ORIGINAL RESEARCH PAPER

Medicine

ASSOCIATION BETWEEN KIDNEY DISEASE AND PRE-DIABETES BY PLASMA GLUCOSE AND HBA1C LEVELS ON NORTH BIHAR

KEY WORDS: Albumin creatinine ratio, Albuminuria, Chronic Kidney Disease, Macroalbuminuria, Microalbuminuria,Prediabetes

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ABSTRACT

Introduction: Chronic kidney disease is recognized as a global health problem. Growing evidence links prediabetes toalbuminuria and CKD and this association is a matter of concern worldwide nowadays.The study aims to find the association between kidney disease and prediabetes and compare it with normoglycemic controls.
Purpose: To study the association between Kidney disease and Prediabetes.
Material And Methods: It is a case control study (100 Prediabetic cases and 50 normoglycemic controls).Both prediabetic menand women >20 years were taken with FBS>100mg/dl but<126mg/dl and/or PPBS>140 mg/dl but<199mg/dl and/or HbA1C 5.7-6.4%as per American Diabetes Association Criteria. CKD was defined by eGFR- 15- 59 per 1.73m2 and/or albumin creatinine ratio 30-300mg/g(microlbuminuria) and>300 mg/g(macroalbuminuria).
Result: Of the total 100 cases and 50 contols 9% cases and none of the controls showed microalbominuria. 7% cases andnone of the controls showed macroalbuminuria (Chi square-8.96, p value- 0.005). 16% cases and none of the controls were under stage 3 and 4 of CKD.(Chi square-9.65, p value-0.05).Overall 18% prediabetic cases and no normoglycemic controls showed evidence of kidney disease.
Conclusion: Kidney disease prevalence is high among people with prediabetes.Prediabetes can be a target for early interventionby lifestyle changes and control of modifiable risk factors for preventing and/or progression of CKD in these individuals.

INTRODUCTION

Chronic Kidney disease (CKD) is recognized as a global health problem. It is increasingly prevalent worldwide, in developing and developed countries alike1 and is associated with substantial burden of morbidity, mortality and health care costs. Concurrently, the incidence of Prediabetes, defined as impaired fasting glucose (IFG) or impaired glucose tolerance (IGT), has reached epidemic proportions worldwide. Growing evidence links prediabetes to albuminuria and CKD and this association is a matter of concern worldwide nowadays.

Pre-Diabetes

- Prediabetes is a precursor stage to Diabetes Mellitus2 in which not all symptoms required to label a person as diabetes are present, but blood sugar is abnormally high. This stage is often referred to as "Grey area".3
- Prediabetes is a high risk state for diabetes with an annual conversion rate of 5-10%.
- According to an ADA expert panel, upto 70% of individuals with prediabetes will
- eventually develop diabetes.
- According to the most recent clinical practices recommendations published in 2010 by the American Diabetes Association (ADA), Prediabetes is defined as4:-

Impaired fasting glucose (IFG) with fasting plasma glucose levels of 100 to 125 mg/dl (5.6 to 6.9 mmol/L)
2. Impaired glucose tolerance (IGT) with plasma glucose levels of 140 to 199 mg/dl (7.8 to 11.0 mmol/L) 2 hours Post Prandial.

3. An HbA1c of 5.7 to 6.4%.
Association of CKD with diagnosed diabetes is known to be high, but little is known about the prevalence of CKD in those with undiagnosed diabetes or Prediabetes.

- People with prediabetes often have unrecognised CKD. Many people with Prediabetes are found to have 2 signs of kidney disease.
- Protein in urine (called albuminuria)
- Reduced estimated Glomerular Filteration Rate (eGFR)

In people with Prediabetes the stage of CKD can be as advanced as people with diabetes many people with prediabetes can have stage 3 or 4 of CKD. And so Prediabetes may be a target for early intervention, to prevent CKD caused by hyperglycemia. If a patient has borderline elevated glucose levels found by the primary physician, they should start lifestyle changes with respect to diet and physical activity and control of modifiable risk factors like smoking, hypertension and obesity to prevent diseases like diabetes and kidney disease.

MATERIAL AND METHODS

The present study was conducted at the Department of Medicine with both outdoor & indoor patient at Darbhanga Medical College and Hospital, Laheriasarai, Bihar as per criteria recommended by ADA on 100 prediabetic cases and 50 normoglycemic controls.

Inclusion Criteria: Cases -1.Patients willing to be a part of study 2.Both men and women > 20 years of age.3.Patients with FPG ≥ 100 mg/dl but ≤ 126 mg/dl and/or PPBS ≥ 140mg/dl but ≤ 199mg/dl and/or HBA1C 5.7 - 6.4% as per American Diabetes Association (ADA) criteria.

