

# Evaluation of Serum Electrolyte Status among Normal Healthy Individuals and Newly Diagnosed Cases of Pulmonary TB in Tertiary Care Hospital in Bidar: An Observational Study

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## ABSTRACT

**Background:** Diarrhea, vomiting, and excessive sweating are common features of tuberculosis (TB) infection and have been described as possible cause of loss of water and electrolyte fluid–electrolyte and acid–base derangement frequently encountered in TB and have been found to be a major factor for development of acute renal failure. In view of this associated water and electrolytes derangement and cytochemical changes in TB, this study was undertaken to evaluate common electrolytes status in patients with TB from that of normal healthy individuals.

**Objectives:** The objective of this study was to evaluate the imbalance of some electrolytes like serum sodium, potassium, chloride, and bicarbonate among patients infected with mycobacterium TB in comparison with the normal healthy individuals at BRIMS Teaching Hospital, Bidar.

**Materials and methods:** This was observational study conducted among the patients attending department of pulmonary medicine at BRIMS Teaching Hospital, Bidar. Demographic data and serum electrolytes levels were analysed among those diagnosed with TB patients and compared with normal individuals.

**Results:** Fifty normal individuals (group I) and 50 newly diagnosed TB patients (group II) were included in the study. In the newly diagnosed TB patients, there was a significant ( $p < 0.001$ ) decrease in sodium and potassium levels and increase in chloride and bicarbonate values compared with normal control group. The odds of having hyponatremia and hypokalemia among the newly diagnosed TB patients were 2.57 and 0.92, respectively, as compared to normal healthy individuals.

**Conclusion:** Our results revealed that the electrolyte imbalance was significantly associated with the newly diagnosed TB patients as compared to the normal healthy individuals. Because of the high incidence of the electrolyte disturbances in TB patients, close monitoring and aggressive management are mandatory.

**Keywords:** Cytochemical changes, Electrolyte, Mycobacterium tuberculosis.

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## INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium*, which generally affects the lungs but also can affect the other parts of the body. The classical symptoms of active pulmonary TB include chronic productive cough with blood-stained sputum, fever, night sweats, and weight loss. TB is a major cause of morbidity, disability, and death. It accounts for 2–3 million deaths per annum globally.<sup>1</sup> One-third of the world population has been exposed to the TB bacterium, and new infection occurs at a rate of one per second. In 2006, a total of 1.7 million people died of TB. India is the country with high burden of TB with WHO statistics for the year 2013 estimated incidence of 2.1 million cases of TB in India out of global incidence of 9 million.<sup>2</sup> In addition to accelerating the annual decline in TB incidence, reaching the 2020 milestone for a 35% reduction in TB deaths requires reducing the global proportion of people with TB who die from the disease (the case fatality ratio or CFR), from 17% in 2015 to 10% by 2020. The factors contributing to the resurgence of TB in the developing countries include coinfection with HIV, emergence of multidrug-resistant TB, inadequate treatment, malnutrition, overcrowding, armed conflict, and increasing numbers of displaced person.<sup>3</sup> Electrolytes play a vital role in maintaining homeostasis within the body. Electrolyte imbalance can lead to impaired functions of heart, nervous system, muscular system, as well as lead to acid–base disorders. Hyponatremia is considered as one of the most common and important electrolyte abnormalities. Hyponatremia must be considered in all seriously ill

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hospitalized pulmonary TB patients.<sup>4</sup> Hyponatremia is defined as depletion in the serum sodium (Na) concentration to a level below 136 mmol/L and severe hyponatremia defined as serum sodium concentration lesser than 115 mmol/L, which can be considered as life-threatening condition.<sup>5</sup> The prevalence of severe hyponatremia and its nonsevere form is estimated as 1–4% and 15–30% of inpatients,<sup>6</sup> respectively. Similarly, other electrolytes imbalance like hypochloremia and hypokalemia and reduced bicarbonate levels are also seen in pulmonary TB patients.

