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A CROSS-SECTIONAL RESEARCH TO EVALUATE INSULIN RESISTANCE AMONG THE PATIENTS OF CHRONIC KIDNEY DISEASE (CKD)

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Abstract:

Objective: *The objective of this research study was to evaluate insulin resistance among CKD patients.*

Patients and Methods: *This cross-sectional research was carried out on a total of 50 patients being treated for structural renal abnormalities or deranged renal functions at Jinnah Hospital, Lahore (February 2019 to January 2020). All the recruited patients did not show any dialysis or diabetes history. Another fifty healthy controls were also included in the research of the same age group. All the patients were screened for lipid profile, renal function tests, complete blood count (CPC), serum insulin levels and fasting plasma glucose. HOMA-IR method was used for the calculation of insulin resistance. We made a statistical analysis of research outcomes on SPSS software.*

Results: *We enrolled controls and cases having fifty in each group. Males dominated females in number in cases. Total of 34% of the cases were females; whereas, 66% were males. On the other hand, in controls 26% were females and 74% were males. The mean age of controls and cases was respectively (49 ± 9) years and (50 ± 10) years. CKD patients showed higher levels of fasting insulin and significantly higher HOMA-IR in comparison to controls (P-Value 0.001). The lipid profile showed a significant difference in the levels of triglycerides in statistical analysis.*

Conclusion: *HOMA-IR was significantly higher among CKD patients which clearly shows an association between insulin resistance and CKD.*

Keywords: *Insulin Resistance, CKD, HOMA-IR, and Hypertriglyceridemia.*

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INTRODUCTION:

National Kidney Foundation estimates a 10% onset of CKD in the total population causing morbidity and mortality as a global disease burden. The number of deaths is always on an increase from 2010 onwards due to CKD. The position of this disease drastically rose from 27th position to 18th position in the global estimates from 1990 to 2010. Its magnitude is just higher next to the occurrence of AIDS and HIV among the world population [1]. In Pakistan, the economy is seriously suffering from the ever-increasing burden of CKD. Advanced treatment centres and scarcity of screening facilities are adding more to the disease burden and helplessness of the healthcare department. Estimates indicate that 100 in every million have already reached end-stage renal disease [2].

National Kidney Foundation criteria enumerate three months of more than three months of disease period as CKD whether the damage is functional impairment or structural impairment of kidney with or without glomerular filtration rate reduction. Such pathological derangements manifest the increase in the biochemical markers resulting in kidney disease [3]. CKD is more likely to develop among the patients already suffering from uncontrolled diabetes mellitus. The more the onset of uncontrolled diabetes the more risk of CKD development. Higher insulin resistance also develops among CKD patients. Vitamin 'D' deficiency, systematic inflammation, depressed serum erythropoietin, elevated serum adipokines, oxidative stress, fetuin-A, endoplasmic reticulum stress, metabolic acidosis, etc. cause the onset of CKD [4]. Insulin resistance also predicts energy malnutrition and coronary artery disease. Moreover, insulin resistance is also caused by skeletal muscles' post-receptor alterations [5]. Insulin resistance is also a contributory factor in the metabolic syndrome associated with biochemical abnormalities.

The role of the kidney is important in insulin degradation and metabolism. Insulin renal clearance routes include pre-tubular capillaries diffusion and binding of peritubular cells with contra luminal membrane; whereas, the second route passes through luminal insulin re-absorption by proximal tubular cells. After being diffused the insulin degrades into amino acids and oligopeptides by insulin protease process. Mechanism clearance breach prolongs insulin metabolism and its half-life [6]. CKD patients also show lipid profile derangement as another vital abnormality. The triglycerides clearance impairs because of lipoprotein lipase activity reduction and hepatic triglyceride lipase. This clearance defect increased triglycerides levels [7, 8]. Lipid abnormalities manifestation is normal as metabolic syndrome among CKD patients which leads to insulin resistance. This ultimate increase in insulin resistance also increases atherogenic dyslipidemias [9, 10]. The existing renal condition also aggravates insulin resistance development and attributes to CVD risk. Timely insulin resistance diagnosis is helpful to limit the chances of a disability and increase health outcomes. Therefore, the objective of our research was to evaluate insulin resistance among CKD patients.

PATIENTS AND METHODS:

This cross-sectional research was carried out on a total of 50 patients being treated for structural renal abnormalities or deranged renal functions at Jinnah Hospital, Lahore (February 2019 to January 2020). All the recruited patients did not show any dialysis or diabetes history. Another fifty healthy controls were also included in the research of the same age group. The study population was enrolled through convenient sampling. The total population was subdivided into Group A & B comprising of deranged renal functions and structural renal abnormality patients respectively. We did not include all those patients on dialysis and who were already diagnosed with diabetes mellitus. Age-matched healthy individuals were placed in Group B. Every patient was told about the purpose and process of this research and they also gave their informed consent before the commencement of this research. We observed strict septic conditions for sample collection. All the patients were screened for lipid profile, renal function tests, complete blood count (CPC), serum insulin levels and fasting plasma glucose. HOMA-IR method was used for the calculation of insulin resistance. We made a statistical analysis of research outcomes on SPSS software.

