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Evaluation of Biochemical Markers and Oxidative Stress in Females of Acute Renal Failure

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ABSTRACT

Acute renal failure is a challenging problem. Acute renal failure as the complication of in-patient care is connected with worsened survival, increased morbidity and cost of hospitalization. Reactive oxygen intermediates have been demonstrated to play an etiological role in renal failure. Renal failure term primarily denotes failure of the excretory functions of the kidney, leading to retention of nitrogenous waste products of metabolism. The present study was undertaken to evaluate and compare the severity of serum electrolytes, glucose, protein, creatinine, urea, antioxidant enzymes and oxidant products in females suffering from acute renal failure. For the present study, 58 female subjects of acute renal failure aged from 30 - 80 years and 60 control subjects of same age group healthy females were assessed. A Significant ($P<0.001$) increase in serum potassium, creatinine, urea, and plasma malondialdehyde levels were found in females with acute renal failure groups while serum sodium, protein and antioxidant enzymes were found to be decreased significantly ($P<0.001$) when compared to female healthy control groups. This review also discuss diagnostic tools, strategies for improved design of clinical and therapeutic interventions that will be needed to properly treat acute renal failure in the 21st century.

Key words: Acute renal failure, oxidative stress.

INTRODUCTION

Over the last three decades, several experimental models have identified pathophysiologic mechanisms associated with acute renal failure and have enhanced our understanding of the disease[1, 2, 3] Acute renal failure result from alteration in renal perfusion, changes in glomerular filtration, and tubular dysfunction and correction of these factors can ameliorate the effects of acute renal failure[4] Acute renal failure usually occurs as the results of a sudden interruption in the blood supply to the kidney or toxic overload of the kidney[5] Oxidative stress has been reported with increasing age[6] Reactive oxygen species are important mediators of injury in acute renal failure. Under normal physiologic conditions, a homeostatic balance exists between the formation of reactive oxygen species and their removal by endogenous antioxidant compounds[7] A major lesson from all of these studies reveals that acute renal failure is frequently reversible[8]

MATERIALS AND MATHODS

The clinical material for present study comprised 58 female patients of acute renal failure admitted in G. M. and S. G. M. Hospital, S. S. Medical College, Rewa (M. P.), India. 60 healthy female subjects of same age group were selected as control. The age range was taken from 30 to 80 years. Blood samples were collected from the patients at the time of admission as well as from individuals of female healthy control groups. Clinical investigations were performed in the Department of Biochemistry, S. S. Medical College, Rewa (M. P.), India. Serum protein (Total), creatinine, urea, and superoxide dismutase

were estimated by biuret, jaffe's, diacetyl monoxime, and Mishra H P et al methods respectively. Plasma malondialdehyde and haemolysate glutathione reductase, glutathione peroxidase, and catalase, were estimated by Jean C D et al method (1983), Horn H D (1963), Hafeman D G method (1974), and Asror K sinha method (1972) respectively. Serum electrolytes were estimated by electrolyte analyzer. Obtained data were analyzed statistically by using student "t" test.

RESULTS

1. We observed, highly significant ($p<0.001$) increased biochemical values in serum potassium ions, glucose, creatinine, urea and plasma malondialdehyde when compared to female healthy control groups (Table: 1 and 2).
2. Biochemical markers such as serum sodium ions, protein (Total), superoxide dismutase, and haemolysate glutathione reductase, glutathione peroxidase and catalase were decreased showing highly significant ($p<0.001$) in female acute renal failure when compared to control groups (Table: 1 and 2).
3. Comparative study of acute renal failure between age 30 – 50 and 51 – 80 years shows levels of sodium ions, superoxide dismutase, glutathione reductase, glutathione peroxidase, and catalase were decreased, highly significant ($p<0.001$) in age 51 – 80 years of acute renal failure when compared to acute renal failure age 30 – 50 years. Highly significant ($p<0.001$) increased levels of potassium ions, urea and plasma malondialdehyde were observed in age 51 – 80 years of females suffering from acute renal failure. Serum creatinine was increased significantly (< 0.05) in acute renal failure between age 51 – 80 years.

DISCUSSION

Acute renal failure is usually considered a disease of the hospitalized patients. Although this is often true, acute renal failure may occur in the outpatients setting[8] Acute renal failure in the hospital setting is often iatrogenic, a result of medical intervention. Incidence of acute renal failure in hospitalized patients is between 2 to 5 per

Table 1: Comparative study of biochemical parameters between female healthy control and female acute renal failure group (age 30 – 50 years).

