MICROALBUMIN STATUS IN RELATION TO GLYCATED HAEMOGLOBIN AMONG TYPE 2 DIABETES MELLITUS IN SOUTH KERALA POPULATION-A COMPARATIVE STUDY

Biochemistry

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ABSTRACT

Diabetes mellitus (DM) is a group of metabolic diseases which if not controlled can cause life threatening complication. The objective of the study is to assess the correlation of urine microalbumin (MAU) with (HbA1C) in type 2 DM patients. Total 180 patients diagnosed for type 2 DM, age 30-60 years were selected and fasting plasma glucose, creatinine, HbA1C and MAU were estimated. HbA1C levels and MAU levels shows significant positive correlation ($r = 0.429$, $p < 0.01$) and the relationship is significant for all the three age groups. The study concluded that there was an increased prevalence of MAU and high HbA1C level among the patients with type 2 DM, and also highlights that there is a significant correlation between MAU levels and HbA1C for all the three age groups which necessitates for early detection of nephropathy and uncontrolled diabetes.

KEYWORDS

HbA1C, Microalbumin, Type 2 DM.

OBJECTIVES

The present study was planned to assess the correlation of urine microalbumin (MAU) with glycosylated hemoglobin (HbA1C) in type 2 DM patients.

INTRODUCTION

Diabetes mellitus (DM) is a chronic, widely prevalent endocrine disease, comprises a group of common metabolic disorders that share the phenotype of hyperglycemia. Chronic hyperglycemia in this disease is caused due to defect either in insulin secretion or insulin action, decreased glucose usage, and increased glucose production (1, 2).

Diabetes Mellitus has become a major health problem in India. It has been estimated that the burden of type 2 DM for India is projected to increase to 87 million by the year 2030. The impacts of type 2 DM are considerable (as a lifelong disease). It increases morbidity and mortality and decreases the quality of life. At the same time, the disease and its complications cause a heavy economic burden for diabetic patients themselves, their families and society (3, 4).

One of the leading causes of diabetes mellitus morbidity and mortality is diabetic nephropathy (5).

According to the International Diabetic Foundation (IDF), 2019 approximately 463 million adults (20-79 years) were living with diabetes; by 2045 this will rise to 700 million (6). Due to the alarming increase in the incidence and prevalence of diabetes in India, WHO has declared India as "the Diabetes Capital of the World".

HbA1C, is widely touted as the "diabetic truth detector." Measuring the percentage of red blood cells that have been "glycated," or permanently chemically joined to sugar, HbA1C is a good indicator of how well diabetics have kept their blood glucose levels in control over the preceding 90 to 120 days. Sometimes, however, HbA1C can be elevated even in people who do not have diabetes (7).

Microalbuminuria is decisive indicator of early stages of DN. Microalbuminuria is common and is a well-established risk factor for macrovascular diseases in type 2 diabetics. The laboratory test for early detection of diabetic nephropathy is the measurement of MAU in urine. Microalbuminuria predicts progression to diabetic nephropathy and cardiovascular diseases (8).

Till date, different studies have been performed to find out the relationship between MAU, HbA1C and duration of diabetes. All the studies have not shown similar results and the relation between these parameters are not clear. This study was conducted to explore the underlying relationship between these parameters in our context.

METHODOLOGY:

Total 180 patients diagnosed for type 2 DM between the age group of 30-60 years with no evidence of any other pathology involving proteinuria were selected.

Patients with newly diagnosed type 2 DM (within 1 month) according to WHO criteria and ADA recommendations for diabetes mellitus (Age > 30 years & < 60 years) were included in this study. Diabetic patients suffering from any other medical problems were excluded from the study.

Total 5 ml venous blood was taken in fasting conditions (as per WHO criteria) and the major investigations were done.

Plasma Glucose, creatinine and HbA1c.

Spot urine sample (25 ml) were collected for urinary MAU estimation.

Plasma glucose by hexokinase method and creatinine by enzymatic method were done in fully auto analyzer Beckman Coulter AU 480. HbA1c done by HPLC method in Aspen-Labnovation analyzer. Microalbumin was estimated by immunoturbidimetric method in Agappe Nephleometer.

RESULT

The study was conducted to compare the HbA1C levels in subjects with and without MAU.

Total 180 subjects were participated in this study including 111 (61.7%) males and 69 (38.3%) females. The study subjects were categorized into three groups according to their age as subjects less than 50 years, subjects between the age group of 50 years and 60 years and subjects above the age of 60 years. The percentage distribution of the study subjects according to age is given in the following (Table 1).

