-9 percent which is unsatisfactory control. Only 11 percent of subjects have fairly good control. It was observed that women have somewhat good control as compared to the males. A total of 16% subjects had a very high percent of HbA1c level and 13.5% of subjects had a very poor control on their HbA1c levels. (Table 3)

Table 3: Distribution of subjects according to their Glycated Haemoglobin (HbA1c) range

Group	Male	Female	Total
Below 6	2 (1.31)	0 (0)	2 (1)
6-7%	14 (9.2)	8 (16.6)	22 (11)
7-8%	30 (19.7)	20 (41.6)	50 (25)
8-9%	51 (33.5)	16 (33.3)	67 (33.5)
9-10%	30 (19.7)	2 (4.16)	32 (16)
10% and above	25 (6.57)	2 (4.16)	27 (13.5)
Total	152	48	200

Association of HbA1c and BMI

Maximum (141) respomdents out of total 200 were in obese category and had an average HbA1c of 8.71 which in unsatisfactory control. Only 20 subjects had a normal BMI and had an average HbA1c 0f 8.6, and a total of 37 subjects were overweight and had average HbA1c of 8.2. So, almost average of all the subjects had unsatisfactory control of HbA1c level. The average HbA1c was effected as a large population is in obese category (Table 4).

Table 4: Association of BMI with HbA1c

	Average HBA1C	Frequency
BMI (15-19)	8.00	2
BMI (19-23)	8.60	20
BMI (23-25)	8.20	37
BMI (>25)	8.71	141

t Stat 74.338**

Association of Waist Hip Ratio with HbA1c

Waist hip ratio has been categorized in WHR I, WHR II, and WHR III. Most of the subjects around 67 percent were in III category and only 8 percent of them were in I category. So majority of the subjects are on the higher side of the waist hip ratio. Out of which more females were on higher side of the reference value. When the average HbA1c was studied to establish a association between HbA1c and Waist Hip Ratio than it was observed that the subjects in WHR III category and WHR II category had slightly higher range of average HbA1c than the WHR I category of the subjects. Maximum subjects were in the category of WHR III category. (Table 5)

Table 5: Association of WHR with HbA1c

	Average HBA1C	Frequency
WHRI	8.25	34
WHR II	8.76	60
WHR III	8.62	106

t Stat -71.109**

Renal profiles

BUN (Blood Urea Nitrogen)

It is a common blood test, the blood urea nitrogen (BUN) test reveals important information about how well our kidneys and liver are working. A BUN test measures the amount of urea nitrogen that's in our blood. BUN in Diabetes Management: Kidney failure is a complication of diabetes. The BUN (blood urea nitrogen) level in the blood is used to monitor the progression of kidney failure. BUN may also be monitored if given drugs that may impair kidney function. Out of total subjects 89 percent of the patients were having normal BUN level and only 5 percent were above normal range, out of which percent of male is slightly higher than the females (Fig 2)

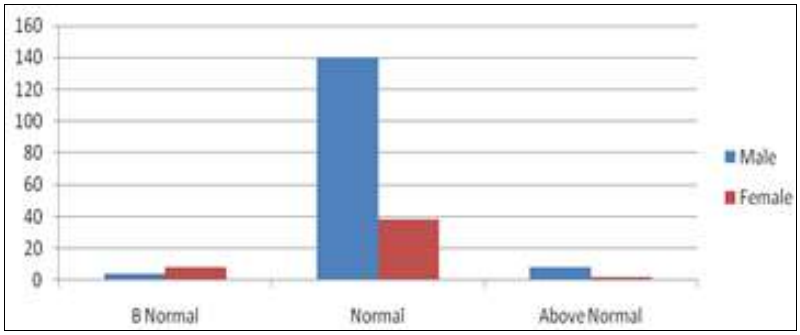

Fig 2: Distribution of blood urea in diabetic patients

Association of BUN with HbA1c

The respondents having normal BUN level had an average HbA1c level 8.68%. More than 8.7 are more susceptible towards abnormal BUN values and kidney problems. Long period of higher HbA1c level affects the kidney (Table 6).

