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Study of Insulin Resistance in Chronic Kidney Disease

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Abstract
Background- In this study, we tried to find out insulin resistance in chronic kidney disease in its various stages.
Material and Methods- This study was conducted in 100 chronic kidney disease patients (both inpatient and outpatient) in the Department of General Medicine, GRMC Gwalior during the period from August 2011- October 2012. Data was collected using a standardized questionnaire, personal interview, physical examination and biochemical investigations.
Results- In our study 100 patients were taken, 57% of the patients were males and 43% were females) with mean age of 44.2 years. The majority of the patients in the study group presented with vomiting and edema. Insulin resistance demonstrated an ascending pattern of prevalence as 27.6%, 31.1%, and 41.4% in stage 3, stage 4, and stage 5 chronic kidney disease respectively. More than half of the hyperinsulinemic patients in stage 5 were overweight). Proteinuria was present in 8 patients out of 9 (88.8%) in stage 4 and 8 out of 12 (66.7%) in stage 5 insulin resistant patients.
Conclusion- Insulin resistance was found in the patients of chronic kidney disease in ascending pattern from stage 3 to 5.

Keywords: Insulin Resistance, Chronic Kidney Disease, Hyperinsulinemia and Proteinuria.

1. Introduction
Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiologic processes associated with abnormal kidney function and a progressive decline in glomerular filtration rate (GFR) [1, 2]. Stages of CKD are stratified by both estimated GFR and the degree of albuminuria, in order to predict risk of progression of CKD. The responses to a reduction in nephron number are mediated by vasoactive hormones, cytokines, and growth factors. Eventually, these short-term adaptations of hypertrophy and hyperfiltration become maladaptive as the increased pressure and flow predisposes to sclerosis and drop out of the remaining nephrons. Reduction in renal mass from an isolated insult may lead to a progressive decline in renal function over many years [3]. Stages of CKD with GFR are: Stage 1- Kidney damage with normal or ↑ GFR (≥90 mL/min/1.73 m^2), Stage 2- Kidney damage with mild ↓ GFR (60-89), Stage 3- Moderate ↓ GFR (30-59), Stage 4- Severe ↓ GFR (15-29), Stage 5- Kidney failure (GFR<15) [4].
Insulin resistance (IR) generally refers to resistance to the metabolic effects of insulin, including the suppressive effect of insulin on endogenous glucose production, the stimulatory effect of insulin on peripheral glucose uptake and glycogen synthesis, and the inhibitory effect of insulin on adipose tissue lipolysis [5]. Insulin resistance results from a combination of genetic susceptibility and environmental exposure [6]. Insulin resistance precedes the development of type 2 diabetes mellitus by 10 to 20 years [7]. IR manifests itself in two complementary pathological sets of derangements. First, manifestations occur due to IR in certain tissues such as the muscles and adipose tissues. Second, heightened responses by other organs occur due to the increased insulin level, such as the kidney and blood vessels [8].

2. Aims and objectives -1. To study the prevalence of Insulin Resistance (IR) in non-diabetic Chronic Kidney Disease (CKD) patients, 2.To compare Insulin Resistance (IR) in various stages of non-diabetic Chronic Kidney Disease (CKD) and 3.To compare various clinical and biochemical parameters in Chronic Kidney Disease (CKD) patients with and without Insulin Resistance (IR).

3. Materials and methods- This open prospective study was conducted in 100 Chronic Kidney Disease patients (both inpatient and outpatient) in the Department of General Medicine, GRMC, Gwalior during the period from August 2011- October 2012. Data was collected using a standardized questionnaire, personal interview, physical examination and biochemical investigations. Inclusion criteria: Non diabetic chronic kidney disease patient with age ≥18 years. Exclusion criteria: 1.Patients having major intercurrent illness at the time of study 2. Patients receiving treatment with drugs with significant anti insulin action (glucocorticoids, antipsychotics, protease inhibitors, diazoxide).