Table 1. Percentage distribution of the sample according to age		
Age	Count	Percent
<50	50	27.8
50 - 60	74	41.1
>60	56	31.1
Mean $\pm$ SD	55.8 $\pm$ 10.9	

Table 2. Percentage distribution of the sample according to HbA1C		
HbA1C	Count	Percent
Normal	20	11.1
Pre diabetes	17	9.4
Diabetes	143	79.4
Mean $\pm$ SD	8.5 $\pm$ 2.3	

The study subjects were classified into three groups as normal, pre

Table 3. Distribution of HbA1C based on age and gender									
HbA1C	<50		50 – 60		>60		Male		Female
	Count	Percent	Count	Percent	Count	Percent	Count	Percent	Count
Normal/Pre diabetes	16	32.0	9	12.2	12	21.4	19	17.1	18
Diabetes	34	68.0	65	87.8	44	78.6	92	82.9	51
Mean $\pm$ SD	8.2 $\pm$ 2.5		8.6 $\pm$ 2.1		8.5 $\pm$ 2.3		8.6 $\pm$ 2.3		8.2 $\pm$ 2.3

Relationship between HbA1C and MAU level is given in figure no 1. HbA1C levels and MAU levels shows significant positive correlation ($r = 0.429$, $p < 0.01$) in the study subjects. The relationship is significant for all the three age groups (Table 6).

Table 4. Percentage distribution of the sample according to Microalbumin		
Microalbumin	Count	Percent
≤ 25	116	64.4
>25	64	35.6
Mean $\pm$ SD	47.3 $\pm$ 63.2	

Table 5. Distribution of Microalbumin based on age									
Micro albumin	<50		50 – 60		>60		Male		Female
	Count	Percent	Count	Percent	Count	Percent	Count	Percent	Count
≤ 25	35	70.0	49	66.2	32	57.1	64	57.7	52
>25	15	30.0	25	33.8	24	42.9	47	42.3	17
Mean $\pm$ SD	47.9 $\pm$ 67		41.2 $\pm$ 58		54.8 $\pm$ 66.7		56 $\pm$ 68.4		33.3 $\pm$ 51.4

Figure 1. Relationship between HbA1C and Microalbumin level
Scatter diagram for HbA1C and Microalbumin level

Table 6. Relationship between HbA1C and Microalbumin level based on age		
Age	R	Sig.
<50	0.458	$p < 0.01$
50 – 60	0.339**	0.003
>60	0.507	$p < 0.01$

** Highly significant

Comparison of HbA1C based on MAU level for different age groups were done (table no 7) and it was significant in the age group of < 50 age.

Table 7. Comparison of HbA1C based on Microalbumin level for different age groups						
Age	HbA1C	≤ 25		>25		p
		Count	Percent	Count	Percent	
<50	Normal/Pre diabetes	14	40.0	2	13.3	3.43
	Diabetes	21	60.0	13	86.7	
50 - 60	Normal/Pre diabetes	8	16.3	1	4.0	2.35
	Diabetes	41	83.7	24	96.0	

diabetes, diabetes according to the levels of HbA1C (Table 2). Majority of the study subjects (79.4 %) were diabetic.

Distribution of HbA1C based on age and Gender is given in the table no 3. Most of the diabetic subjects were in the age group of 50 – 60 years in that 82.9% male subjects were diabetes whereas among the female subjects 73.9% were diabetes.

Percentage distribution of the sample according to MAU is given in table no 4. Majority of the study subjects (64.4%) were have high microalbumin level (≥ 25 mg/l) and are in the age group of 50 – 60 years. The levels of MAU was highest in the age group of >60 years (54.8 $\pm$ 66.7). Majority of the females (75.4%) and (57.7%) of males have high microalbumin levels (≥ 25 mg/l) is given in table no 5. The level of MAU was highest in male group (54.8 $\pm$ 66.7).

>60	Normal/Pre diabetes	9	28.1	3	12.5	1.99	0.158
	Diabetes	23	71.9	21	87.5		

** Highly significant

DISCUSSION

HbA1C in Type 2 DM is said to be an indicator of poor glycemic control which in turn is a risk factor for progression of DN. The present study was therefore planned to assess the association of HbA1c with MAU and hence with progression of DN in Type 2 patients.