S. No.	Particulars	Female healthy control (30) Mean ± S. D.	Female acute renal failure (30) Mean ± S. D.	t-test	P-value
1	Serum Sodium ions (mEq / L)	139.99 ± 2.46	127.07 ± 3.05	18.060	< 0.001
2	Serum Potassium ions (mEq / L)	4.42 ± 0.32	6.13 ± 0.28	22.027	< 0.001
3	Serum Glucose (mg / dl)	87.61 ± 4.63	119.87 ± 3.84	29.375	< 0.001
4	Serum Protein (Total) (gm / dl)	7.19 ± 0.17	6.14 ± 0.21	21.286	< 0.001
5	Serum Creatinine (mg / dl)	0.8 ± 0.11	3.05 ± 0.35	33.591	< 0.001
6	Serum Urea (mg / dl)	29.82 ± 1.85	44.97 ± 1.30	36.699	< 0.001
7	S-Superoxide dismutase (EU / mg protein / ml)	13.06 ± 1.34	9.50 ± 0.29	14.222	< 0.001
8	Glutathione reductase (EU / gm protein)	19.65 ± 0.16	17.99 ± 0.06	53.208	< 0.001
9	Glutathione peroxidase (EU / mg % Hb)	9.62 ± 0.28	7.52 ± 0.08	39.499	< 0.001
10	Catalase (EU / mg protein / ml)	6.09 ± 0.19	4.79 ± 0.06	35.736	< 0.001
11	Plasma Malondialdehyde (nano mole- ml)	3.97 ± 0.77	9.55 ± 0.28	37.302	< 0.001

cent[9] Advance age, liver diseases, underlying renal insufficiency and diabetes (especially in the presence of vascular disease) have been implicated as risk factor for the development of acute renal failure[8] Acute tubular necrosis is the most common cause of intrinsic acute renal failure in hospitalized patients. Ischemia or toxins usually induce this condition. Ischemic acute tubular necrosis is frequently reversible, but if the ischemia is severe enough to cause cortical necrosis, irreversible renal failure can occur[10,11] Acute tubular necrosis may be prevented by promptly treating patients with reversible causes of ischemic or pre-renal acute renal failure and by maintaining appropriate hydration in patients who are receiving nephrotoxins[12]

Acute renal failure, the kidneys are unable to perform their normal excretory function leading to accumulation of renally eliminated electrolytes.[13] Hyponatremia is a relatively common complication of acute renal failure due to a dilution effect by retained water[14] E*uvolemic hyponatremia t*he most common type of hyponatremia seen in hospitalized acute renal failure patients[15,16,17] A 38.6 per cent incidence of hyperkalemia is seen in azotemic patients[18] Acute renal failure is potential complication of hyperkalemia, affects potassium excretion due to reduced nephron mass (number of functioning collecting ducts) and intrinsic impairment of active potassium secretion[19], because the number of collecting ducts is directly related to the glomerular filtration rate, renal failure whether acute or chronic, leads to impaired renal potassium secretion[20] Pathophysiology of hyperglycemia is associated with hyponatremia in advanced renal failure. Hyperglycemia causes disturbances in the tonicity of body fluids, the distribution of body water between major body fluid compartments and the external balance of body solute and water[21] The prevalence of proteinuria was three times as great among those individuals with a self-reported family history of kidney disease and proteinuria is directly reduces serum protein levels[22] Elevated serum creatinine levels are common in the community and strongly associated with older age[23] Nitrogenous waste products from protein metabolism are retained in the body, resulting in azotemia, as evidenced by the increased serum levels of urea nitrogen[24] Similar results were observed in our study (Table: 1 and 2).

Oxygen is required by various systems for the release of energy and to detoxify xenobiotics.