4. Results & Discussion

The present study was done with an aim to assess the insulin resistance in non-diabetic CKD patients in Indian scenario. In our study 100 patients were taken, 57% of the group were males and 43% were females (table 1). 49% of the study population belonged to 25-54 years (table 3) with a mean age of 44.2 years, Bancha Satarapoj *et al.* [9] screened 84 non diabetic CKD patients in stage 2-4 for IR and mean age of the patient was 59 yrs. Majority of the patients in the study group presented with vomiting and edema, which was closely followed by decreased urine output (table 3). 29% of the study population showed evidence of insulin resistance. Insulin resistance demonstrated an ascending pattern of prevalence as 27.6%, 31.1%, and 41.4% in stage 3, stage 4, and stage 5 CKD respectively (table 4). Stefikova *et al.* [10] studied IR in 66 non diabetic CKD patients and found that although the prevalence of IR is more in CKD patients compared to the general population. 21% of the study population showed fasting hyperinsulinemia with majority of patients in stage 5 CKD (table 5). Lindblad *et al.* [11] also found hyperinsulinemia in CKD paediatric population. More than half of the insulin resistant patients in stage 5 were overweight (table 6). More than half of the hyperinsulinemic patients in stage 5 were overweight (table 7). Proteinuria was present in 8 patients out of 9 (88.8%) in stage 4 and 8 out of 12 (66.7%) in stage 5 insulin resistant patients (table 8). Caracava *et al.* [12] who studied IR in 365 non diabetic CKD patients as the stage of CKD advances, the capacity of the kidneys to excreate protein decreases as evidenced in the study. Proteinuria was present in 100% (7 out of 7) of stage 4 and 50% (5 out of 10) of stage 5 non diabetic hyperinsulinemic CKD patients (table 9). Dyslipidemia was evenly distributed in different stages of CKD in relation to insulin resistance and hyperinsulinemia (table 10 and 11). Among the 18 males with insulin resistance, 7 patients were overweight (38.8%) while one person was obese (table 12).
Out of the 18 male patients with insulin resistance, 13 patients had hypertriglyceridemia (72.2%) table 13.

5. Tables

Table 1: Gender distribution of Chronic Kidney Disease patients

Sex	Stage 3	Stage 4	Stage 5	Total	
				N	%
Male	24	17	16	57	57
Female	11	14	18	43	43
Total	35	31	34	100	

Table 2: Age distribution of Chronic Kidney Disease patients

Age distribution	Stage 3	Stage 4	Stage 5	Total	
				N	%
15-24	9	5	3	17	17
25-34	11	3	10	24	24
35-44	4	9	8	21	21
45-54	2	6	6	14	14
55-64	3	2	3	08	08
65-74	5	4	1	10	10
>75	1	2	3	06	06
Total	35	31	34	100	

Table 3: Symptomatology in Chronic Kidney Disease patients

Symptom	Percentage
Vomiting	50
Edema	48
Decreased urine output	40
Dysuria	27
Breathlessness	26

Table 4: Prevalence of Insulin Resistance (IR) in Chronic Kidney Disease patients

Insulin resistance	Chronic Kidney disease						Total	
	Stage 3, N=35		Stage 4, N=31		Stage 5, N=34			
Present	8	27.6%	9	31.1%	12	41.4%	29	29%
Absent	27	82.4%	22	68.9%	22	58.6%	71	71%
Total	35		31		34		100	

Table 5: Prevalence of Hyperinsulinemia (HI) in Chronic Kidney Disease patients

Hyper Insulinemia (HI)	Stage 3	Stage 4	Stage 5	Total	
				N	%
Present	4	7	10	21	21
Absent	31	24	24	79	79
Total	35	31	34	100	

Table 6: Body Mass Index and insulin resistance (IR) in Chronic Kidney Disease patients

BMI (in kg/m^2)	Stage 3		Stage 4		Stage 5	
	IR		IR		IR	
	Y	N	Y	N	Y	N
<18.5	0	0	0	0	1	2
18.5-24.9	6	23	8	15	3	12
25-29.9	2	3	1	7	7	8
30-34.9	0	1	0	0	1	0
Total	8	27	9	22	12	22