RESULTS:

We enrolled controls and cases having fifty in each group. Males dominated females in number in cases. Total of 34% of the cases were females; whereas, 66% were males. On the other hand, in controls 26% were females and 74% were males. The mean age of controls and cases was respectively (49 ± 9) years and (50 ± 10) years. The anthropometric data shows mean BMI value (23 ± 2) kg/m² for Group 'A' cases and (24 ± 3) kg/m² for Group 'B' controls. Mean serum urea value for cases was (17.84 ± 11) mmol/L and (3.7 ± 0.7) mmol/L for controls. The serum creatinine value for cases was (345 ± 255) umol/L and (71 ± 9) umol/L for controls. Mean fasting insulin level for cases was calculated (19.4 ±9.1) uU/ml and (9.3 ± 6.6) uU/ml for controls. Insulin levels and fasting glucose were calculated through the HOMA-IR method. CKD patients showed higher levels of fasting insulin and significantly higher HOMA-IR in comparison to controls (P-Value 0.001). The lipid profile showed a significant difference in the levels of triglycerides in statistical

analysis. Detailed comparison of research outcomes for both cases and controls is given in Mean and SD values in the tabular form for anthropometric data, glycemic parameter and lipid profile along with P-Values and HOMA-IR correlation.

Table: Lipid Profile, Anthropometric Data, and Glycemic Parameters

(Mean±SD)		Case	Control	P-Value	Correlation with HOMA-IR
Anthropometric data	Age	50.780 ± 14.810	49.700 ± 9.830	Not applicable	
	Weight	63.700 ± 10.800	65.200 ± 9.850		
	Height	164.460 ± 8.630	164.760 ± 10.570		
	BMI	23.380 ± 2.280	24.220 ± 3.400	0.005	0.113
	Hb Level	10.010 ± 1.940	13.620 ± 1.340	0.125	0.551
Glycemic Parameters	Fasting Glucose	5.590 ± 0.930	5.520 ± 0.740	0.073	0.019
	Fasting Insulin	19.460 ± 9.130	8.530 ± 3.060	<0.001	0.953
	HOMA-IR	2.640 ± 1.300	1.150 ± 0.390	<0.001	
	HbA1C	5.850 ± 0.500	5.290 ± 0.560	0.261	0.399
Lipid Profile	Cholesterol	4.6220 ± 1.007	4.017 ± 0.809	0.064	0.061
	Triglycerides	1.989 ± 0.650	1.297 ± 0.454	0.005	0.25
	LDL-C	2.583 ± 0.597	2.209 ± 0.502	0.059	0.146
	HDL-C	1.014 ± 0.168	1.004 ± 0.203	0.329	-0.035

DISCUSSION:

CKD patients' biochemical profile shows insulin resistance as an early marker. CKD patients develop insulin resistance from a very early stage but every patient is developing insulin resistance towards the end-stage failure of the kidney. We evaluated insulin resistance among the patients of CKD. HOMA-IR and renal functions showed positive correlations for both serum creatinine and urea (P-Value < 0.05). Both groups showed a difference in the mean levels of fasting insulin especially cases with a higher mean HOMA-IR score. Another author also finds similar outcomes for the HOMA-IR score with a mean value of (2.24 ± 1.06) [11]. Deranged lipid profile and BMI also attribute in insulin resistance development which is why we also included both factors in our research. The outcomes of this research indicate a positive correlation between body mass index and HOMA-IR score. Similar research also found a correlation between BMI and HOMA-IR (28 versus 3.06) [12]. In those cases where diabetes was absent, hypertension played its part in CKD development. Two studies showed 74% and 80% prevalence of hypertension among the patients of CKD while our outcomes report 74% hypertension score among CKD patients [12, 13]. There was a positive correlation between HOMA-IR and serum triglycerides levels (P-Value 0.005). Lipid profile variables indicated mean value differences in both cases and controls along with positive HOMA-IR correlation except an inverse association between insulin resistance and HDL-C. Mean value differences and insignificant P-values of HDL-C, LDL-c, and total cholesterol are because of the small sample population selected for this particular research. Studies have also shown a positive correlation between HOMA-IR, plasma creatinine levels, triglyceride and cholesterol [14]. Another study has reported a mean triglyceride value of (1.68 ± 1.02) [15]. Our reported reduced haemoglobin levels refer to the small population numbers. Different groups studied by various authors also report a decrease in the levels of haemoglobin [16]. Residual renal cell functioning directly attributes in the development of anaemia [17]. Numerous other factors are also contributing to the development of anaemia among CKD patients with attribution of hepcidin, tumour necrosis factor (TNF-alpha) and interleukins (IL1-6) [17].

CONCLUSION:

Management strategies need serious modulation of therapeutic interventions for an increased presence of insulin resistance among CKD patients. HOMA-IR was significantly higher among CKD patients which clearly shows an association between insulin resistance and CKD.

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