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Original Research Article

A prospective study indicating that fractional excretion of sodium is a good marker for fluid loss

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ABSTRACT

Background: Pre-renal failure, a reversible form of acute renal failure (ARF), accounts for 60-70% of all cases of ARF. To study the factors affecting fractional excretion of sodium (FE_{Na}) in patients with pre-renal failure.
Methods: The study involved patients with pre-renal failure, admitted in a multi-speciality hospital in south India for a period of two years. The demographic and clinical data were collected using a standard pro forma. The correlation between FE_{Na} and factors such as age, diabetes mellitus, fluid loss, fever, urine output and creatinine of pre-renal failure were statistically evaluated.
Results: The prospective study involved 24 patients diagnosed as pre-renal failure with a mean age of 52.75±18.78. The subjects included 14 males and 10 females, with a median FE_{Na} of 0.55 (0.10-0.90). A moderate negative correlation was observed between FE_{Na} and fluid loss in pre-renal failure patients (r -0.646, P=0.0007).
Conclusions: The level of FE_{Na} may assist in estimating fluid loss in patients with pre-renal failure.

Keywords: Acute tubular necrosis, FE_{Na}, Pre-renal failure

INTRODUCTION

Pre-renal failure, a reversible form of acute renal failure (ARF), accounts for 60-70% of all cases of ARF.[1,2] The early diagnosis and management of pre-renal failure assists in preventing ARF. Sodium is the key component of the extracellular fluid volume. In a patient following sodium-restricted diet (40 to 50 mEq/d), urinary sodium level decreases to <10 mEq/L within 3-5 days. If the person was earlier on normal sodium diet (150 to 200 mEq/d), the resultant decrease in sodium is sensed by the kidney and thereby tries to conserve sodium.[3] These modest changes in total body sodium and thus in extracellular fluid volume would not be reflected on physical examination and in the assessment of sodium in serum. Fractional excretion of sodium (FE_{Na}), a measure of the percentage of the sodium filtered by the kidney, is one of the helpful tools for assessing the same. It is also used to distinguish pre-renal failure from acute tubular necrosis (ATN).[4] A FE_{Na} <1% indicates pre-renal azotemia, and >1% indicates ATN.[3] Since FE_{Na} works on the principle that sodium reabsorption is enhanced with volume depletion; use of diuretics that decrease the sodium reabsorption can elevate the level of FE_{Na}, thereby producing misleading values.[4] In addition, inaccurate results of FE_{Na} has been reported in patients with metabolic alkalosis.[5]

Fractional excretion of urea nitrogen (FEUN), another diagnostic tool used for differentiating pre-renal failure from acute tubular necrosis, is less influenced by diuretic therapy.[1,4] There are studies showing improved sensitivity, specificity, and overall accuracy of FEUN in differentiating pre-renal failure from acute tubular necrosis than FE_{Na}. Moreover, studies indicate good correlation between FEUN and FE_{Na}, and a weak

correlation between FE_{Na} and serum creatinine. The correlation of FE_{Na} with other variables in patients with pre-renal failure has not been clearly established.[6]

In addition to sodium intake, other patient characteristics may influence the level of FE_{Na}. However, as per the literature review, there are no studies evaluating the factors influencing the FE_{Na}, in a pre-renal failure state. The present study evaluated the correlation between FE_{Na} and factors such as age, diabetes mellitus, fluid loss, fever, urine output and creatinine, and its clinical value in classifying renal patients.

METHODS

The prospective study was conducted in a multi-specialty hospital from South India for a period of two years. Subjects diagnosed with pre-renal failure were selected for the study. Other inclusion criteria considered were: subjects having reduced central venous pressure (CVP), urinary spot sodium <20 mmol/L, renal failure index (RFI) <1, FE_{Na} <1%, and plasma urea creatinine ratio >20.

Clinical features, details on laboratory and imaging investigations, and drug history were collected using a standard pro forma. The laboratory investigations involved blood examination, urine analysis and CVP. The blood examination included: Hb%, TC, DC, ESR, RBS, blood urea, serum creatinine, serum electrolytes and liver function test. The urine analysis included: urine spot sodium, urea, and creatinine. The inclusion criterion considered was renal failure patients with clinical and biochemical evidence of pre-renal failure like low central venous pressure suggesting hypovolemia, urinary spot sodium <20 Mmol/ml, FE_{Na} <1%, and renal failure index <1. Exclusion criteria included patients with established acute tubular necrosis, having signs of chronic renal failure, central venous pressure recording >8 cm of water, urinary spot sodium >20Mmol/ml, and FE_{Na} >1% and renal failure index >1.