In our study done on randomly selected patients the incidence of microalbuminuria was found to be 64.4% and (79.4 %) were diabetic. In NIDDM patients, the prevalence has been reported in between 8-46% in European and 36.7 % in India (9). But according to Afhami-Ardekani et al. (10) study, no statistically significant correlation was found between the prevalence of microalbuminuria and the fasting blood sugar or HbA1c, which was similar to findings reported by Huraib *et al.* However, Varghese *et al.* reported a correlation of the prevalence of microalbuminuria with the fasting blood sugar and with HbA1c levels. The previous study conducted in Yazd also showed that the HbA1c level was associated with microalbuminuria (9). Similarly, Gupta et al performed an independent study and reported strong association of HbA1c level with urinary microalbumin excretion (11). According to a report of World Health Organisation (WHO) the number of people with diabetes has risen from 108 million to 422 million, and the global prevalence of diabetes among adults, over 18 years, has risen from 4.7 % to 8.5 % from the year 1980 to 2014. Diabetes prevalence has increased by 64% across India over the quarter-century, according to November 2017 report by the Indian Council for Medical Research, Institute for Health Metrics and Evaluation, both research institutes, and the Public Health Foundation of India, an advocacy. The overall prevalence of diabetes in India to be 7.3% and the prevalence of prediabetes to be 10.3% (WHO criteria) or 24.7% (ADA criteria) (3). According to Thankappan KR, Shah B, Mathur P, et al. studies Kerala is the state with the highest reported

prevalence of diabetes in India so far(12).

According to Chowta et.al (13) the higher percentage of prevalence of microalbuminuria in the present report can have a number of reasons, one of the main causes is, “irregular treatment with poor glycemic control and also may be due to the “small sample size” in their study. The sample size in the above report and the present study is almost similar, being 100 and 180 respectively. However, we feel that, sample size does not play much role in this and agree with them in suggesting that, “the level of glycemic control seems to be the strongest factor influencing transition from normoalbuminuria to microalbuminuria.” They further suggest that, “ethnic differences also play a role in giving a higher prevalence of microalbuminuria” with which the present study agree.

Mean age of patients with diabetes in the present study was 50.57 years, which is similar to that, reported by Chowta et al.(13) , Kanakmani et al(14) and Maskari et al. (15). Generally, diabetic nephropathy affects both males and females equally. This was also confirmed by the present study. The level of HbA1C has been widely accepted as an indicator of mean daily blood glucose concentration over the preceding 8–12 weeks. The glycated hemoglobin (HbA1C) assay is the most commonly used measure of chronic glycaemia, since its introduction more than 25 years ago. HbA1C levels equal to or less than 6.5% in diabetes reflects good glycemic control and more than 8.0% will put patient at greater risk of developing disease related complications, including nephropathy (16).

In the present study the prevalence of microalbuminuria was 13.3% with HbA1C value more than 6.5 in the age group of <50 and 86.7% with HbA1C value more than 8.0%. HbA1C levels and MAU levels shows significant positive correlation ($r = 0.429$, $p < 0.01$) in the study subjects. The relationship is significant for all the three age groups. Our study also evaluated relationship between HbA1C levels and serum creatinine level and found insignificant correlation ($r = -0.028$, $p = 0.711$).

The present study also found that diabetics with poor glycemic control had higher microalbumin levels compared with those of diabetics with good glycemic control. This study also highlights that there is a significant correlation between MAU levels and HbA1C.

Acharya K.Regmi S et.al showed positive correlation of MAU with HbA1C but statistically insignificant ($r = 0.245$, $p > 0.05$) (17). Varghese et al. carried out study among type 2 diabetic people and found a positive correlation between microalbuminuria and HbA1C but did not find any statistical difference between microalbuminuria and two sexes (9).

CONCLUSION

The diabetes epidemic in India is in a state of transition. The pool of people with prediabetes seems to be shrinking in many of the more economically advanced states, raising the possibility of stabilisation of the epidemic in the near future. However, we can expect further increases in diabetes prevalence among the people of low socioeconomic status in urban areas, as well as in rural India, which accounts for the majority of the country's population.

In the Present study there was an increased prevalence of Microalbuminuria and high HbA1c level among the patients with type 2 DM, also highlights that there is a significant correlation between MAU levels and HbA1C for all the three age groups, which necessitates for early detection of nephropathy and uncontrolled diabetes to reduce the burden of diabetes induced kidney disease in the future.

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