Controls - Apparently healthy individuals both males andfemales who are > 20 yrs of age with FPG < 100 mg/ dl and/or PPBS < 140mg/dl and/or HBA1C < 5.7%. (Normoglycemic Patients)

Exclusion Criteria: 1. Patients who are pregnant.
2. Patients who are known diabetic 3.Patients on Angiotensin Converting Enzyme Inhibitors (ACEI) or Angiotensin Receptor Blockers (ARB) use to treat hypertension/CKD 4.Patients who do not give consent Patients with risk factors for Pre -diabetes on OPD(SpecialityOPD) basis or from wards were taken and screened for Prediabetes as per the ADA criteria Under aseptic precautions blood samples were drawn in morning (after 12 hours of fasting) and were analysed for plasma glucose.

Blood samples were also drawn 2hrs post meal and were analysed for Post Prandial Blood sugar.

Blood sugar was estimated by Randoxautoanalyser using colorimetric method without deproteinisation using glucose oxidase and peroxidase reaction. The values were measured in mg/dl.

Blood samples were drawn for HBA1C (Glycated Hemoglobin). HbA1c was measured using Latex agglutination inhibition assay.

To Establish Kidney Disease:-
Definitions:
Estimated Glomerular Filtration Rate
eGFR was calculated according to Modification of Diet in Renal disease (MDRD) Study by measuring serum creatinine.

Stages
- Stage I - eGFR> 90 ml/min per 1.73 m2 & presence of Albuminuria at single measurement.
- Stage II - eGFR 60 to 89 ml/min per 1.73 m2 & presence of Albuminuria at single measurement.
- Stage IIIA - eGFR 45 to 59 ml/min per 1.73 m2.
- Stage IIIB - eGFR 30 to 44 ml/min per 1.73 m2
- Stage IV - eGFR 15 to 29 ml/min per 1.73 m2.

Blood Samples were drawn for Serum Creatinine which was applied in above formula. Serum creatinine level was estimated by Jaffe's method and was measured in mg/dl.

Albuminuria
- Urinar y albumin creatinine ratio of 30 to 300 mg/g (microalbuminuria) and > 300 mg/g (macroalbuminuria).
- Spot urine sample was collected and measured for urine albumin creatinine ratio (UACR).

Statistical Analysis
All the records were rechecked for their completeness and consistencies. Non numeric entries were coded numerically into nominal/ordinal distribution before analysis. Categorical variables were summarized in frequency and percent distribution and Chi-square or Fishers exact test was performed as appropriate. Continuous variable were analyzed using mean ± SD or median with inter quartile range as appropriate. P value<0.05 was considered to be significant.

RESULTS
In the present study, mean age of prediabetic cases was (49.05±14.71) years and mean age of controls was (44.82±14)years.The difference in age group between cases and controls was found statistically significant(Chi Square- 8.08 p value- 0.018) and thus as age advances, the prevalence of prediabetes increases. There was no significant difference recorded in distribution of sexes between cases and controls. (Chi Square- 0.34 p value- 0.56).Thus, there was noassociation between sex and prevalence of prediabetes. 16% cases and none of the controls were in stage 3 and 4 of kidney disease. Maximum cases and controls were having eGFR> 90 ml/min/1.73m2. This difference in eGFR between cases and controls was statistically significant. (Chi Square- 9.65 p value- 0.05). 9% cases and none of the controls showed microalbominuria. 7% cases and none of the controls showed macroalbuminuria.Thus there was association between albuminuria and Prediabetes.(Chi square- 8.96

Table 1: Characterstics of study population

Parameters	Mean±SD	
	Prediabetic cases	Normoglycemic controls
AGE (years)	49.05±14.71	44.82±14
FBS (mg/dl)	111.28±7.06	77.62±10.2
PPBS (mg/dl)	171.4±13.63	116.52±12.86
HbA1C(%)	6.03±0.19	4.56±0.61
UACR (mg/g)	32.45±76.69	9.61±7.16
eGFR (ml/min/1.73 m2)	75.8±21.94	87.52±15.58

Table 2: Overall assessment of prediabetic cases

	GFR (ml/min /1.73m2)	Macroalbuminuria	Microalbuminuria	No albuminuria
>90	2 (2%)	Nil	54	(54%)
60-89	Nil	Nil	28	(28%)
30-59	2 (2%)	6 (6%)	2	(2%)
15-29	3 (3%)	3 (3%)	0	(0%)
<15	Nil	Nil	0	(0%)

Table 3: Overall assessment of controls

	GFR (ml/min/ 1.73m2)	Macroalbuminuria	Microalbuminuria	No albuminuria
>90	Nil	Nil	35	(70%)
60-89	Nil	Nil	15	(30%)
30-59	Nil	Nil	0	(0%)
15-29	Nil	Nil	0	(0%)
<15	Nil	Nil	0	(0%)