Table 2: Comparative study of biochemical parameters between female healthy control and female acute renal failure group (age 51 – 80 years)

S. No.	Particulars	Female healthy control (30) Mean ± S. D.	Female acute renal failure (28) Mean ± S. D.	t-test	P-value
1	Serum Sodium ions (mEq / L)	141.36 ± 2.97	123.07 ± 3.24	22.431	< 0.001
2	Serum Potassium ions (mEq / L)	5.08 ± 0.32	6.73 ± 0.39	17.664	< 0.001
3	Serum Glucose (mg / dl)	99.48 ± 2.96	121.36 ± 3.53	25.604	< 0.001
4	Serum Protein (gm / dl)	7.47 ± 0.29	6.09 ± 0.23	19.985	< 0.001
5	Serum Creatinine (mg / dl)	0.89 ± 0.09	3.28 ± 0.34	37.154	< 0.001
6	Serum Urea (mg / dl)	35.52 ± 2.77	48.89 ± 2.51	19.216	< 0.001
7	S-Superoxide dismutase (EU / mg protein / ml)	12.41 ± 1.61	8.93 ± 0.45	11.036	< 0.001
8	Glutathione reductase (EU / gm protein)	18.79 ± 0.27	17.71 ± 0.05	20.824	< 0.001
9	Glutathione peroxidase (EU / mg % Hb)	8.9 ± 0.15	6.99 ± 0.06	62.822	< 0.001
10	Catalase (EU / mg protein / ml)	5.39 ± 0.17	4.33 ±0.09	29.365	< 0.001
11	Plasma Malondialdehyde (nano mole / ml)	3.35 ± 0.36	9.91 ± 0.25	80.055	< 0.001

The products of partial reduction of oxygen are referred to as 'reactive oxygen species' which are highly reactive.[25] Generation of reactive oxygen species contribute to oxidative and the renal damage in ischemic- acute renal failure (iARF).[26] Oxidative stress was measured by reduced level enzymatic activity of superoxide dismutase and catalase.[27] Oxygen free radical scavengers protect against ischemia / reperfusion injury of the kidney in vivo and against hypoxia / re-oxygenation (H / R) injury of renal cells in several in vitro systems acute injury.[28] Oxygen free radicals have been implicated in the pathogenesis of ischaemic acute renal failure. Plasma glutathione peroxidase levels were significantly lower in the patients with post diarrhoeal acute renal failure[29] Malondialdehyde is a terminal product of lipid peroxidation, which can be measured in plasma and serves as an effective lipid peroxidation marker and an indirect index of reactive oxygen species activity[30] Acute renal failure can be triggered or aggravated by reactive oxygen species but established ARF per se might also affect the antioxidant defense mechanisms of the organism. In patients with associated ARF was even more pronounced and plasma malondialdehyde levels were higher[27, 31] Similar results were observed in our study (Table: 1 and 2).

Acute renal failure is most commonly seen in older adults and its associated with significant mortality and morbidity, with death rates among hospitalized acute renal failure patients ranging from 25 to 70 per cent[32, 33] Acute renal failure is characterized by tubular dysfunction with impaired sodium and water re absorption and it has associated with the shedding and excretion of proximal tubule brush border membranes and epithelial tubular cells into the urine[11] An evolving understanding of epidemiology and patho physiology of acute organ dysfunction in the setting of critical illness has give rise to new concepts and terminology for a syndrome once known as either acute tubular necrosis or acute renal failure[34]

Hyperkalemia could be caused by an overall excess of body potassium or by a shift from inside to outside cells or hyperkalemia could be caused by the sudden release of potassium ions from muscle into the surrounding fluids[35, 36] With acute renal failure, sustained decline in the glomerular filtration rate,

Table 3: Comparative study of biochemical parameters between 30 – 50 and 51 – 80 years age group of female acute renal failure patients

S. No.	Particulars	Female acute renal failure		t-test	P-value
		(30–50^{Yr}) Mean ± S. D. (30)	(51–80^{Yr}) Mean ± S. D. (28)		
1	Serum Sodium ions (mEq / L)	127.07 ± 3.05	123.07 ± 3.24	4.843	< 0.001
2	Serum Potassium ions (mEq / L)	6.13 ± 0.28	6.73 ± 0.39	6.765	< 0.001
3	Serum Glucose (mg / dl)	119.87 ± 3.84	121.36 ± 3.53	1.535	0.130
4	Serum Protein (Total) (gm / dl)	6.14 ± 0.21	6.09 ± 0.23	0.865	0.390
5	Serum Creatinine (mg / dl)	3.05 ± 0.35	3.28 ± 0.34	2.536	< 0.05
6	Serum Urea (mg / dl)	44.97 ± 1.30	48.89 ± 2.51	7.542	< 0.001
7	S-Superoxide dismutase (EU / mg protein / ml)	9.50 ± 0.29	8.93 ± 0.45	5.773	< 0.001
8	Glutathione reductase (EU / gm protein)	17.99 ± 0.06	17.71 ± 0.05	19.233	< 0.001
9	Glutathione peroxidase (EU / mg % Hb)	7.52 ± 0.08	6.99 ± 0.06	28.383	< 0.001
10	Catalase (EU / mg protein / ml)	4.79 ± 0.06	4.33 ± 0.09	23.047	< 0.001
11	Plasma Malondialdehyde (nano mole / ml)	9.55 ± 0.28	9.91 ± 0.25	5.151	< 0.001

