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GENDER DIFFERENCES IN THE PROGRESSION OF ACUTE RENAL FAILURE

G. Yasmeen[1]., Z. Hussain[1] and M.L. Bharwani[2]

[1]*Department of Physiology, University of Karachi, Karachi. 75270, Pakistan*
[2] *Department of Nephrology, JPMC, Karachi, Pakistan.*

ABSTRACT

The present study was planned to investigate the alteration in renal function of ischemic ARF patients and to compare the magnitude of these variations in men and women. The study was conducted in collaboration with the department of Nephrology, Jinnah Postgraduate Medical Centre, Karachi. The consent and personal history were taken from the patients of ischemic ARF. Then they were scrutinized to eliminate the influence of potential systemic disorders and blood samples from selected individuals were collected & tested for blood urea nitrogen, plasma urea, creatinine, and electrolytes. The percent elevation from the base line value in the plasma urea and creatinine concentration was found significantly higher in males. Moreover, men have insignificant high level of creatinine while difference in blood urea nitrogen and plasma urea reached the level of statistical significance when compared with women. The findings lead to the conclusion that worsening of renal function in ischemic ARF is more in men. Faster disease progression in males may be in part caused by the sex hormones.

Key Words: Acute renal failure, Blood urea nitrogen, Creatinine, Male sex

INTRODUCTION

Acute renal failure (ARF) is an abrupt deterioration of renal function which is sufficient to result in failure of urinary elimination of nitrogenous waste products i.e. urea nitrogen and creatinine. This deterioration of renal function results in elevations of blood urea nitrogen and serum creatinine concentrations. Commonly used descriptions of acute renal failure include an increase in serum creatinine of >0.5 mg per deciliter (44 µmol per liter) over the base-line value, an increase of more than 50 percent over the base-line value, a reduction in the calculated creatinine clearance of 50 percent, or a decrease in renal function that results in the need for dialysis (Moore *at. al.*, 1984; Solomon *at. al.*, 1994). There are substantial differences in diagnostic criteria, various clinicians use to define ARF as magnitude of rise of serum creatinine concentration. From a clinical perspective, for persons with normal renal function and serum creatinine concentration, glomerular filtration rate must be dramatically reduced to result in even modest increments (*e.g.*, 0.1 to 0.3 mg/dL) in serum creatinine concentration.

Acute renal failure can result from decreased renal perfusion without cellular injury; an ischemic, toxic, or obstructive insult to the renal tubule; a tubulointerstitial process with inflammation and edema; or a primary reduction in the filtering capacity of the glomerulus (Thadhani *et al.,* 1996). The major reisk factors for ARF are hypotension, congestive heart failure, diabetes, septic shock, volume depletion, aminoglycoside use and radiocontrast procedures (Hou *et al.,*1983; Shusterman *et al.,* 1987). It is a morbid disorder that causes mortality in 7-23% patients without any other complication and 50 – 80% in ICU patients (Thadhani *et.al.,* 1996; Chertow *et.al.*, 1997) Ischemia contributes to about 50% in ARF. Ischemia/reperfusion (I/R) injury is a leading cause of acute renal failure (ARF) which is a frequent clinical syndrome with high morbidity and mortality.

The substantial data suggests that sex differences exist in different renal diseases. A meta-analysis by Neugarten *et al.,* (2000) showed that males had a rapid rate of progression of renal disease in membranous nephropathy, IgA nephropathy and autosomal dominant polycystic kidney disease and had worse outcome in chronic renal disease. Consistent with the clinical studies in ARF, animal studies have also shown females to be protected against renal ischemic/reperfusion injury. These findings suggest that the rate of ARF advancement is not similar in both genders and sex may be a discriminating factor. The previous studies did not involve particularly the ischemic ARF patients but they worked upon renal failure or injuries in general.

The routine diagnostic estimations may be helpful in the evaluation of damage intensity and their difference from base line values in both genders may be used as an indicator to predict the progression and severity of renal failure in ischemic insults. The present study was planned with the objective to investigate the alteration in renal function of ischemic ARF patients and to compare the magnitude of these variations in men and women.

METHODOLOGY

Study Type: It was a case-control study that has been conducted at Jinnah Post Graduate Medical Centre, Karachi in collaboration with department of Nephrology.

Inclusion Criteria: Only those patients and normal individuals were included in the study that has no previous personal history of hypertension, diabetes mellitus and heart abnormalities. The basic mechanism of acute renal failure was ischemia but not the toxins. All of the selected participants had to be non-smoker, non-alcohol user and females in reproductive phase of life. None of the partaker was overweight.

Patients & Control: All admitted patients of acute renal failure were clearly explained the purpose of study and their consent was taken prior to questioning and sampling. A detailed personal history was collected through a questionnaire that was asked and filled by the interviewer itself. Special care was taken to ask it as simple as possible to avoid misunderstanding by the patients leading to the gathering of wrong information. The same procedure was practiced with healthy normal individuals.

A total of 100 patients with acute renal failure from both sexes were interviewed initially, 28 of them were excluded from the study because they did not match the basic criteria of study including negative personal history of cardiovascular disease, diabetes mellitus and non-ischemic ARFs. Left over were classified in classes of males (n = 40) and female (n = 32). Forty normal individuals following the same criteria were also included equally in both groups to obtain the base line values for reference.

