

**Analyze the Prevalence of Hyponatremia in Adult Patients with Pulmonary Tuberculosis****Prakash Sinha<sup>1</sup>, Laxmi Niwas Tiwari<sup>2</sup>, Ritesh Kamal<sup>3</sup>**<sup>1</sup>Associate Professor, Department of Pulmonary Medicine, Katihar Medical College and Hospital, Katihar, Bihar.<sup>2</sup>Assistant Professor, Department of Pulmonary Medicine, Katihar Medical College and Hospital, Katihar, Bihar.<sup>3</sup>Professor and Head of Department, Department of Pulmonary Medicine, Katihar Medical College and Hospital, Katihar, Bihar

Received: 25-09-2023 / Revised: 28-10-2023 / Accepted: 30-11-2023

Corresponding author: Dr. Laxmi Niwas Tiwari

Conflict of interest: Nil

**Abstract:****Background:** One of the main causes of morbidity and death in developing and poor nations is pulmonary tuberculosis (PTB). The nation with the greatest PTB load is India. Hyponatremia is one of the most prevalent electrolyte imbalances, and it increases morbidity and mortality. The prevalence of hyponatremia in adult pulmonary tuberculosis patients was investigated in this study.**Methods:** Patients who presented to the pulmonary medicine department at Katihar Medical College and Hospital in Katihar, Bihar between September 2019 and August 2020 and who were above the age of 18 were included in this retrospective analysis. PTB was identified in accordance with the institutional protocol, which took into account the patient's clinical presentation, microscopic investigation results suggesting the presence of acid-fast bacilli (AFB), and abnormal chest radiograph findings. During the study period, all patient case files with PTB were gathered, and pertinent laboratory results and demographic information were recorded and examined.**Results:** In all, 150 PTB patients between the ages of 18 and 86 were enrolled in this study. The patients' average age was  $50.92 \pm 17.76$ . Thirty-six (26%) and eighty-four (74%) of the 150 patients who had hyponatremia—that is, serum sodium levels less than 135 mmol/l were female. A total of 150 patients were found to have mild hyponatremia in 59 (39%), moderate hyponatremia in 41 (27%) and severe hyponatremia in 14 (9%) of them. Males constituted the majority in all groups with hyponatremia. Sputum tested positive for AFB in 27 cases (46%) of mild hyponatremia, 34 cases (83%) of moderate hyponatremia, and 11 cases (79%) of severe hyponatremia. All patients but four had severe hyponatremia and needed vasopressor therapy due to hypotension; the other patients were asymptomatic.**Conclusion:** Hyponatremia should be assessed in patients with PTB as early detection and therapy may be able to lower morbidity and death.**Keywords:** AFB; Hyponatremia; Mortality; Pulmonary tuberculosis.This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.**Introduction**

One of the main causes of morbidity and death in developing and poor nations is pulmonary tuberculosis (PTB). One of the top 10 causes of death worldwide and the most common infectious agent is tuberculosis. 10.0 million individuals worldwide 5.8 million men, 3.2 million women, and 1.0 million children—developed tuberculosis in 2017. According to a prior study, roughly 23% of people on the planet have a latent tuberculosis infection, putting them at risk of ever having active tuberculosis [1]. One of the most prevalent infections in India is tuberculosis, which has a high death rate. India is ranked 14th out of the top 22

nations with a high rate of tuberculosis infections [2]. As per the Global TB report 2017 the estimated incidence of TB in India was approximately 28,00,000 accounting major part of the world's TB cases. In clinical practice, hyponatremia defined as serum sodium levels below 135 mmol/litre is the most prevalent electrolyte abnormality [3]. Because hyponatremia can have serious consequences and may indicate an underlying medical condition, it is crucial to identify it [4]. A biochemical finding of a serum sodium concentration between 130 and 135 mmol/L, between 125 and 129 mmol/L, and less than 125 mmol/L, respectively, is defined as mild,

moderate, and severe hyponatremia. Up to 20% of critically ill patients experience hyponatremia, which is seen in 15-20% of emergency room admissions [5].

The most frequent cause of hyponatremia is the syndrome of inappropriate secretion of antidiuretic hormone (SIADH), which is characterized by decreased serum osmolality in a euvolemic patient without edema, hyponatremia, excessive urine sodium, and inappropriately elevated urine osmolality [6]. A common side effect of cancer, lung diseases, neurosurgical conditions, heart failure, liver failure, and renal failure is SIADH [2]. PTB has a strong correlation with SIADH in addition to other infections [7].

Numerous mechanisms have been proposed to explain how tuberculosis (TB) can cause hyponatremia. These include direct effects on the adrenal glands, local invasion of the hypothalamus or pituitary gland, meningitis [12–14], and inappropriate ADH secretion as a result of pulmonary infection [15–17]. One of the most frequent causes of Addison's disease in India is tuberculosis (TB), which can destroy the adrenal glands and result in overt or subclinical adrenal insufficiency [2]. In the KMCH in Katihar, Bihar, the prevalence of hyponatremia in adult PTB patients was investigated and analyzed in the current study.