Table 6: Association of serum BUN level with HbA1c

	Average HBA1C	Frequency
BUN < Normal	7.02	12
BUN Normal	8.68	178
BUN > Normal	8.98	10

t Stat 10.460**

Serum creatinine (Cr)

Serum Creatinine is a waste product in our blood that comes from muscle activity. It is normally removed from our blood by our kidneys, but when kidney function slows down, the creatinine level rises. It was observed that 79.5 percent subjects had normal range of serum creatinine levels where about 16 percent were below the normal range and only 4 percent had high serum creatinine level serve as a surrogate marker of muscle mass, and a possible relationship between low serum creatinine and type II diabetes (Fig 3).

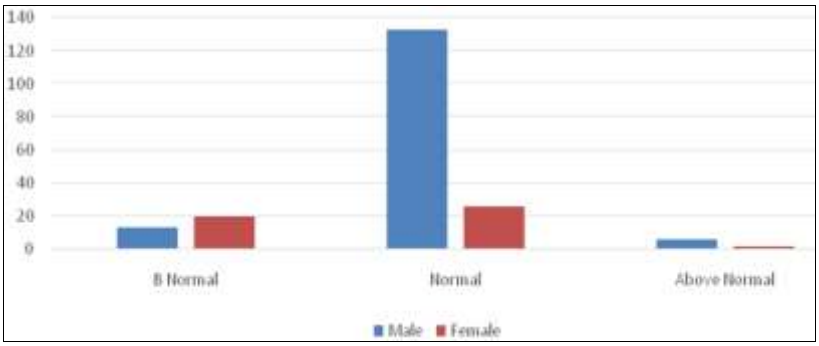

Fig 3: Distribution according to serum Creatinine in diabetic patients.

Association of creatinine with HbA1c

When the serum creatinine level was associated with glycated hemoglobin, it was observed that subjects having poor control of sugar levels had high level of serum creatinine level. Maximum subjects that are 113 out of 200 had a normal serum Creatinine level.

Table 7: Association of serum creatinine and average HbA1c in diabetic patients**.**

	Average HBA1C	Frequency
Creatinine (0.4-0.6)	9.07	41
Creatinine (0.6-0.8)	8.24	113
Creatinine (0.8-1.0)	8.45	30
Creatinine (1-1.2)	10.92	10
Creatinine (1.2-1.4)	9.07	6

t Stat -74.334**

Conclusion

The anthropometric parameters play an important role in the management of sugar level. In our study when different parameters were studied and correlated with the average sugar level of the subjects it was observed that these play a very significant role in diabetes management. When physical activity was studied it was observed that those who do no regular physical activity have a higher average HbA1c level and those who were involved in physical activity had comparatively less average HbA1c. Whereas subjects doing physical activity more than 5 time a week also have a higher HbA1c which may contribute to other contributory parameters like medicines and insulin resistance. When the dietary pattern and management of the subjects were studied it was found that those who adhere to a diabetic diet have comparatively lowHbA1c level than who occasionally does. The average HbA1c level was found higher in males as compared to females. More than 60% of subjects have deranged value that is above 8%. When BMI was studied it was observed that obese subjects have higher average HbA1c level than the normal subjects. Similarly in case of Waist Hip Ratio when association was studied it was observed that as the WHR is increasing the HbA1c level is also increasing. Waist hip ratio has been categorized in WHR I, WHR II, and WHR III, most of the subjects around 67 percent were in III category and only 8 percent of them were in I category. So majority of the subjects are on the higher side of the waist hip ratio. Out of which more females were on higher side of the reference value.

The renal profile was also studied in the subjects and majority have a normal value of all renal parameters and it was also observed that those having high values or deranged parameters have a high average HbA1c level. So, a controlled HbA1c level plays a vital role in complete diabetes management program and its complications. Monitoring the HbA1c and having a control over it reduces the chances of complications and promotes the quality of life of the patients.

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