

# Impairments in Renal Functions in Relation with Obesity

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## ABSTRACT

**Background** Obesity is recently acknowledged as an important independent risk factor for kidney disease, in which epidemiological evidence played a crucial role. This risk is probably explained by intracellular lipid accumulation in the kidney. Life style factors such as physical activity and diet play a role in the development of kidney disease in several stages. Impaired renal function is strongly related to cardiovascular disease and mortality. One in every 200 adults suffers from chronic kidney disease, and with growing obesity epidemic, this is likely to increase. This means that since kidney disease takes a long time to develop, pre-clinical kidney dysfunction is much more prevalent, and estimates in the general population ranges from 5 to 11%.

**Methods:** The present study is based on a total of 75 subjects comprising 45 patients with renal failure with or without obesity and metabolic syndrome. Patients with acute renal infection, nephrolithiasis or specific cardiovascular disease were excluded from study. Serum creatinine, urea, blood sugar random, (Estimated glomerular filtration rate) eGFR, hemoglobin, calcium, and phosphate were investigated.

**Results:** The mean eGFR level in 45 patients with renal disease were markedly higher than those of controls, NO significant difference was shown between levels of obese without (Renal disease) RD and of control subjects. Serum creatinine was higher in patients with renal disease. The level in obese renal patients was not significantly different from those with non obese patients with renal failure.

**Conclusion:** Our results based on measurement of various peripheral markers of CKD, failed to suggest a further aggravation of renal dysfunction due to obesity or in the presence of metabolic syndrome, in this cohort of patients.

**Key words:** Chronic kidney disease, cardiovascular disease, C- Reactive protein, End stage renal disease

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## INTRODUCTION

CKD also called as chronic renal failure (CRF), results in loss of normal renal function over a period of months and years. The most important symptoms are feeling of generally weak and experiencing a decreased anorexia, nausea, fatigue<sup>1</sup>. More often subject known to be at higher risk of kidney diseases are those with high blood pressure, diabetes, obesity and a family history with known renal disease.<sup>1</sup> CKD may also be diagnosed when it develops to one of its important complications such as cardiovascular disease, anemia or pericarditis<sup>2,4</sup>. Chronic kidney disorder is diagnosed by a blood test for serum creatinine and eGFR. Increased levels of serum creatinine showed a lower glomerular filtration rate due to a decreased capability to excrete the waste products by both kidneys. In the early stages of chronic renal failure the creatinine levels may within be normal and the CKD is identified if there is presence of proteins or red blood cells in urine

analysis (testing of a urine sample)<sup>3</sup>. As the kidney function lowers, blood pressure raises and leads to fluid overload Mild edema to life-threatening pulmonary edema<sup>4</sup>. associated with hyperphosphatemia, due to decreased phosphate excretion<sup>5</sup> and hypocalcemia due to 1-25 dihydroxy vitamin D<sub>3</sub> insufficiency, and secretion of vasoactive hormones secreted by the kidneys through the RAS (renin-angiotensin system), thus elevates one's risk of producing blood pressure and suffering from congestive cardiac failure. CKD leads to urea accumulation leading to the condition of azotemia and finally (uremic encephalopathy). In such cases urea is also present in sweat and production of crystallizes on skin called "uremic frost"<sup>6</sup>. Erythropoietin production is lowers and leading to chronic anemia, developing severe body aches<sup>2</sup>. In most parts of the world since from last two decades obesity has assumed proportion of an epidemic. Almost 49% of the population in most of the countries having as obesity and a raising increase proportion of small children and young adults are following the same way of obesity. Obesity is concerned with an increase in number of other serious metabolic disorders such as diabetes, CVD and some forms of

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cancers. Obesity associated with metabolic syndrome (MS) has also been regarded as independent single risk factors for CRF<sup>7</sup>. Clinically, some obese patients may present as nephrotic syndrome, although, more commonly, they do not suffer nephrosis. A study on obese patients reports the absence of features of the nephrotic syndrome in spite of high proteinuria<sup>3</sup>. The histopathology of proteinuric obese individuals provides evidence of glomerulomegaly with or without focal segmental glomerular sclerosis (FSGS). These glomerular changes have together been identified as obesity-related glomerulopathy<sup>8</sup>. These changes have been related to impaired renal hemodynamics that includes raised renal blood flow, hyperfiltration, and an increase in filtration fraction. Hypertension, which is nearly associated to obesity, is probably an important cause of kidney malfunction in obese individuals but is likely not the single hemodynamic risk factors.