The variables examined included: age, gender, FE_{Na}, fluid loss, fever, diabetes mellitus, hypertension, and creatinine. The FE_{Na} of pre-renal failure patients, where compared with clinical and demographic variables such as age, diabetes mellitus, fluid loss, fever, urine output and creatinine, using Spearman's correlation coefficient. The linearity of the correlations was graphically analyzed.

RESULTS

The prospective study enrolled 25 subjects, out of which one expired during the study. Hence only 24 subjects with pre-renal failure were considered. The mean age of the study participants was 52.75±18.78. The total subjects included 14 males and 10 females. The median FE_{Na} of the subjects was 0.55 (0.10-0.90). Fluid loss, fever, and DM were observed in 19, 9 and 2 subjects respectively. The mean creatinine noted was 2 (1.4-4.5). None of the subjects reported hypertension. The corresponding percentage of events of fluid loss, fever, DM, and creatinine noted were 79.16, 37.50, 8.33 and 8.33 (Table 1).

Table 1: Distribution of variables among pre-renal failure patients.

Demographic and clinical characteristics	Values (total n=24)	Percentage of events
Age (Mean±SD)	52.75±18.78	-
FE_{Na} (Median)	0.55 (0.10-0.90)	-
Gender (M/F)	14/10	-
Fluid loss (Y/N)	19/5	79.16
Fever (Y/N)	9/15	37.50
DM (Y/N)	2/22	8.33
HTN (Y/N)	0/24	0.00
Creatinine (Median)	2 (1.4-4.5)	8.33

Comparison of different variables demonstrated a moderate negative correlation between fluid loss and FE_{Na}. This was found to be statistically significant (P= 0.0007, r -0.646, 95%CI: -0.832 to -0.327). Even though a moderate negative correlation was observed between FE_{Na} and fever (r -0.359), urine output (r -0.327) and creatinine (r -0.344), the observations were not statistically significant. However, a tending to be significant correlation was observed between FE_{Na} and fever (P=0.0850, 95% CI: -0.666 to 0.0520), and also between FE_{Na} and creatinine (P= 0.0994, 95%CI: -0.657 to 0.0686). A weak positive correlation was observed between age and FE_{Na} (r 0.13, P= 0.5444, 95% CI: -0.288 to 0.507), and a weak negative correlation between DM and FE_{Na} (r -0.0993, P= 0.6445, 95%CI: -0.483 to 0.317), but neither of them was statistically significant (Table 2).

Table 2: Spearman's correlation between FE_{Na} and different variables.

Factors	r	P value	95% CI
Age	0.13	0.5444	-0.288 to 0.507
DM	-0.0993	0.6445	-0.483 to 0.317
Fever	-0.359	0.0850	-0.666 to 0.0520
Fluid loss	-0.646	0.0007	-0.832 to -0.327
Urine output	-0.327	0.1186	-0.645 to 0.0878
Creatinine	-0.344	0.0994	-0.657 to 0.0686

The regression analysis showed a comparatively strong linear negative correlation between fluid loss and FE_{Na} (Figure 1), compared to other factors such as fever (Figure 2), urine output (Figure 3), and DM (Figure 4). The correlation was very minimal between FE_{Na} and DM. No linear positive association was observed between FE_{Na} and mean age of the subjects and with creatinine (Figure 5 and 6).

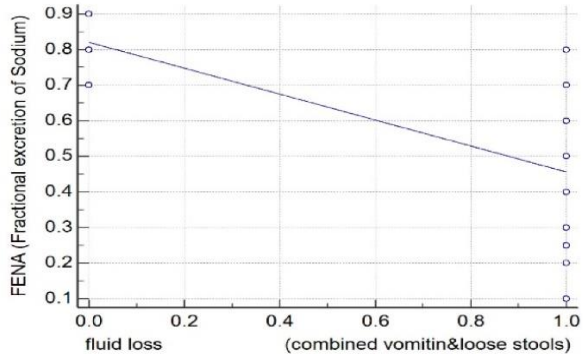

Figure 1: Correlation between FE_{Na} and fluid loss.

