Section: Respiratory Medicine

Original Research Article

ELECTROLYTE ABNORMALITIES IN PULMONARY TUBERCULOSIS – A RETROSPECTIVE ANALYSIS OF 86 PATIENTS

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Received : 15/05/2023
Received in revised form : 19/06/2023
Accepted : 01/07/2023

Keywords:
Tuberculosis, electrolytes, hyponatremia, hypochloremia.

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DOI: 10.47009/jamp.2023.5.4.144

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (4); 722-725

Abstract

Background: India has a high prevalence of tuberculosis. Various serum electrolyte abnormalities are commonly seen in pulmonary tuberculosis (PTB) patients including hyponatremia, hypokalemia, hypochloremia and low serum bicarbonate levels. At present, our National Tuberculosis Elimination Program (NTEP) is not insisting on testing serum electrolytes in PTB patients. **Aim:** To study the electrolyte abnormalities in patients diagnosed with pulmonary tuberculosis. **Settings and design:** A retrospective record-based analysis of data of microbiologically confirmed pulmonary TB patients was done at the department of Respiratory Medicine, at a tertiary care center. **Materials and Methods:** The medical records of the diagnosed PTB patients from the year 2021-2022 were collected. Data regarding demography, diabetic status, blood urea, serum creatinine, serum electrolytes (sodium, potassium, chloride) were collected from the records of 86 patients was anonymized and analyzed. **Statistical Analysis:** Continuous variables were calculated using mean and standard deviation. Frequency in percentage was calculated for categorical variables. Correlation and statistical significance were calculated using t test, Pearson correlation, and Fisher exact test. SPSS version 23.0 was used for statistical analysis. **Results:** In our analysis, we found that the majority of the patients were males, and the commonest electrolyte abnormality was hyponatremia (59.3%) followed by hypochloremia (24.4%) and hypokalemia (15.1%). We also found that hyponatremia was independent of the patient's age, sex, diabetic status, and serum creatinine values. **Conclusion:** We found that the majority of the patients had at least one electrolyte abnormality, the most common being hyponatremia. Hence, we recommend measuring serum electrolytes routinely in all patients with pulmonary tuberculosis to improve the outcomes.

INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by the bacteria Mycobacterium tuberculosis. As per the World Health Organization's (WHO) Global TB Report 2022, an estimated 10.6 million people developed tuberculosis in 2021. Of these, India accounted for 28% of the new TB cases, which translates to 2.95 million cases.[1] Pulmonary TB (PTB) accounts for the majority of TB cases, but TB can also affect any part of the body, and it is termed as 'extrapulmonary TB' (EPTB).

Electrolytes are vital for maintaining homeostasis. Electrolyte imbalance may result in impaired functioning of vital organs such as the heart, nervous system, and other organs such as muscles, and may also lead to acid-base imbalance. Hyponatremia, hypokalemia, hypochloremia, hypercalcemia, and reduced bicarbonate levels are seen in PTB patients, with hyponatremia being the most common electrolyte abnormality and the syndrome of inappropriate antidiuresis (SIAD) being the commonest cause of hyponatremia.(2)

Currently, performing serum electrolytes for tuberculosis patients is not mandatory as per the National Tuberculosis Elimination Programme (NTEP) in India. Hence, this study was carried out to assess the magnitude of electrolyte abnormalities among PTB patients.

MATERIALS AND METHODS

This is a retrospective record-based study conducted at the department of Respiratory Medicine at a tertiary care center. The medical records of the microbiologically confirmed PTB patients who were admitted from the year 2021-2022 were collected. Patients with EPTB and incomplete data were excluded.

Out of 134 microbiologically diagnosed PTB patients, 48 were excluded due to incomplete data, and the remaining 86 patients' data was analyzed. Data regarding patients' demography, blood glucose (random blood sugar, fasting blood sugar, post-prandial blood sugar, HbA1C), blood urea, serum creatinine, and serum electrolytes (sodium, potassium, and chloride) were collected.

Serum sodium concentration < 136 mmol/L was considered as hyponatremia and < 115 mmol/L was considered as severe hyponatremia.(3) Serum potassium concentration of 3.5 to 5.1 mmol/L was considered normal. Serum chloride concentrations of 96 to 106 mmol/L were considered normal. Electrolytes were measured by Ion selective electrode-direct method. A diagnosis of diabetes was considered when fasting blood glucose was ≥126 mg/dL or 2-hour post-glucose load ≥200 mg/dL or random blood glucose ≥200 mg/dL with symptoms or HbA1c > 6.5%.(4) Blood urea levels of 15 – 40 mg/dL (Urea Urease-GLDH Kinetic) and serum creatinine values of 0.7 – 1.2 mg/dL (Jaffe's Kinetic method) were considered normal.