## MATERIAL AND METHODS

This is a cross-sectional study. The current study is mainly on a total of 75 subjects comprising 45 patients with renal failure with or without obesity and/or metabolic syndrome. The patients 25-50 years of age were recruited from the out-patient departments of the Social Security Health Management Company Hospital Manga Raiwind Road Lahore, Participation of subjects was voluntary and a signed written informed consent to participate in the study was obtained from each subject. The subjects with acute renal infection, nephrolithiasis or specific cardiovascular disease (CVD) were excluded from the study. Also, patients who had developed renal disease before onset of obesity were not included. All biochemical parameters were determined in using standard procedures. Serum creatinine, urea, random blood sugar, calcium, phosphate, and urinary proteins were determined by biochemical procedures. Erythropoietin (Epo) concentrations were analyzed by enzyme-linked immunosorbent assay (ELISA) using commercial kits (MD Biosciences Morwell Diagnostics GmbH, Zurich Switzerland). Samples were processed and analyzed following the manufacturers' recommendations for each assay. The subjects were divided in following five groups: Group A: normal subjects (control=C)(n=15; M :8; f: 7), Group B: patients with renal failure(n=15; M :11; F:4) (Renal Disease=RD), Group C: patients with obesity and with normal renal function (n=15;M:10;F:5) (Obese=Ob), Group D: patients with renal disease and obesity(n=15;M:9;F:6) (RD+Ob),

Group E: patients with renal failure and metabolic syndrome(MS), Diabetes mellitus (DM), and Hypertension (HTN) (n=15;M:7;F:8)(RD+MS)

## RESULTS

The mean BMI of control subjects and non obese patients with renal disease range between 23 and 26. The BMI of obese subjects with or without renal disease and of those with metabolic syndrome ranged between 34 and 36. Both systolic and diastolic BP (mean SBP 159-DBP 101) were significantly higher in patients with MS as compared in the rest of the four groups in which the values were in the normal range (SBP:114-121, DBP: 68-76 mm Hg). No significant gender differences were found in either BMI or BP in all the five groups. Mean random blood sugar levels were 272 mg/dl in patients with MS but were within the normal range in all other groups regardless of obese condition. As expected, creatinine levels were higher in patients with renal disease. The level in obese renal patients was not significantly different from those with non obese patients with renal failure. Also, mean creatinine levels in obese subjects were not significantly different from the control group (0.6±0.1 vs. 0.6±0.0, mg/dl respectively). The mean urea levels were higher in patients with renal disease regardless of the presence of obesity or MS. Also, mean urea levels in obese subjects were not significantly different from control group (26.4±1.7 vs. 27.7±1.1 mg/dl). The mean eGFR levels in all 3 groups with RD were markedly higher than those of controls. No significant difference was shown between levels of obese subjects without RD and of control subjects. The average hemoglobin level of normal subjects and obese subjects without RD were similar, but were significantly different from patients with RD. (13.0±0.5 vs. 19.5±0.5mg/dl). The average calcium levels were found higher in obese subjects and lower levels in patients with renal disease. The average calcium levels in obese subjects were not significantly different from control group (9.7±0.1 vs. 9.2±0.1mg/dl). The mean phosphate levels were higher in renal disease regardless of presence of obesity or presence of MS. Also phosphate levels in obese subjects were not significantly different from control values (4.0±0.1 vs. 3.7± 0.2mg/dl). The mean erythropoietin levels in normal and obese subjects were found decrease in renal disease and higher in obese and control group, also mean EPO level in obese subjects were not significantly different from control group (23.0±1.2 vs. 27.3±0.6 miu/ml)

Biochemical parameters in both males and females

(n = each g)	BSR (mg/dl)	Creatinine (mg/dl)	Urea (mg/dl)	eGFR (ml/min/1.73m <sup>2</sup> )	Hb (mg/dl)	Ca (mg/dl)	PO4 (mg/dl)	EPO (mIU/ml)
	Mean ±	Mean ±	Mean ±	Mean ±	Mean ±	Mean ±	Mean ±	Mean ±
Group (control)	127.5	0.6 ±	27.7 ±	151.7	13.0 ±	9.2 ±	3.7 ±	23.0 ±
Group (N-Obese)	108.6	2.8 ±	126.3 ±	35.8	9.3 ±	7.9 ±	6.1 ±	12.7 ±
Group (OBE)	104.7	0.6 ±	26.4 ±	165.2	13.2 ±	9.7 ±	4.0 ±	27.3 ±
Group (Obese)	108.4	2.5 ±	105.1 ±	61.4 ±	9.5 ±	8.3 ±	5.6 ±	13.2 ±
Group (RD)	272.1 ±	2.7 ±	109.8 ±	58.4 ±	9.8 ±	8.0 ±	6.0 ±	11.4 ±

