CORRELATION OF HbA1C WITH MICROALBUMINURIA IN TYPE-2 DIABETES MELLITUS PATIENTS

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Abstract
Background: Diabetes is a very common disease nowadays. It has adverse effects on many human organs as its duration increases. Many studies exist to show its bad effects on body organs in different parts of the world. We have studied if there is any relation between microalbuminuria with HbA1c levels.

Methods: We have done a cross-sectional study from January 2016 to March 2017 in a tertiary health care hospital located in Jhalawar, Rajasthan. Our study includes all the known case of type 2 diabetes mellitus patients of age group of 45 years and above.

Results: Total 69 patients had urinary albumin level less than 30 mg/dl out of which HbA1c was less than 6.5% present in 20.2% of patients and 79.7% of patients had more than 6.5%. Total 31 patients had urinary albumin level more than 30 mg/dl out of which only 3% had HbA1c value less than 6.5% whereas 96% had HbA1c value more than 6.5%. This association was found to be clinically significant (Pearson Chi-Square- 4.888, df is 1 and p value is 0.027, Fishers Exact test is 0.033)

Conclusion: Patients having microalbuminuria were associated with high level of glycosylated hemoglobin.

Keywords: Diabetes Mellitus, Microalbuminuria, Glycosylated Hemoglobin.

Abbreviations:
DM: Diabetes Mellitus
HbA1C: Glycosylated Hemoglobin
Mcps: Microscopy
OPD: Out door patients
IPD: Indoor patients
ACE: Angiotensin converting enzymes
ARB: Angiotensin Receptor Blocker
T2DM: Type2 Diabetes Mellitus
eGFR: Estimated Glomerular Filtration Rate
INTRODUCTION:
Diabetes mellitus (DM) is a group of metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of diabetes mellitus are caused by a complex interaction of genetic and environmental factors. Depending on the etiology of diabetes mellitus, factors’ contributing to hyperglycemia includes reduced insulin secretion, decreased glucose utilization, and increased glucose production. The metabolic deregulation associated with DM causes secondary pathophysiologic changes in multiple organ system.

Microalbuminuria occurs when the kidney leaks small amounts of albumin into the urine, in other words, when there is Microalbuminuria, it is an important adverse predictor of glycemic outcomes in pre-diabetes and diabetes. Prediabetes is the precursor stage before diabetes mellitus in which not all of the symptoms required to diagnose diabetes are present, but blood sugar is abnormally high. Prediabetes individuals with increased microalbuminuria even in the so-called normal range are associated with increased progression to diabetes and decreased reversal to normoglycemia. Hence prediabetes individuals with microalbuminuria warrant more aggressive intervention to prevent diabetes in them. A microalbumin urine test determines the presence of the albumin in urine. In a properly functioning body, albumin is not normally present in urine because it is retained in the bloodstream by the kidneys.

Microalbuminuria can be diagnosed from a 24-hour urine collection (between 30–300 mg/24 hours) or, more commonly, from elevated concentrations in a spot sample (30 to 300 mg/L). Both must be measured on at least two of three measurements over a two- to three-month period.

| Table 1: Microalbuminuria |
|---------------------------|
| **Individual** | **Lower limit** | **Upper limit** | **Unit** |
| 24h urine collection | 30$^4$ | 30$^4$ | mg/24h (milligram albumin per 24 hours) |
| Short-time urine collection | 20 | 200 | µg/min (microgram albumin per minute) |
| Spot urine albumin sample | 30$^3$ | 300$^3$ | mg/L (milligram albumin per liter of urine) |
| Spot urine albumin/creatinine ratio | | | |
| Women | 3.5$^4$ | 25$^4$ or 35$^4$ | mg/mmol (milligram albumin per millimole creatinine) |
| | 30 ($^4$) | 400$^4$ | µg/mg (microgram albumin per milligram creatinine) |
| Men | 2.5$^4$ or 3.5$^4$ | 25$^4$ or 35$^4$ | mg/mmol |
| | 30$^4$ | 300$^4$ | µg/mg |