TB is one of the rare pulmonary infections which can induce electrolytes imbalance. TB can induce electrolytes imbalance via several mechanisms containing local invasion to the adrenal glands (adrenal insufficiency<sup>7</sup>), local invasion to hypothalamus or pituitary gland,<sup>8</sup> tubercular meningitis<sup>9</sup> and inappropriate ADH secretion via pulmonary infection,<sup>10</sup> and excessive loss of these ions since diarrhea, vomiting, and sweating are frequently seen in PTB.<sup>11</sup> Other electrolyte disturbances such as hypercalcemia have been reported as one of the most common electrolyte imbalance in 25.7% of patients with TB although hyponatremia developed lower prevalence (22.15%)<sup>12</sup>. The disease has become rare in the developed countries, but is still a major public health problem in low- and middle-income countries.<sup>13</sup>

It is estimated that between the years 2000 and 2010, eight to nine million new cases emerged each year. Approximately 1.5 million people die from the disease each year. In adults, TB is the second leading cause of death due to an infectious disease (after AIDS), with 95% of deaths occurring in low-income countries. TB is a major problem of children in poor countries where it kills over 100,000 children each year.<sup>14</sup>

Taking this into account, this observational study was conducted among the patients attending pulmonary medicine OPD of BRIMS Teaching Hospital, Bidar. With the objective to evaluate the imbalance of some electrolytes like serum sodium, potassium, chloride, and bicarbonate among the patients infected with mycobacterium TB in comparison with the normal healthy individuals at BRIMS Teaching Hospital, Bidar.

Socio-demographic, clinical, and laboratory investigations data were collected from the study participants by the investigator by the predesigned and pretested questionnaire.

## MATERIALS AND METHODS

This observational study was carried out during May 2016 to May 2017 at BRIMS Teaching Hospital, Bidar. Sample size was calculated using the following formula:<sup>15</sup>  $[Z_{1-\alpha/2}(SD)^2]/D^2$ , where  $Z_{1-\alpha/2}$  is standard normal variate (at 5% type 1 error ( $p < 0.05$ ) and is 1.96.

Standard deviation (SD) of variable. The value of SD can be taken from the previously done study or through a pilot study.  $D$  = absolute error or precision (5%) in the present study, we are interested in knowing the electrolyte imbalance in TB patients at 5% of type 1 error and SD, based on the previously done studies. Hence, the sample size was taken as 50 per group. The participants were allocated into two group of 50 each.

### Group I (Normal Healthy Individuals)

50 normal healthy individuals between the age group of 14 years and 60 years, both the sex were included on the basis of history and clinical examination.

### Group II (Newly Diagnosed TB Patients)

Fifty newly diagnosed cases of pulmonary TB were included, with age and sex matched with healthy controls. Pulmonary TB was confirmed in this group by chest physician on clinical examination along with sputum smear examination by Z-N staining technique and chest X-ray.

### Exclusion Criteria

Based on the history and clinical examination, patients with diabetes mellitus, liver disease, endocrine disease, HIV, renal disease, intestinal infections, severe malnutrition, and any other acute/chronic illness were excluded. Pregnant women, women using oral contraceptive pill, patients receiving drugs like antidiuretics were also excluded.

## METHODOLOGY

Parameters to be studied were serum sodium, potassium, chloride, and bicarbonate.

### Sample Analysis

5–7 mL of venous blood samples from cubital vein was collected from both groups at the beginning of the study using sterile needle and syringe into a lithium heparin bottle. The plasma was extracted by centrifugation at 4,000 rpm for 10 minutes and stored at  $-20^{\circ}\text{C}$ . Serum sodium, potassium, chloride, and bicarbonate levels were estimated in Group II at the beginning of the study and were compared with Group I. Sodium, potassium, chloride, and bicarbonate analyses were carried out on electrolyte analyzer, which is based on principle of ion-selective electrode. The sputum of the patients and controls were collected for Ziehl–Neelsen staining.

The estimation of sodium and potassium was done using flame emission spectrophotometry method, whereas estimation of chloride was done using colorimetric method, and estimation of bicarbonates was done using back titration method.

### Statistical Analysis

All values were analyzed by Student's *t* test (both paired and unpaired) and one-way analysis of variance (ANOVA) using the Brown–Forsythe statistic followed by Games–Howell *post hoc* comparisons tests to study the differences between groups. The level of statistical significance was set at  $p < 0.05$ . Data are expressed as mean  $\pm$  SD.

### Ethical Clearance

The ethical clearance was obtained from Institutional Ethical Committee of BRIMS before the commencement of the study, and informed consent was obtained from the study participants.