Hb; males 14-16mg/dl, females 11-13mg/dl, BSR 100-180mg/dl, Creatinine 0.2-1.3, Urea 15-45, Ca 8.1-10.4, Po4 2.5-5.0, EPO 3.22-31.9

## DISCUSSION

The present study was conducted to evaluate the biochemical spectrum of CKD patients and to examine whether presence of diabetes and overweight in such patients leads to a further aggravation of renal dysfunction. In addition, we have attempted to assess a possible predisposition of kidney disease in obese subjects. The mean eGFR is mainly used to diagnose for early renal injury and to detect kidney function. The mean GFR estimated in our subjects was lowest in the lean CKD patients and the levels were just under the cut off values in CKD patients who had a BMI of >30. Furthermore, obese subjects without CKD had a GFR slightly higher than those of the normal weight controls. These observations lead to the interesting speculation that adiposity per se may have a slightly protective effect on overall kidney function. Contrary to our findings a number of previous investigations indicate that individuals with other metabolic disorders like diabetes and obesity are at increased risk of developing CKD. It has been suggested that kidney function may decrease with time as a part of the normal old aging process.<sup>9</sup> in this study also; we observed a gradual decline in GFR subsequent to 40 years of age. We, therefore, chose a cut-off value for abnormally decrease renal function at eGFR less than 60 ml/min to decrease the likelihood of elderly adult patients being erroneously classified as having abnormal kidney status.<sup>10</sup> In our present study we did not find a significant difference between eGFR values of CKD patients with or without MS.

In this investigation serum creatinine levels were significantly raised in all the three groups of patients with renal disease, compared to those of controls. Previous studies indicate that for each 0.2 mg/dl (18 µmol/l) rise in the serum creatinine level, the risk of end stage renal disease is raised by 4.31% in

males and 2.92% in females. In our study we did not find a significant difference between creatinine values of CKD patients with and without MS. Previous studies demonstrated that older age, diabetes, hypertension and obesity MS are associated with a higher risk factor for CKD. Epidemiological studies indicate that pre-existing anemic condition or its development during early stages of renal dysfunction worsens the outcome of patients with CKD. In this investigation, mean hemoglobin levels in obese subjects were not significantly different from controls whereas in the rest of groups of patients with CKD, hemoglobin levels were significantly compromised. In CKD patients random blood glucose levels were within the normal with or without increased adiposity. Our results, therefore, demonstrate that presence of obesity did not worsen the glycemic response of the renal disease patients and the increase observed in CKD+MS subjects was exclusively due to the diabetic condition of these individuals. Peripheral calcium levels though slightly variable in different groups, were within the normal range, Phosphate levels in patients with CKD were slightly but significantly increased over values in control and obese subjects. However, the levels in obese subjects were identical from control values. Previous studies based on cohort data regard serum phosphate as a poor biomarker for CKD

The mean EPO level will be highest in control ,obese group and lower levels will be noticed in, Obs RD, RD, MS. Hypo regenerative anemia is a most common symptom of CRF and has an important impact on morbidity and mortality of kidney patients. Recently two large studies with more than 12,000 patients each have investigated the incidence of anemia in patients with various degrees of renal insufficiency and observed a higher incidence already in individual with mild to moderate kidney dysfunction (creatinine clearance <60 mL/min)

## CONCLUSION

Taken together, our results based on measurement of various peripheral markers of CKD; do not suggest a further aggravation of renal dysfunction due to obesity or in the presence of metabolic syndrome, in our cohort of patients. Also, we did not find a predisposition to renal disease due to increased adiposity but without any co-morbidity. In addition, the study provides normative values of a wide spectrum of biochemical markers of kidney function in a small sample of healthy subjects drawn randomly from the local population. Further studies are necessary to confirm the relationship between MS and CKD over time, and may identify the target level of clinical intervention.

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