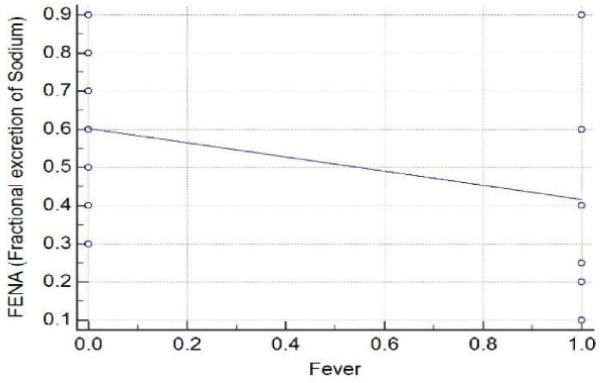

Figure 2: Correlation between FE_{Na} and fever.

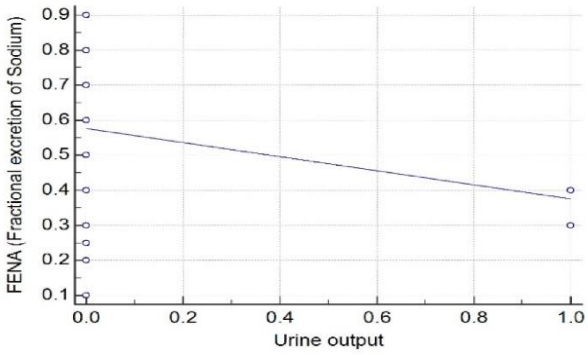

Figure 3: correlation between FE_{Na} and urine output.

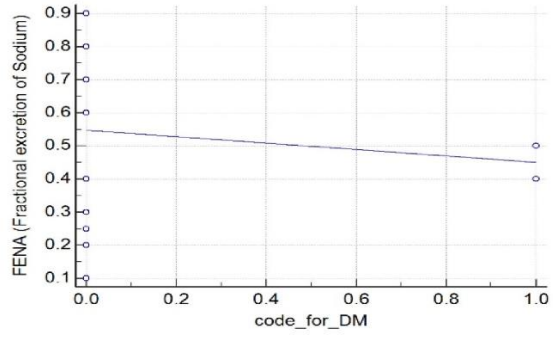

Figure 4: correlation between FE_{Na} and DM.

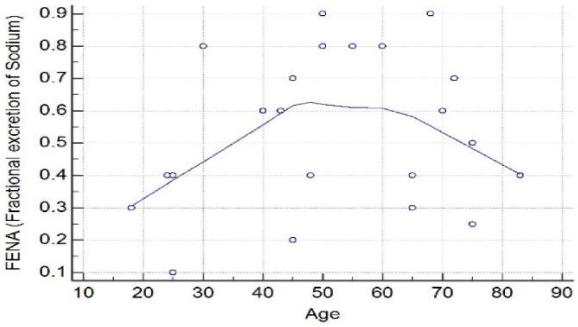

Figure 5: Correlation between FE_{Na} and age.

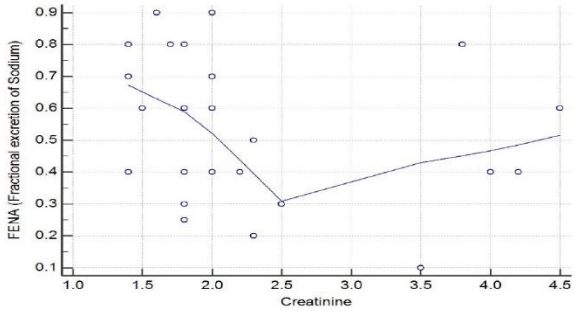

Figure 6: Correlation between FE_{Na} and creatinine.

DISCUSSION

Literature studies on correlation between FE_{Na} and other clinical variables are very limited, especially in patients with pre-renal failure. The present study showed a statistically significant negative correlation between fluid loss and FE_{Na}. Even though a weak negative correlation was observed between FE_{Na} and factors like creatinine and fever, they were not found to be statistically significant. These observations are in concurrence with the findings of Yassin et al. The study conducted in Egyptian population also demonstrated a weak correlation between serum creatinine level and FE_{Na}, with a correlation coefficient of 0.36, closer to the present study (0.34). Other factors such as age, DM and urine output did not show any statistically significant correlation with FE_{Na}.

