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Medicine

Study of Insulin Resistance by Homeostatic Model Assessment (Homa) in Type 2 Diabetes Mellitus Patients and Its Correlation with Diabetic Nephropathy

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Original Research Article

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Abstract: Many studies showed that Insulin resistance is present in chronic renal failure and evidences suggest that Insulin resistance can also occur in early stages of renal disease. In Indian Scenario there is paucity of data available, so this study was conducted to establish relationship between Insulin Resistance with various stages of Diabetic nephropathy, if any. Study subjects and methods: This is cross sectional study where total 100 subjects are included and are divided into three groups according to their renal status, Group 1 (control) n=19, group 2 (Normoalbuminuria) n=21, group 3 (Microalbuminuria) n=39 and group 4 (Macroalbuminuria) n=21. Seem Insulin measurement was estimated by chemiluminescence method. Insulin resistance was calculated using Homeostatic Model Assessment (HOMA method). The normal cut off value for HOMA IR (2.4) was derived using mean+2SD of control group. Subjects on Insulin therapy was kept in exclusion crieteria. Results: Mean HOMA IR increased significantly with decreasing renal function. Larger percentage of subjects had HOMA IR (≥2.4) at different stages of diabetic kidney disease (Normo albuminuria: 60%; Microalbuminuria: 76%, Microalbuminuria: 92%) compared to normal (32%). There was no significant difference between the study groups with respect to age, BMI, duration of diabetes, duration of nephropathy, habits, glycemic control. The results of multiple logistic regression analysis showed an association between HOMA IR and diabetic nephropathy. Conclusion: There is an association between Insulin Resistance and diabetic kidney disease in type 2 diabetes. In day to day practice clinicians must think about insulin resistance in diabetic patients. It should be measured in all the diabetic patients because it is cheap and easily measurable from FPI and fasting blood sugar level. Its measurement will help to prevent the development of various complications of diabetes at early stages.
Keywords: HOMA, Diabetes mellitus, Diabetic nephropathy, Insulin resistance.

INTRODUCTION

Type 2 Diabetes is an increasing cause of morbidity and mortality in both the industrialized as well as the developing countries. In India approximately 50 Million people are diabetic, > 90 % of them with type 2 diabetes; hence India is rightly called the diabetes capital of the world. Epidemiological studies among migrant Asian Indians in many countries showed higher prevalence of type 2 diabetes compared with the host populations and other migrant ethnic groups.

Diabetic nephropathy is characterized by persistent proteinuria (total urinary protein) 0.5 g/24 h), arterial hypertension, declining glomerular filtration rate and plasma lipid abnormalities. DN is a public health concern of increasing proportions and reasons for a significant reduction in life expectancy of diabetic patients. 2 Without any intervention in Type 2 diabetic patients, 20-40% with microalbuminuria (MA) progress to manifested nephropathy after 20 years from the onset of diabetes; approximately 20% develop end-stage renal disease (ESRD).

Homeostasis model assessment, first described by Matthews et al., is a method for estimating insulin sensitivity [6]. This model is based on the theory of a feedback loop between β cells and the liver [7]. The homeostasis model assessment of insulin resistance (HOMA-IR), calculated from fasting plasma glucose level and immunoreactivity insulin (IRI), is a simple method for evaluation of insulin sensitivity and correlates with the results of glucose clamp test in subjects with mild diabetes without significant hyperglycemia

Hence the present study was done at our tertiary care centre to assess insulin resistance at different stages of diabetic nephropathy and to study the correlation between HOMA-IR & HOMA-β and various stages of diabetic nephropathy.

According to the results of a 10-year longitudinal prospective study, it was observed that insulin resistance is most predictive of diabetic nephropathy in the long-term. Blood pressure and lipids were only predictive of nephropathy in the short-term.

There is a paucity of data on insulin resistance at different stages of diabetic nephropathy in India population; hence in this study we evaluated insulin resistance at different degrees of renal impairment among type 2 diabetic patients in pts visiting D Y Patil Hospital Kolhapur.

METHODOLOGY

This was a prospective cross-sectional study where 100 patients having Diabetes mellitus Type 2 attending medicine O.P.D. and admitted in the medicine ward at D. Y. Patil hospital & research center, Kadamwadi, Kolhapur for evaluation of their glycemic control will be studied. Family history of diabetes mellitus, duration of diabetes, treatment for diabetes and nephropathy, habits like smoking and alcohol noted. The study will be done from July 2015 to October 2017.