Glycated hemoglobin (HbA$_{1c}$) is a form of hemoglobin that is measured primarily to identify the three month average plasma glucose concentration, because the lifespan of a red blood cell is three months. It is formed in a non-enzymatic glycation pathway by hemoglobin’s exposure to plasma glucose. HbA$_{1c}$ is a measure of the beta-N-1-deoxy fructosyl component of hemoglobin. Normal levels of glucose produce a normal amount of glycated hemoglobin. As the average amount of plasma glucose increases, the fraction of glycated hemoglobin increases in a
predictable way. This serves as a marker for average blood glucose levels over the previous three months before the measurement as this is the lifespan of red blood cells. In diabetes mellitus, higher amounts of glycated hemoglobin, indicating poorer control of blood glucose levels, have been associated with cardiovascular disease, nephropathy, neuropathy, and retinopathy.

**Measuring HbA1c**

A number of techniques are used to measure hemoglobin A1c. Laboratories use:

- High-performance liquid chromatography (HPLC): The HbA1c result is calculated as a ratio to total hemoglobin by using a chromatogram.
- Immunoassay, Enzymatic, Capillary electrophoresis, Boronate affinity chromatography.

The United States, HbA1c testing laboratories are certified by the National Glycohemoglobin Standardization Program (NGSP) to standardise them against the results of the 1993 Diabetes Control and Complications In Trial (DCCT). An additional percentage scale, Mono S is in use by Sweden and KO500 is in Japan.

| HbA1C (%) | (mmol/mol) | Estimated average glucose (mmol/L) | (mg/dL) |
|-----------|------------|-----------------------------------|---------|
| 5         | 31         | 5.4 (4.2–6.7) | 97 (76–120) |
| 6         | 42         | 7.0 (5.5–8.5) | 126 (100–152) |
| 7         | 53         | 8.6 (6.8–10.3) | 154 (123–185) |
| 8         | 64         | 10.2 (8.1–12.1) | 183 (147–217) |
| 9         | 75         | 11.8 (9.4–13.9) | 212 (170–249) |
| 10        | 86         | 13.4 (10.7–15.7) | 240 (193–282) |
| 11        | 97         | 14.9 (12.0–17.5) | 269 (217–314) |
| 12        | 108        | 16.5 (13.3–19.3) | 298 (240–347) |
| 13        | 119        | 18.1 (15–21) | 326 (260–380) |
| 14        | 130        | 19.7 (16–23) | 355 (290–410) |
| 15        | 140        | 21.3 (17–25) | 384 (310–440) |
| 16        | 151        | 22.9 (19–26) | 413 (330–480) |
| 17        | 162        | 24.5 (20–28) | 441 (460–510) |
| 18        | 173        | 26.1 (21–30) | 470 (380–540) |
| 19        | 184        | 27.7 (23–32) | 499 (410–570) |

**Inclusion Criteria:**

1. All patients of type 2 diabetes mellitus 45 years and above
2. Patients with or without micro vascular complications

**Exclusion Criteria:**

2. Proteinuric conditions like congestive cardiac failure, renal failure and proven renal diseases,
3. Pregnancy.

**MATERIAL AND METHOD:**

We have planned to select approximately 100 diabetic patients from OPD as well as IPD of medicine department. All the patients will go through the investigations for microalbuminuria and HbA1C. The samples were centrifuged, separated and stored at 4°C until analysis. For
glycosylated hemoglobin estimation, EDTA blood samples were used. Glycosylated hemoglobin (HbA1c) by the cation exchange resin method and micro albumin levels in the urine sample by using the turbilatex method.

The present cross sectional study is conducted from January 2016 to March 2017 in a tertiary health care hospital located in Jhalawar, Rajasthan. Our study includes all the known case of type 2 diabetes mellitus patients of age group of 45 years and above (according to American diabetes association). All the patients were fully informed about the purpose, the procedures and the hazards of the study.