An earlier study by Lam et al has also reported that FE_{Na} may serve as a guide to volume loss during the recovery in acute renal failure patients. The researchers have noted that a prominent decrease in Fe_{Na} in patients with acute tubular necrosis may indicate a superimposed sodium-retaining state such as fluid loss. The study had shown that FE_{Na} was significantly lower (0.4% to 0.8%) in volume-depleted patients than non-volume depleted subjects. The vigorous intravenous fluid therapy had contributed to increase in urine volume and improved renal function. However, a recent prospective multicenter observational study Legrand et al has concluded that routine urinary biomarkers have lesser predictive value towards fluid responsiveness in oliguric normotensive

ICU patients. The study has found that there was no statistically significant difference between the subjects who responded and did not respond to the fluid challenge with reference to uNa+ (37±38 mmol/L vs 25±75 mmol/L, p=0.44) and FE_{Na} (2.27±2.5% vs 2.15±5.0%, p=0.94).[7]

In a volume-depleted patient without kidney failure, increased reabsorption of sodium and water, results in a decreased excretion of urinary sodium, which in turn reflects in the level of FE_{Na}.[8] The sodium reabsorption is higher in pre-renal state due to the increase in proximal tubular reabsorption of water. Elevated aldosterone level, secondary to hypovolemia, also contribute to increase in reabsorption.[9] Maintenance of renal perfusion and optimization of volume status through the administration of isotonic fluids are imperative to prevent the progression of prerenal ARF to intrinsic renal failure.

The smaller sample size is the major limitation of the study. Due to the limited number of patients, it was difficult to perform reliable statistical tests to explore the relation between FE_{Na} and assessed clinical variables. Hence further research involving larger population size is warranted to corroborate the external validity of their results.

CONCLUSION

In conclusion, FE_{Na} is independent of factors such as age, urine output, diabetes mellitus, fever and creatinine. Since a statistically significant negative correlation was observed between fluid loss and FE_{Na}, the latter may serve as a marker to optimize the status of fluid volume in patients with pre-renal failure.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Hoste EAJ. Pre-renal acute kidney failure. In: Jorres A, Ronco C, eds. Management of acute kidney problems. New York: Springer; 2010:33.
2. Needham E. Management of Acute Renal Failure. Am Fam Physician. 2005;72(9):1739-46.
3. Schrier RW. Diagnostic value of urinary sodium, chloride, urea, and flow. J Am Soc Nephrol. 2011;22(9):1610-3.
4. Carvounis CP, Nisar S, Guro-Razuman S. Significance of the fractional excretion of urea in the differential diagnosis of acute renal failure. Kidney Int. 2002;62(6):2223-9.
5. Nanji AJ. Increased fractional excretion of sodium in prerenal azotemia: need for careful interpretation. Clin Chem. 1981;27(7):1314-5.
6. Yassin AR, Sherif HM, Mousa AY, Esmat A. Comparison between fractional excretion of sodium and fractional excretion of urea in differentiating prerenal from renal azotemia in circulatory shock. Egyptian J Critical Care Med. 2013;1(2):69-77.
7. Legrand M, Le Cam B, Perbet S, Roger C, Darmon M, Guerci P, et al. Urine sodium concentration to predict fluid responsiveness in oliguric ICU patients: a prospective multicenter observational study. Crit Care. 2016;20(1):165.
8. Nguyen MT, Maynard SE, Kimmel PL. Misapplications of commonly used kidney equations: renal physiology in practice. Clin J Am Soc Nephrol. 2009;4(3):528-34.
9. Macedo E, Mehta RL. Prerenal Failure: From Old Concepts to New Paradigms. Curr Opin Crit Care. 2009;15(6):467-73.
10. Lam M, Kaufman CE. Fractional excretion of sodium as a guide to volume depletion during recovery from acute renal failure. Am J Kidney Dis. 1985;6(1):18-21.
11. Demirjian S. Nally J. Acute Kidney Injury, 2010. Available at: http://www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/nephrology/acute-kidney-injury/.

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