Statistical analysis

Statistical analysis was done using SPSS version 23.0 software (SPSS Inc., Chicago, Illinois, USA). Continuous variables were reported in terms of mean and standard deviation. Frequency in percentage was calculated for categorical variables. Pearson correlation, t-test, and Fisher's exact test was used to evaluate correlation and statistical significance wherever applicable. A p value < .05 was considered statistically significant.

RESULTS

All 86 patients were microbiologically confirmed cases of MTB by either sputum microscopy or Cartridge Based Nucleic Acid Amplification Test (CBNAAT) or both. None of the patients were HIV positive.

Out of 86 patients, 66 (76.74%) were males and 20 (23.26%) were females. The mean age was 51.54 ± 14.67 years, and the minimum and maximum ages of the patients were 18 years and 85 years, respectively. Males had a higher mean age (54.4 ± 13.56 years) compared to females (42.1 ± 14.55 years), and the difference was statistically significant (P 0.0008).

Thirty-eight patients (44.2%) were non-diabetics, and 48 patients (55.8%) were diabetics diagnosed as per the WHO criteria. The incidence of diabetes was higher among males (38 out of 66, 57.6%) compared to females (10 out of 20, 50%) but the difference was not statistically significant (P 0.6124). The association between diabetic status and serum sodium levels was not statistically significant (P 0.0507).

Electrolyte abnormalities

Of the 86 patients, 20 (23.25%) had no electrolyte abnormality, and 66 (76.74%) had at least one electrolyte abnormality. Table 1 and Figure 1 shows the overall electrolyte abnormalities observed in our study, and Table 2 shows the mean values of the electrolytes, urea, and creatinine based on sex and their statistical significance.

Serum Sodium

Overall, 57 patients (66.3%) had hyponatremia, of which one patient (1.16%) had severe hyponatremia. Twenty-nine patients (33.7%) had normal serum sodium ion concentrations. Forty-four out of sixty-six (66.7%) male patients had hyponatremia, whereas 13 out of 20 (65%) females had hyponatremia. The difference was not statistically significant (P 1). The overall mean serum sodium ion concentration among the patients was 132.62 ± 5.75 mmol/L (range: 113 to 143 mmol/L). Among males, the mean sodium levels were 132.56 ± 5.94 mmol/L, and among females, they were 132.85 ± 5.2 mmol/L and this difference was not statistically significant (P 0.8451).

Our analysis revealed that there was a negative correlation between age and serum sodium levels and the correlation was not statistically significant (r -0.08, P 0.447). It was also observed that the relationship between serum creatinine and serum sodium values had a weak positive correlation and was not statistically significant (r 0.13, P 0.214).

Serum Potassium

In total, 13 patients (15.1%) had hypokalemia, 68 patients (79%) had normal levels of serum potassium, and five patients (5.8%) had hyperkaliemia. The mean potassium ion concentration was 4.21 ± 0.68 mmol/L (range: 2 to 5.7 mmol/L). Among males, the mean potassium levels were 4.25 ± 0.66 mmol/L, and among females, they were 4.12 ± 0.72 mmol/L and this difference was not statistically significant (P 0.454).

Serum Chloride

Twenty-one patients (24.4%) had hypochloremia, three patients (3.5%) had hyperchloremia, and 62 patients (72%) had normal serum chloride levels. The mean chloride ion concentration was 97.3 ± 11 mmol/L (range: 10 to 108 mmol/L). Among males, the mean potassium levels were 97.09 ± 12.22 mmol/L, and among females, they were 98 ± 5.6

ISSN (O): 2687-5365; ISSN (P): 2753-6556

mmol/L and this difference was not statistically significant (P 0.7486).

Table 1: An overview of electrolyte abnormalities observed in our study

Electrolyte abnormality	Males (n=66)	Females (n=20)	Total (N=86)
Hyponatremia	44 (66.7%)	13 (65%)	57 (66.3%)
Hypokalemia	10 (15.15%)	3 (15%)	13 (15.1%)
Hyperkalemia	4 (6%)	1 (5%)	5 (5.8%)
Hypochloremia	16 (24.24%)	5 (25%)	21 (24.4%)
Hyperchloremia	2 (3%)	1 (5%)	3 (3.5%)

Table 2: Mean serum electrolytes, urea and creatinine values among males and females

	Males (n=66)	Females (n=20)	Total (N=86)	P value
Sodium (Mean ± SD)	132.56 ± 5.94 mmol/L	132.85 ± 5.2 mmol/L	132.62 ± 5.75 mmol/L	0.8451*
Potassium (Mean ± SD)	4.25 ± 0.66 mmol/L	4.12 ± 0.72 mmol/L	4.21 ± 0.68 mmol/L	0.454*
Chloride (Mean ± SD)	97 ± 12.2 mmol/L	98 ± 5.6 mmol/L	97.3 ± 11 mmol/L	0.7486*
Blood urea (Mean ± SD)	31 ± 17.4 mg/dL	20.8 ± 8.72 mg/dL	28.65 ± 16.34 mg/dL	0.0133#
Sr. creatinine (Mean ± SD)	1.17 ± 0.67 mg/dL	0.81 ± 0.27 mg/dL	1.09 ± 0.62 mg/dL	0.0208#