RESULT

Urinary albumin level less than 30 mg/dl was found in 14 (20.2%) patients in whom Hb1Ac was less than 6.5% and in 55 (79.7%) patients in whom Hb1Ac was more than 6.5%.

Urinary albumin level more than 30 mg/dl was seen in 1 (3%) in whom Hb1Ac was less than 6.5% and 30 (96%) in whom it was more than 6.5%.

Table 3: Comparison of HbA1c with microalbuminuria

| HbA1c       | U.alb | Total |
|-------------|-------|-------|
| less than 6.5% | 14 (20.2%) | 1 (3%) | 15 |
| More than 6.5% | 55 (79.7%) | 30 (96%) | 85 |
| Total       | 69    | 31    | 100  |

Pearson Chi-Square- 4.888, df is 1 and p value is 0.027
Fishers Exact test is 0.033

Graph 1: Comparison of HbA1c with microalbuminuria

DISCUSSION

HbA1c with microalbuminuria

Total 69 patients had Urinary albumin level less than 30 mg/dl out of which Hb1Ac was less than 6.5% present in 20.2% of patients and 79.7% of patients had more than 6.5%.

Total 31 patients had Urinary albumin level more than 30 mg/dl out of which only 3% had Hb1Ac value less than 6.5 % whereas 96% had Hb1Ac value more than 6.5%. This association was found to be clinically significant (Pearson Chi-Square- 4.888, df is 1 and p value is 0.027, Fishers Exact test is 0.033) (Table, Graph)

This results can be compared with the study conducted by Mishra et al in which patients of DM having HbA1c ≤ 7% had mean urinary microalbumin level of 40.27 mg/24hrs and the patients of DM having HbA1c >7% had mean
urinary microalbumin level of 67.95 mg/24 hrs (p ≤0.03). This is statistically significant. The patients of DM having HbA1c ≤ 7% had mean serum microalbumin level of 1.7 mg/dl and the patients of DM having HbA1c >7% had mean serum microalbumin level of 1.64 mg/dl (p ≤0.53).\(^{11}\)

One more study conducted by Alamdari et al on risk factors for microalbuminuria in T2DM patients and reported 30.5% prevalence of microalbuminuria. Alamdari et al also reported significantly high HbA1c levels in patients with microalbuminuria.\(^{12}\) In a study performed on 8,260 subjects at 9 centres reported that prevalence of microalbuminuria and decreased eGFR was highest when HbA1c was above the median and prevalence was lowest when HbA1c median was at lowest.\(^{13}\)

Study conducted by Khan p et al also shows the positive correlation between microalbuminuria and glycemic control as shown by the high frequency of microalbuminuria (33%) in poor glycemic control (HbA1c >7) group as compared to only 10% of microalbuminuria in good glycemic control (HbA1c <7) group.\(^{14}\)

**CONCLUSION**

Recently, attention has been called to atypical presentations of diabetic nephropathy with dissociation of proteinuria from reduced kidney function. Also noted is that microalbuminuria is not always predictive of diabetic nephropathy. Patients having microalbuminuria were associated with high level of glycosylated haemoglobin.

Early detection of diabetic nephropathy, adoption of multifactorial interventions targeting the main risk factors (hyperglycemia, hypertension, dyslipidemia, and smoking), and use of agents with a renoprotective effect (ACE inhibitors and/or ARBs) do indeed reduce the progression of renal disease. Treatment of hypertension is a priority. Attention to these procedures will also ensure the reduction of cardiovascular mortality.

**LIMITATION**

One of the biggest challenges for health care providers today is addressing the continued needs and demands of individuals with chronic illnesses like diabetes.

During study, only 100 patients were agreed and included in the study. More sample size will require generalizing its effect on population.

Many patients didn’t agree to participate in study because of many problems like no time to participate in the study, have ignorance towards the diseases etc. We did not exclude obese patients.

Ours is cross sectional study so we cannot compare efficacy of HbA1c levels in controlling and prevention of microvascular complication in diabetic patients.

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