For all patients included in this study, we intend to record following information Age, sex, height (by using stature meter),weight(on standard weighing machine), body mass index (Quetelet index) calculated by formula ,waist circumference(by using measuring tape at the highest point of iliac crest), waist-hip ratio blood pressure in sitting and standing position after resting for 15 minutes by using standard mercury sphygmomanometer, All the biochemical investigations i.e. Complete Blood Count(CBC) Lipid profile, Blood Urea(BUL), Blood Urea Nitrogen(BUN), Sr.uric acid will done by using standard enzymatic procedures.

Fasting serum insulin will be done on the sample taken after 8 hours of fasting, serum insulin concentration will be measure via Electro-chemiluminescence immunoassay (ECLIA).

HOMA-IR and HOMA-β was calculated by

$$\text{HOMA-IR} = \frac{\text{Glucose x Insulin}}{405}$$

$$\text{HOMA-}\beta = \frac{360 \times \text{Insulin}}{\text{Glucose-63}} \quad \%$$

Spot Urine samples in sterile container will send to laboratory for assessment of albuminuria.

All the study subjects will be evaluated for renal status based on albuminuria and was divided in following groups

Group 1 will be control group in which sample will be diabetes mellitus patients not devolep into diabetic nephropathy.

Group 2 will be normoalbuminuric subjects (albumin-creatinine ratio 30-300 ug/mg)

Group 3 will be the subjects having microalbuminuria expected protein excretion of more than 500mg/dayand albumin to creatinine ratio >300µg/mg.

Group 4 will be subjects having microalbuminuria.
Estimated Glomerular filtration rate (e-GFR) will calculate by Cockcroft and Gault formula.

Insulin resistance was assessed by using the HOMA method. Normal cut off value for insulin resistance was derived from norm glycemic control subjects (mean+2SD).Subjects having HOMA IR value of above 2.4 were considered to have insulin resistance.

STATISTICAL ANALYSES

Mean and standard deviation and proportions are reported as relevant. Significant differences between groups were tested using the t test, Chi-square test and ANOVA as relevant. Multiple logistic regression analysis was done using diabetic nephropathy as the dependent variable. Independent variables included were age, gender, and duration of DM, BMI, systolic and diastolic blood pressure and insulin resistance (HOMA IR). A p value of <0.05 was considered statistically significant. All the statistical analyses are performed using SPSS 10.0 version software.

RESULTS

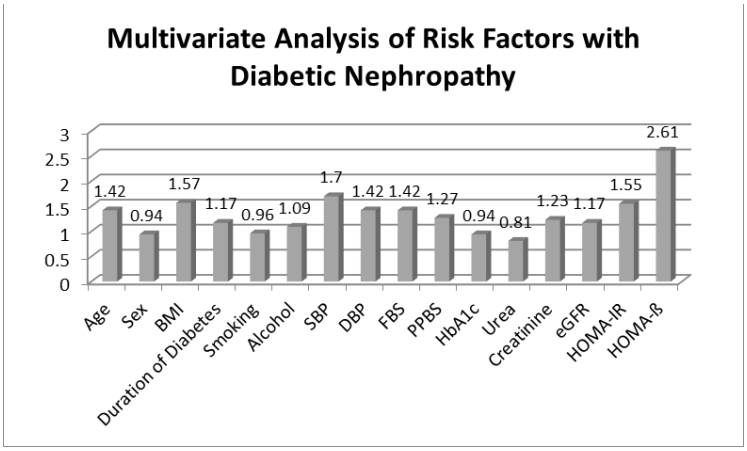
Multivariate Analysis of Risk Factors with Diabetic Nephropathy

It was observed in the present study that there was no significant correlation between serum insulin and demographic parameters (age, sex, BMI, duration of diabetes, smoking and alcohol).

It was observed that Systolic Blood Pressure, Diastolic Blood Pressure, HOMA-IR and HOMA ß were significant risk factors for Diabetic Nephropathy.