IR-Insulin Resistance, Y –Yes and N - No

Table 7: Body Mass Index and Hyperinsulinemia (HI) in Chronic Kidney Disease patients

BMI (in kg/m^2)	Stage 3		Stage 4		Stage 5	
	HI		HI		HI	
	Y	N	Y	N	Y	N
<18.5	0	1	0	0	0	3
18.5-24.9	3	26	6	17	3	12
25-29.9	1	4	1	7	6	9
30-34.9	0	0	0	0	1	0
Total	4	31	7	24	10	24

Table 8: Proteinuria and insulin resistance (IR) in Chronic Kidney Disease patients

Proteinuria (mg %)	Stage 3		Stage 4		Stage 5	
	IR		IR		IR	
	Y	N	Y	N	Y	N
NIL	4	6	1	1	4	4
<150(trace)	0	7	3	4	2	5
150-500(1+)	2	10	4	8	2	6
500-2000(2+)	1	3	1	7	4	2
>2000(3+)	1	1	0	2	0	4
Total	8	27	9	22	12	21

Table 9: Proteinuria and Hyperinsulinemia (HI) in Chronic Kidney Disease patients

Protei Nuria (mg %)	Stage 3		Stage 4		Stage 5	
	HI		HI		HI	
	Y	N	Y	N	Y	N
NIL	1	9	0	2	5	3
<150 (trace)	0	7	2	5	2	5
150-500 (1+)	2	10	4	8	1	7
500-2000 (2+)	0	4	1	7	2	4
>2000 (3+)	1	1	0	2	0	4
Total	4	31	7	24	10	23

Table 10: Dyslipidemia and insulin resistance (IR) in Chronic Kidney Disease patients

Lipid profile (in mg/dl)	Stage 3		Stage 4		Stage 5	
	IR		IR		IR	
	Y	N	Y	N	Y	N
TG(>150)	5	22	7	17	8	16
TC(>200)	5	19	5	15	8	14
HDL(<40)	0	7	1	4	2	5
LDL(>100)	3	4	2	4	2	4
Total	13	52	15	40	20	39

TG – Triglyceride and TC – Total cholesterol

Table 11: Dyslipidemia and Hyperinsulinemia (HI) in Chronic Kidney Disease patients

Lipid profile (mg/dl)	Stage 3		Stage 4		Stage 5	
	HI		HI		HI	
	Y	N	Y	N	Y	N
TG(>150)	1	26	5	19	8	16
TC(>200)	2	22	4	16	8	14
HDL(<40)	0	2	0	2	1	2
LDL(>100)	2	5	1	5	1	5
Total	05	55	10	42	18	37

Table 12: Correlation between BMI and Gender of Chronic Kidney Disease patients with Insulin Resistance

BMI	Stage 3		Stage 4		Stage 5	
	M	F	M	F	M	F
Overweight	2	0	1	0	4	3
Obese	0	0	0	0	1	0

M – Male and F – Female

Table 13: Correlation between Hypertriglyceridemia and gender of CKD patients with Insulin Resistance

	Stage 3	Stage 4	Stage 5
Males	4	4	5
Females	1	3	3

6. Conclusions

Patients with CKD have an alarmingly high risk for cardiovascular morbidity and mortality. This applies even to patients with minor degree of renal dysfunction. The findings of a positive and significant association between IR, hyperinsulinemia and non-diabetic CKD have clinical and public health implication. First, they suggest that it may be beneficial to detect and treat IR and concomitant hyperinsulinemia in non-diabetic CKD patients. Second, they suggest that a more aggressive approach to reducing IR in individual patients and population would substantially lower the risk of CKD. Integration of clinical and bench science will foster identification of subgroups of patients at risk for CKD and provide new treatments based on a more thorough understanding of CKD pathophysiology that helping the patients to lead a better quality life in the coming years.

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