P value-0.005). 54% cases showed eGFR>90 ml/ min/1.73m2 of which 2% showed macroalbuminuria. 28% cases showed eGFR 60-89 ml/min/1.73m2.10% cases showed eGFR 30-59 ml/min/1.73m2 of which 2% showed macroalbuminuria and 6% showed microalbuminuria. 6% cases showed eGFR 15-29 ml/min/1.73m2 of which 3% showed macroalbuminuria and 3% showed microalbuminuria. None of the cases showed eGFR<15 ml/min/1.73m2.70% controls showed eGFR>90 ml/min/1.73m2. 30% controls showed eGFR 60-89 ml/min/1.73m2.None of the controls showed eGFR 30-59, 15-29, <15 ml/ min/1.73m2. 9% cases showed Microalbuminuria and none of the controls showed Microalbuminuria.7% cases showed Macroalbuminuria and none of the controls showed Macroalbuminuria.16% cases and none of the controls were under stage 3 and 4 of CKD. Overall 18% Prediabetic Cases and no Normoglycemic Controls showed evidence of Kidney Disease. (Chi square- 19.78 p value- <0.0001) [Figure 1-3 and Table 1-3].

DISCUSSION
In the present study, 5% cases in stage 3A, 5% in stage 3B, 6 % in stage 4 of eGFR was found.None of the controls were in stages 3 and 4 of eGFR. This difference in eGFR between cases and controls was significant. (Chi Square- 9.65 p value- 0.05).Overall 16% cases were in stage 3 and 4 of CKD.

A study conducted by Platinga LC et al on "Prevalence of Chronic Kidney Disease in US Adults with Undiagnosed Diabetes or Prediabetes".(2010)5 showed that of total 17.7% patients with prediabetes and CKD,56.2% had stage 3 and 4 of CKD.This means 9.95% showed stage 3 and 4 of CKD.

In contrast study by Zhou et al (2013)6 showed 14.1% prevalence of CKD in Prediabetes in which only 2.6% showed reduced eGFR. This difference in eGFR in various studies may be due to difference in study population and different methods of eGFR calculation used.Also duration of hyperglycemia in study population which was not known may causehyperfiltration followed by reduced eGFR which may also contribute to differences in eGFR.

In the present study albuminuria was found in 16% cases. Microalbuminuria was found in 9% cases (UACR- 30– 300 mg/g).Macroalbuminiria was found in 7% cases. (UACR->300 mg/g).None of the controls showed microalbuminuria or macroalbuminuria. This difference of albuminuria between cases and controls was statistically significant.(Chi square- 8.96 p value-0.005).

In study conducted by Bahar A, Maklough A et al(2013)7on correlation between Prediabetic conditions and Microalbuminuria, prevalence rate of microalbuminuria was 15.5% in prediabetic group.(p value-0.005).

In Monica study on Italian subjects(2007)8,the prevalence of Microlbuminuria were 6.9%,5.6%and4.3% in IFG,IGT and NGT group respectively.

Whereas in Robyn study in Australia (2004)9 prevalence of microalbuminuria was 8.3%, 9.9% and 4.3% in IFG, IGT and NGT group respectively.

In study by Zhou et al (2013)6 Albuminuria was found in 12.9% with Prediabetes (Microalbuminuria-12%, Macroalbuminuria-1%).

This difference in prevalence of albuminuria in various studies may be attributed to differences in the population indices, laboratory techniques for urine albumin measurement, differences in

definitions of albuminuria and prediabetes and laboratory techniques to measure it.

The overall evidence of kidney disease was found in 18% cases and none of the controls.This difference in evidence of kidney disease between cases and controls was found to be statistically significant.(chi square – 19.78, p value-<0.0001).

A study conducted by Zhou et al(2013)6 showed 14.1% prevalence of CKD in Prediabetes and 9.2% in normoglycemic patients.(p value-<0.05).

Similarly study conducted by Platinga LC et al (2010)5 showed that 17.7% with prediabetes had CKD.

A study by Caroline S. Fox et al on "Glycemic Status and Development of Kidney Disease"(The Framingham Heart Study)(2005)10 showed that IFG or IGT conferred a 65% increased odds of developing CKD.

Also a study by Shottker B et al on "Prognostic associationof HbA1C and fasting plasma glucose with reduced kidney function in subjects with and without diabeticmellitus."(2013)11 showed that Relative Risk (RR) of IFG to develop reduced kidney function (RKF) was 0.97(95%CI: 0.75-1.25) and HbA1C defined prediabetes was 1.03 (95%CI:0.86-1.23).

CONCLUSION

Kidney disease prevalence is high among people with prediabetes. Thus, prediabetes can be a target for early intervention by lifestyle changes and control of modifiable risk factors for preventing and/or progression of CKD in these individuals which is the need of the hour in countries like India, which is experiencing the epidemiological transition of chronic non-communicable disease.

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