Table-1: Multivariate Analysis of Risk Factors with Diabetic Nephropathy

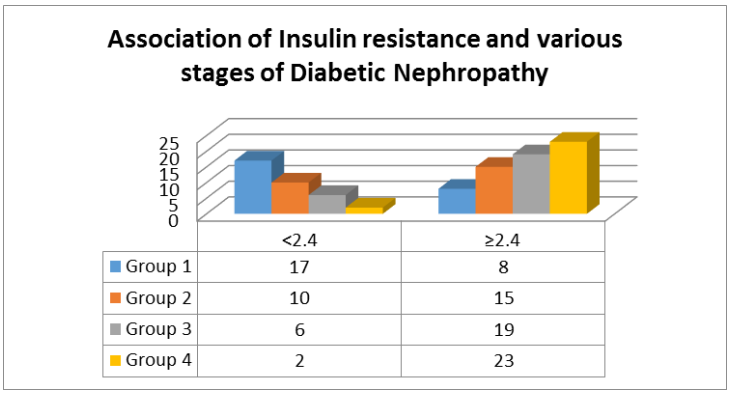
Parameters	OR	95% CI	p Value
Age	1.42	0.54 - 4.61	p>0.05
Sex	0.94	0.31 - 2.98	p>0.05
BMI	1.57	0.87-3.13	p>0.05
Duration of Diabetes	1.17	0.45– 2.85	p>0.05
Smoking	0.96	0.32-2.97	p>0.05
Alcohol	1.09	1.43 – 3.89	p>0.05
SBP	1.70	1.15-2.50	p<0.05
DBP	1.42	1.26-1.60	p<0.05
FBS	1.42	0.54 - 4.62	p>0.05
PPBS	1.27	0.96– 1.53	p>0.05
HbA1c	0.94	0.31 - 2.98	p>0.05
Urea	0.81	0.26-2.75	p>0.05
Creatinine	1.23	1.00– 1.51	p>0.05
eGFR	1.17	0.45– 2.85	p>0.05
HOMA-IR	1.55	1.17– 2.05	p<0.05
HOMA-ß	2.61	1.19 - 4.58	p<0.05



Graph-1: Multivariate Analysis of Risk Factors with Diabetic Nephropathy

Table-2: Association of Insulin resistance and various stages of DiabeticNephropathy

HOMA-IR	Group 1		Group 2		Group 3		Group 4	
	N	%	N	%	N	%	N	%
<2.4	17	68%	10	40%	6	24%	2	8%
≥2.4	8	32%	15	60%	19	76%	23	92%
Total	25	100%	25	100%	25	100%	25	100%



Graph-2: Association of Insulin resistance and various stages of Diabetic Nephropathy

DISCUSSION

To our knowledge, no studies have previously investigated the association between insulin resistance and diabetic kidney disease in Indian population with type 2 diabetes. Our findings demonstrated that insulin resistance was significantly associated with diabetic kidney disease. In our study, insulin resistance increased with worsening renal status in type 2 diabetic subjects.

Mean HOMA IR values also increased with deteriorating eGFR stages. Svensson *et.al.* reported that several mechanisms which include circulating hormones, neuro endocrine pathways and chronic inflammation can contribute to the worsening of insulin resistance at different stages of diabetic nephropathy. The author also concluded that IR is a consequence, and potentially also a cause of diabetic nephropathy. Genetic and environmental background factors may also predispose to both IR and diabetic nephropathy. Our study is a cross sectional design so it is still unclear whether IR is a cause of the decline in renal function. Another Japanese study findings suggested that insulin resistance and hyperinsulinemia are relevant factors of renal function in the general population after taking into account other relevant risk factors.10 They showed that IR and hyperinsulinemia cause glomerular hypertension and hyperfiltration which may predispose an individual to progressive glomerulosclerosis, resulting in renal dysfunction.

Albumin creatinine ratio is important indicator of nephropathy. VishwanathanV *et al*. studied insulin resistance in different stages of diabetic renal dysfunction. They found that insulin resistance increases with worsening of renal function. It was observed in our study that Systolic Blood Pressure, Diastolic Blood Pressure, HOMA-IR and HOMA ß were significant risk factors for Diabetic Nephropathy.

CONCLUSION

There is an association between Insulin Resistance and diabetic kidney disease in type 2 diabetes. In day to day practice clinicians must think about insulin resistance in diabetic patients. As insulin resistance is an independent risk factor in diabetic patients in addition to all well-established risk factors i.e. CAD, Hypertension, and Obesity. It should be measured in all the diabetic patients because it is cheap and easily measurable from FPI and fasting blood sugar level. Its measurement will help to prevent the development of various complications of diabetes at early stages.

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