which leads to accumulation of nitrogenous waste products and uremic toxin[37] Acute renal failure can be triggered or aggravated by reactive oxygen species but established acute renal failure per se might also affects the antioxidant defense mechanisms of the organism[38] Superoxide dismutase is generally thought to play a central role because it scavenges superoxide anion at the initial step of the radical chain reaction[39]

Therefore, from above study we are concluding that acute renal failure are associated with increased serum potassium (hyperkalemia), creatinine, urea and plasma malondialdehyde and decreased serum sodium (hyponatremia), antioxidant enzymes are also associated with the disease. The main novel finding of this study is that oxidative stress leads to acute renal failure. Oxidative stress in elderly patients intensified especially if the patients have associated with renal complications especially in middle age.

REFERENCES

1. Lieberthal W, Nigam S K. Acute renal failure. II Experimental models of acute renal failure: Imperfect but indispensable. *Am J Physiol Renal.* **278**: F1- F12 (2000).
2. Ueda N, Kaushal G P, Shah S V. Apotopic mechanism in acute renal failure. *Am J Med.* **108**: 403-415 (2000).
3. Rosen S, Heyman S N. Difficulties in understanding human "Acute tubular necrosis" limited data and flawed animal models. *Kidney Int.* **60**: 1220 -1224 (2001).
4. Sulton T A, Fisher C J, Molitoris B A. Microvascular endothelial injury and dysfunction during ischemic acute renal failure. *Kidney Int.* **62**: 1539 -1549 (2002).
5. Hegarly J, Middleton R J, Krebs M, et al. Sever acute renal failure in adults: Place of care, incidence and outcomes. *QJM.* **98** (9): 661- 666 (2005).
6. Victor Manuel Mendoza-Nunez, Mirna Ruiz-Romos, Martha A Sanchez-Rodriguez. Aging-Related Oxidative Stress in Healthy Humans. *The Tohoku Journal of Experimental Medicine*. **213** (3): 261-268 (2007).
7. Gutteridge J, Mitchell J: Redox imbalance in the critically ill. *Br Med Bull.* **55**: 49-75 (1999).
8. Josheph A, Mindell, Glenn M, Chertow. A practical approach to acute renal failure. *MCNA.* **81** (3): 731-748 (1997).
9. Shusterman N, Stron B L, Murray T C, et al. Risk factors and out come of hospital – aquired acute renal failure. *Am J Med.* **83**: 65-71 (1987).
10. Brady H R, Singer G G. Acute renal failure. *Lancet*. **346**: 1533-1540 (1995).
11. Thadhani R, Pascual M, Bonventre J V. Acute renal failure. *N Engl J Med*. **334**: 1448-1460 (1996).
12. Brezis M, Rosen S, Epstein F H. Acute renal failure due to ischemia (acute tubular necrosis): In Lazarus J M, Brenner B M. Acute renal failure. 3rd edn. *New York: Churchill Livingston.* 207-229 (1993).
13. Brian L Erstad. General therapeutic consideration in patients with acute renal failure. *Am J Pharma Ed.* **63**: 209-213 (1999).
14. Fraser C L and Ariff A I. Epidemiology, pathophysiolgy, and management of hyponatremia encephalopathy. *Am J Med*. **102**: 67-77 (1997).
15. Bartter F C, Schwartz W B. The syndrome of inappropriate secretion of antidiuretic hormone. *Am J Med*. **42**: 790-806 (1967).
16. Robertson G L, Aycinena A, Zerbe R L. Neurogenic disorders of osmoregulation. *Am J Med*. **72**: 339-353 (1982).
17. Wong L L, Verbalis J G. Vasopressin V_2 receptor antagonist. *Cardiovasc Res.* **51**: 391-402 (2001).
18. Ahuja T S, Freeman D Jr, Mahnken J D, Agraharkar M, Siddiqui M, Memon A. Predictors of the development of hyperkalemia in patients using angiotensin-converting enzyme inhibitors. *Am J Nephrol*. **20**: 268-272 (2000).
19. Daphnis Egene, Stylicnou Kostas. Acute renal failure, translocation hyponatremia and hyperkalemia following intravenous immunoglobulin therapy. *The Nephrol Journal*. **106**(4): c143-c148 (2007).