## RESULTS

### Demographic Data

The mean age of patients was  $52 \pm 13.6$  years (in the range of 14–78 years), and 42 patients were men. Women had slightly higher mean age than men ( $53.1 \pm 14.3$  vs  $50.9 \pm 14.3$ ) but this difference was not statistically significant (Table 1). In control group ( $n = 50$  with 1:1 male to female ratio), 25 (50%) were men and 25 (50%) were women. In the newly diagnosed TB patients, there was a significant ( $p < 0.001$ ) decrease in serum sodium, potassium, chloride, and bicarbonate values compared with normal control group.

Plasma sodium levels were monitored in both groups at the time of diagnosis. Mean sodium value was significantly ( $p < 0.001$ ) lower in the newly diagnosed patients than in normal control group (Table 2). The mean chloride value was significantly ( $p < 0.001$ ) lowered in the newly diagnosed TB cases when compared with the normal control. The mean potassium value was significantly ( $p < 0.001$ ) lower in the newly diagnosed TB cases when compared

**Table 1:** Patient distribution based on age and gender

| Gender | No. of patients N (%) |          | Mean age $\pm$ SD (years) |                 |
|--------|-----------------------|----------|---------------------------|-----------------|
|        | Group I               | Group II | Group I                   | Group II        |
| Male   | 25 (50%)              | 17 (34%) | $49.1 \pm 13.4$           | $50.9 \pm 12.3$ |
| Female | 25 (50%)              | 33 (66%) | $48.9 \pm 12.8$           | $53.1 \pm 14.3$ |
| Total  | 50 (100%)             | 50       | $49 \pm 12.9$             | $52.3 \pm 13.6$ |

**Table 2:** Serum electrolyte levels

| S. no. | Electrolyte (mmol/L) | Group I      |          | Group II     |          | Chi-square, p value | Odds ratio |
|--------|----------------------|--------------|----------|--------------|----------|---------------------|------------|
|        |                      | Mean         | Hypo     | Mean         | Hypo     |                     |            |
| 1      | Sodium               | 140.4 ± 3.30 | 0 (0%)   | 124.0 ± 2.17 | 36 (72%) | 53.35, p < 0.001    | 2.57       |
| 2      | Potassium            | 4.2 ± 0.5    | 0 (0%)   | 3.4 ± 0.7    | 24 (48%) | 28.73, p < 0.001    | 0.92       |
| 3      | Chloride             | 101.9 ± 6.1  | 5 (10%)  | 97.7 ± 8.4   | 12 (24%) | 3.47, p < 0.001     | 0.41       |
| 4      | Bicarbonate          | 20.6 ± 2.0   | 26 (52%) | 19.4 ± 1.9   | 36 (72%) | 4.24, p < 0.001     | 2.57       |

with the control. Similarly, the mean bicarbonate value was also decreased significantly ( $p < 0.001$ ) in the newly diagnosed TB cases when compared with the normal control (Table 2).

The hyponatremia seen among the normal healthy individuals was 0%, whereas the hyponatremia seen among the newly diagnosed TB patients was 72%; the odds of having hyponatremia was 2.57 higher among the newly diagnosed TB patients as compared to normal healthy patients. Hypokalemia seen among the normal healthy individuals was 0%, whereas among the newly diagnosed TB patient, it was 48%, with the odds being 0.92. Hypochloremia seen among the normal healthy individuals was 10% whereas among the newly diagnosed TB patient, it was 24%, the odds being 0.41. Low serum bicarbonate among the normal healthy individual was 52%, whereas among the newly diagnosed TB patient, it was 72%, the odds being 2.57.

## DISCUSSION

In the present study, a total of 50 new positive cases of pulmonary TB attending pulmonary medicine outpatient department were enrolled. For comparison, normal persons (control) without pulmonary TB with sex ratio of 1:1 were enrolled, and these patients were screened by Ziehl–Neelsen technique and were confirmed negative.

Gender-related problems of access to health care are more difficult to assess and may need a combination of epidemiological research (population-based prevalence survey) and social science research on health-seeking behavior.<sup>16</sup> Alternatively, at the time of diagnosis, smear-positive patients could be requested to bring in all other household members for sputum smear examination. In the absence of gender bias, one would expect the female/male ratio among smear-positive household members to be approximately equal to that among index patients. This may apply in particular to spouses, who are likely to share possibly confounding characteristics (such as approximate age) with the index patient. Thus, if in the majority of cases the index patient in double-positive couples is husband, gender bias, either in access to health care or within the health system, can be suspected.