* Statistically not significant. # statistically significant. p value <0.05 is considered significant

DISCUSSION

Electrolyte abnormalities, the most common being hyponatremia, were reported in various studies. In tuberculosis, hyponatremia may be a result of excessive loss of Na ions due to vomiting or diarrhea or due to direct invasion of the adrenal glands causing adrenal insufficiency, direct involvement of the hypothalamus and pons in cases of TB meningitis, or inappropriate anti-diuretic hormone secretion (ADH) due to extensive pulmonary disease.[3,5–8] Even among disseminated TB patients, the involvement of the adrenal gland is mostly subclinical.[9] The exact prevalence of hyponatremia among TB patients is uncertain. Various studies have reported a prevalence ranging from 22.15% to 72%.[7,10–14] Jafari et al. in their review of 200 TB patients found that the mean sodium concentration was 134 ± 4 mmol/L without any gender predilection, and the overall prevalence of hyponatremia and severe hyponatremia was 51% and 1%, respectively.[7] In our study, we found that the mean sodium concentration was 132.62 ± 5.75 mmol/L, hyponatremia was present in 66.3% of the patients, and severe hyponatremia was present in one patient (1.1%). Further, in our analysis we found that the serum sodium levels were independent of age, sex, diabetic status and renal function (serum creatinine).In primary adrenal insufficiency or Addison's disease, which occurs secondary to involvement and destruction of the adrenal glands, hyponatremia is usually seen along with hyperkaliemia and increased urinary excretion of potassium.[8,15] Hypokalemia can be explained by the excretion of potassium ions in the sweat, urine, or vomitus without proper dietary replacement, as most PTB patients will suffer from anorexia.[16] Hypokalemia may also be drug-induced in patients treated with drugs such as rifampicin, amikacin, capreomycin, and viomycin-pyrazinamide for the treatment of TB.[17,18] In our study, 5.81% had hyperkaliemia, and 15.11% had hypokalemia. Kaur et al. and Patil et al. reported that hypokalemia was present in 45% and 48% of their study population, which is higher than our observation.[13,14] A study found that serum potassium levels were significantly elevated among HIV-TB patients compared to new TB patients.[19] But, in our study, the serum potassium levels were elevated by 0.1 to 0.6 mmol/L above the reference value, which may not have any impact on the patients.

Hypochloremia in TB patients is due to dehydration and the loss of chloride ions in vomitus. In our study, hypochloremia was seen in 21 out of 86 patients (24.41%), which correlates with a study by Patil et al., where they found that hypochloremia was seen in 24% of the newly diagnosed TB patients.[14] We also found hyperchloremia in 3 patients, but the chloride ion values were only elevated by 1-2 mmol/L from the reference value, which is too small to make an impact on the clinical condition of the patients.

Other electrolyte abnormalities, such as hypercalcemia, and low levels of serum bicarbonate, may be seen in TB, which was not evaluated in this study. Hypercalcemia in PTB is mainly due to excessive extra-renal 1-alpha hydroxylase activity, and the condition is exacerbated by taking vitamin D or calcium supplements.[20] Hypercalcemia may also be seen in disseminated TB and in concomitant renal failure and diabetes.[21] Hypercalcemia in TB is usually mild and self-limiting. Various studies had reported the prevalence of hypercalcemia to be 2-51% among TB patients.(22) Conversely, in a large study on hypercalcemia, 6% of patients with confirmed hypercalcemia had TB.[23] Low levels of serum bicarbonate may be attributed to the body's homeostatic mechanisms to maintain electrochemical neutrality.[2]

Patients with diabetes have a 2 to 3-fold higher risk of developing TB disease, a 2-fold risk of death during TB treatment, a 4-fold risk of relapse and a 2-fold risk of developing multidrug-resistant TB (MDR TB) compared to non-diabetic individuals.[24]

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Globally, about 10% of TB cases are linked to diabetes.[25] WHO and NTEP recommend collaborative care for patients with TB and diabetes.(24) In India, various studies have reported a prevalence of diabetes among TB patients ranging from 13.1 to 44%.[26–30] Balakrishnan et al. found in their study that nearly half of the TB patients in Kerala had diabetes, which holds true for our study too, as we have found that 55.81% of our patients had diabetes.

CONCLUSION

A significant number of our study population had significant electrolyte abnormalities such as elevated hyponatremia, hypochloremia, and hypokalemia which may be due to adrenal insufficiency, reduced oral intake, dehydration, and increased excretion in the form of sweat, vomitus, or diarrhea. Hence, all pulmonary TB patients should be evaluated with renal function testing and serum electrolyte measurement as a part of pre-treatment evaluation, like blood glucose and HIV testing, to improve treatment outcomes.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556