20. David Weiner and Charles S Wingo. Hyperkalemia: A potential silent killer. *J Am Soc Nephrol*. **9**: 1535-1543 (1998).
21. Antonios H Tzamaloukas, Alan R Levinstone, Kanneth D Gardner Jr. Hyperglycemia in advanced renal failure: Sodium and water metabolism. *Nephron.* **31**: 40-44 (1982).
22. Ramirez S P, McClellon W, Part F K, et al. Risk factors for proteinuria in a large multiracial South-East Asian Population. *J Am Soc Nephrol*. **13**: 1907-1917 (2002).
23. Culleton B F, Larson M G, Evans J C, et al. Prevalence and correlates of elevated serum creatinine levels. *Arch Intern Med*. **159**: 1785-1799 (1999).
24. Price S, Wilson L. Pathophysiology: Clinical concepts of disease processes. 6th edn. *St Louis Mo; Mosby.* (2003).
25. Pillai C K, Pillai K S. Antioxidant in health. *Indian J Physiol Pharmacol*. **46**: 1-5 (2002).
26. Noiri E. Oxidative and nitrosactive stress in acute renal ischemia. *Am J Physiol Renal Physiol.* **281**(5): F948-F957 (2001).
27. Chander V, Singh D, Chopra K. Catechin a natural antioxidant protect against rhabdomyolysis-induced myoglobinuric acute renal failure. *Pharmacol Res.* **48** (5): 503-509 (2003).
28. Mark S Paller, John W Eaton. Hazard of antioxidant combination containing superoxide dismutase. *Free Radical Bio Med.* **18** (5): 883-890 (1995).
29. P V L N Srinivas Rao, K V Dakshinamurty, K S S Saibaba, et al. Edidence for oxidant injury in patients with postdiarrhoeal acute renal failure. *Ind J Clin Bioch.* **11**(1): 66 -69 (1996).
30. Gutteridge J M C, Halliwell B. The measurement and mechanism of lipid peroxidation in biological system. *Trends Biochem Sci.* **15**: 129 -135 (1990).
31. Metnitz P G H, Fischer M, Bartena C, et al. Impact of acute renal failure on antioxidant status in multiple organ failure. *Acta Anasthes Scand*. **44** (3): 236-240 (2000).
32. Santacruj F, Barreto S, Mayor M M, Cabrera W, Breuer N. Mortality in elderly patients with acute renal failure. *Ren Fail*. **18**: 601-605 (1996).
33. Obialo C I, Crowell A K, Okonofua E C. Acute renal failure mortality in hospitalized Affrican – Americans: Age and gender considerations. *J Natl Med Assoc*. **94**: 127-134 (2002).
34. John A Kellum, Eric A J Hoste. Acute kidney injury. *Epidemiology & assessment*. **68** (S241): 6-11 (2008).
35. Greenberg A. Hyperkalemia: Treatment opinions. *Seminars in Nephrology*. **18**: 46-57 (1998).
36. Venzin R M, Cohen C D, Maggiorinin M, Wutherich R P. Aliskiren-associated acute renal failure with hyperkalemia. *Clin Nephrol*. **71** (3): 326 -328 (2009).
37. Nissenson A R. Acute renal failure: Definition and pathogenesis. *Kidney Int.* **53** (Suppl 66): S7-S10 (1998).
38. Metnitz P G H, Fischer M, Bartena C, et al. Impact of acute renal failure on antioxidant status in multiple organ failure. *Acta Anasthes Scand.* **44** (3): 236-240 (2000).
39. Takaya Yamanobe, Futoshi Okada, Yashihito Iuchi, et al. Deterioration of ischemia / reperfusion-induced acute renal failure in SOD-1 deficiency mice. *Free Radical Research*. **41** (2): 200-207 (2007).