Biochemical Assessments: Blood sample was collected in a heparinized tube and centrifuged at 3000r/m for 5minutes. Plasma was isolated and kept in frozen form till used for biochemical estimations. Later all the routine diagnostic assays were performed spectrophotometrically including blood urea nitrogen, plasma urea, plasma creatinine, bilirubin total. All values were shown as Mean ± standard error of mean (S.E.M). Student's t-test was applied with $\alpha = 0.05$ level of significance for statistical analysis.

RESULTS

There is significant increase in the plasma values of blood urea nitrogen, urea, creatinine, bilirubin in the ARF patients as compared with the base line values obtained from the gender matched control groups. It was found that there is markably high elevation in the plasma indicators of kidney dysfunction in the male patients as compared with normal males, while the same difference is observed less in females as shown in table 1. The percent variation from base line values in these parameters was observed more in males as compare to females (fig. I) depicting that the magnitude of damage to kidney because of the underlying factors and conditions leading to ARF is higher in males. The difference was found to be statistically significant for all diagnostic parameters except plasma creatinine ($p<0.8$), (Table 1).

Table 1. Gender-wise Average variation in the values of kidney diagnostic parameters in acute renal failure patients.

Parameters	Males		Difference	Females		Difference
	Control (n=20)	Patients* (n=40)		Control (n=32)	Patients* (n=20)	
Plasma Urea (mg/dl)	35±0.2	146±0.6	111**	28±5.2	112±4.1	84
Plasma Creatinine (mg/dl)	0.89±.05	14.79±1.8	14$	0.75±2.2	9.07±.02	08
BUN (mg/dl)	19.5±1.9	99.4±2.9	80**	17±4.1	73.5±0.7	56
Billi D (mg/dl)	0.2±3.2	10.37±3.2	10**	0.08±2.3	0.9±2.1	01
Billi Tot (mg/dl)	0.45±0.9	21.6±0.8	21**	0.78±3.2	2.5±0.6	02

* Statistically significant as compared with respective control.
** Statistically significant as compared with difference in females.
$Non-significant, Values are shown as Mean ± S.E.M.

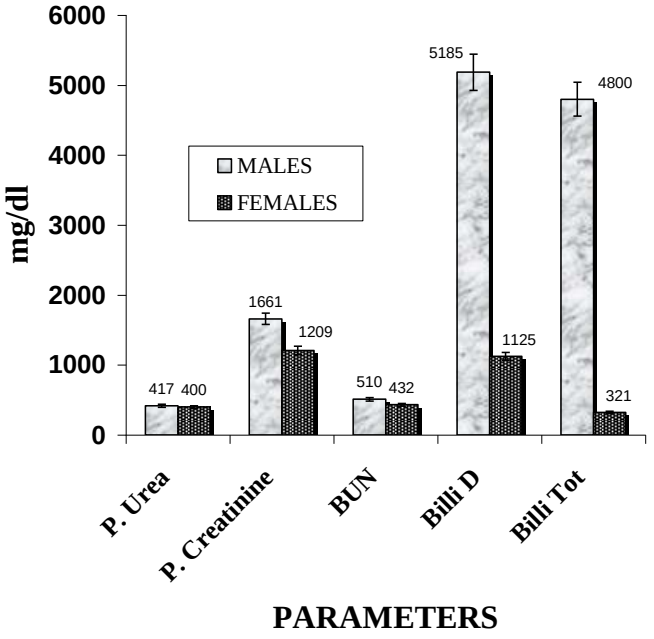

Fig. I. Comparison between the percent alterations of major renal parameters from normal in male and female patients of acute renal failure.

DISCUSSION

Acute renal failure is characterized by a deterioration of renal function over a period of hours to days, resulting in the failure of the kidney to excrete nitrogenous waste products and to maintain fluid and electrolyte homeostasis (Thadhani *et al.,* 1996).

Our study showed that the renal dysfunction is comparatively more in males. This difference may be due to the principal sex hormones of males or females. Testosterone in males may have deteriorating effect causing renal damage and leading to high prevalence or the estrogen in females may have protective effects against ischemic injuries. A study by Park *et al.,* (2004) showed that males had deterioration of kidney function after bilateral renal ischemia of 30 min while females were relatively protected and developed dysfunction only after 60 min of ischemia supports the positive contribution of estrogen in females. They also showed males to have a higher mortality rate. Similarly, Muller *et al.,* (2002) reported that 8% males compared with 75% females survived seven days after ischemia is also in agreement with our study. The same sort of findings are reported in another study by Fekete *et al.,* (2004) who showed that females have lower blood urea nitrogen, serum creatinine and less severe tubular necrosis after renal I/R compared to males. These studies support the hypothesis that sex differences in renal I/R injury exist.

The findings reported by Jafar *et al,* (2003) opposes the results of our study and other studies concluding the faster preogression in males, who evaluated the efficacy of angiotensin-converting enzyme inhibitors on the progression of renal disease and found that after adjusting for baseline variables females had faster progression instead of slower. However, the mean age of the patients participated in the study was 52 years and hence the majority of women may have been postmenopausal. While in our study all female partakers were reproductive. The Modification of Diet in Renal Disease (MDRD) study showed that females, especially <52 years, had a slower rate of progression (Coggins, 1998). However, after adjusting for proteinuria, blood pressure and HDL cholesterol the gender differences were no longer significant. In contrast, studies looking at outcomes in ARF patients have shown that men have twice the mortality of women and have found that gender is an independent predictor of mortality in ARF (Chertow, 1998).

CONCLUSION

The present study concludes that acute renal failure progression is faster and severe in males as compared with females.

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