### Electrolytes Levels

There was a significant decrease in sodium level (124 mmol/L vs 140.4 mmol/L), potassium level (3.4 mmol/L vs 4.2 mmol/L), chloride level (97.7 mmol/L vs 101.9 mmol/L), and bicarbonate values (19.4 vs 20.6 mmol/L) in the newly diagnosed patients compared with normal control group. In this study, in TB patient the mean value of serum  $\text{Na}^+$  concentration was found to be 124 mmol/L. The observed significant lower mean values of serum  $\text{Na}^+$  level in the total patients than in control may be attributable to vomiting and dehydration.<sup>17</sup>

In 1969, Chung and Hubbard noted that nearly 11% of patients with active TB (pulmonary or nonpulmonary) are affected with hyponatremia, and it is apparent that the main cause of serum

sodium depletion in these patients is syndrome of inappropriate ADH secretion (SIADH).<sup>18</sup> Vorherr et al. reported a case with PTB and hyponatremia and found antidiuretic agents in tuberculous lung tissues.<sup>19</sup> Bryant suggested the syndrome of inappropriate secretion of antidiuretic hormone for patients with an infectious pulmonary disease such as PTB.<sup>20</sup> Schorn et al. reported two cases of PTB and an abnormal inappropriate antidiuretic hormone level as a justifier mechanism.<sup>21</sup> Cockcroft et al. reported a 74-year-old woman with miliary TB, which had been complicated by severe hyponatremia due to SIADH.<sup>22</sup> Manosuthi et al. and Usalan et al. reported a case of TB who initially presented with lethargy due to hyponatremia evidently resulting from SIADH. Finally, they concluded a case of PTB with refractory hyponatremia due to SIADH.<sup>23,24</sup>

Although in this study we did not evaluate patients for etiology of hyponatremia, it can be beneficial if we concisely review the causes of hyponatremia in patients with PTB; SIADH is a considerable complication of pulmonary infection, inflammatory, and neoplastic disorders. In one of the first reports, Weiss et al. reported hyponatremia resulting from SIADH in patients with PTB.<sup>25</sup> Then, it was declared that an increased ADH level in the presence of hyponatremia in PTB cases is an indicator for ectopic ADH production. The mean value of chloride gave the same pattern as the level of  $\text{Na}^+$  in the patients because  $\text{Na}^+$  is always (in most cases) in association with  $\text{Cl}^-$ ; therefore, the same reason for the level of  $\text{Na}^+$  in the patients also holds for this.

In this study, the mean level of  $\text{K}^+$  was significantly lower in pulmonary TB patients when compared to the normal patients. This agreed with another study.<sup>25</sup> In the stress situation due to severe/chronic illness, there is increased catabolism of protein leading to the movement of  $\text{K}^+$  from the intracellular compartment to the plasma and consequently excreted in the urine, sweat, and vomit without any compensatory replacement through food due to anorexia, a common feature of pulmonary TB. There is lower significant bicarbonate level in the pulmonary TB patients than in the TB patients with coinfections, and the normal patients can be attributed to the body's compensatory mechanism to maintain electrochemical neutrality due to the plasma levels of  $\text{Na}^+$  and especially chloride.<sup>17</sup>

The observed potassium level was significantly lower in pulmonary TB patients as compared to the normal individuals. This is similar to other studies.<sup>26</sup> In chronic infection, due to prolonged illness there is increased catabolism of proteins consequently leading to the excretion of potassium in the urine, sweat, and vomit without compensatory replacement from food due to anorexia.<sup>27</sup> The significant lower level of bicarbonates among pulmonary TB patients can be attributed to the body's compensatory mechanism to maintain electrochemical neutrality.<sup>28</sup> The significant higher level of free radical among the newly diagnosed TB cases can be attributed to the fact that mycobacterium-induced reactive oxygen species (ROS) and nitrogen intermediates (RNI) by activating phagocytes and thus promoting tissue injury and inflammation.<sup>29,30</sup>

## CONCLUSION

This study finding suggests that TB bring about the development of electrolyte imbalances including hyponatremia, hypokalemia, hypochloremia, and hypocarbonemia. The observed significant hyponatremia and hypochloremia in the total patients than in control may be attributable to loss of these ions from vomiting and dehydration.

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