### Material and Methods

It was an analysis done in the past. Over the course of a year, from September 2019 to August 2020, patients with PTB who presented to the pulmonary medicine department of Katihar Medical College and Hospital in Katihar, Bihar, were included. According to the institutional protocol, PTB was diagnosed based on the patient's clinical presentation, microscopic examination suggesting

the presence of acid-fast bacilli (AFB), and abnormal findings on chest radiographs. Patient case files pertaining to PTB patients have been collected. The patients' laboratory results and demographic information were noted and examined. Patients with a history of prior TB, kidney disease, cancer, diuretics, and medications associated with SIADH were also included in the group of adult patients, aged 18 and above, who had been diagnosed with active PTB. Serum sodium concentration less than 135mmol/L were considered as hyponatremia were excluded in this study.

The patients were categorized into three groups based on their serum sodium concentration: 130–134 mmol/L, 125–129 mmol/L, and less than 125 mmol/L for mild, moderate, and severe hyponatremia, respectively. The laboratory used for the microbiological testing is part of our hospital and is approved by the Revised National TB Control Program (RNTCP).

N, mean, standard deviation, and range were used to present the statistical techniques for quantitative data and descriptive statistics in this study. Frequency count, N, and percentage were tabulated for the qualitative data. SPSS (version 20) statistical software was used for all statistical analysis, and a p value of less than 0.05 was considered significant.

### Results

In total, 150 adult patients, ages 18 to 86, with active PTB were included in this study. Patients' average age was  $50.92 \pm 17.76$ ; hyponatremia patients' average age was  $51.42 \pm 17.77$ ; and patients' average age with normal sodium levels was  $49.31 \pm 17.89$  (Table 1). The statistical significance of this was not established (P value = 0.53).

**Table 1: The serum sodium levels and Mean age**

Serum Sodium (mmol/l)	Mean age (years)
<135	$51.42 \pm 17.77$
>135	$49.31 \pm 17.89$
P-value	0.53

The subjects' mean serum sodium levels were  $130.91 \pm 4.59$  overall. Table 2 displays the age distribution and mean serum sodium levels. This table indicates that 33% of the patients were between the ages of 20 and 40, and 33% were between the ages of 60 and 60. Individuals over 60 had mean serum sodium levels ( $130.35 \pm 5.19$ ) that were lower than those in other age groups.

**Table 2: Age distribution and mean serum sodium levels**

Age (years)	Patients (%)	Mean Serum Sodium (mmol/l)
<20	4(2.7)	$134 \pm 1.82$
20-40	49(32.7)	$131.38 \pm 4.49$
40-60	49(32.7)	$131.06 \pm 4.37$
>60	48(32)	$130.35 \pm 5.19$

Out of 150 patients, 114 (76%) had low sodium levels less than 135 mmol/l. Of these, 30 (26%) were female and 84 (74%) had low sodium levels. Table 3 shows the sex distribution and mean serum sodium levels. It is evident that the mean serum sodium levels of males were lower than those of females, at  $130.84 \pm 4.57$ . But with a p value of 0.83, this was not statistically significant.

**Table 3: Sex distribution and mean serum sodium levels**

Sex	Frequency (%)	Mean Serum Sodium (mmol/l)
Male	110(73.3)	130.84±4.57
Female	40(26.7)	131.13±4.70
P-value	0.83	

Table 4 indicates that the majority of patients, or 59 patients (39.3%), had mild hyponatremia, followed by 41 patients (27.3%) with moderate hyponatremia, and 14 patients (9.3%) with severe hyponatremia. When comparing the males to the females in each of the hyponatremia groups, it was found that the majority of the individuals were male.

**Table 4: Serum sodium levels and gender wise distribution**

Serum Sodium Levels (mmol/l)	Males (%)	Females (%)	Total (%)
>135	26 (72)	10 (36)	36 (24)
130-134	43 (73)	16 (27)	59 (39.33)
125-129	30 (73)	11 (27)	41 (27.33)
<125	11 (79)	3 (21)	14 (9.33)
P-value	0.88		

50 patients (33.33%) out of 150 had diabetes, and 20 patients (13.33%) had retroviral illness. 38 (76%) of the 50 patients with diabetes and PTB had hyponatremia, suggesting that patients with diabetes have a higher prevalence of hyponatremia; however, this difference in prevalence was not statistically significant ( $p=0.88$ ). Fifteen (75%) of the twenty patients with pulmonary Kochs and HIV had hyponatremia. Moreover, this did not reach

statistical significance ( $p=0.92$ ). Seventy-two (63%) of the 114 hyponatremia patients had positive sputum AFB.

There is statistical significance in this finding ( $p<0.001$ ). Table 5 indicates that of the 59 patients with mild hyponatremia, 27 (46%) had sputum AFB positive, 34 (83%) had moderate hyponatremia, and 11 (79%) had severe hyponatremia.

**Table 5: Serum sodium levels in relation to sputum AFB status**

Serum Sodium Levels (mmol/l)	Sputum Positive (%)	Sputum Negative (%)
>135	12(33)	24(67)
130-134	27(46)	32 (54)
125-129	34(83)	7 (17)
<125	11(79)	3(21)
P-value	<0.001	

## Discussion

This study included 150 PTB patients, ranging in age from 18 to 86 years, with a mean age of  $50.92 \pm 17.76$  years. Many of these patients were in the 20–60 age range. According to a prior study, sodium's age ranged from 18 to 80 years old, with a mean age of  $44.4 \pm 13.81$  years [2]. In the range of 13–102 years, Jafari et al. reported a mean age of  $59 \pm 20$  years [18], while Khan et al. found that the mean age of all patients was  $51.57 \pm 16.3$ [7].

The results of our study indicated a preponderance of men: 40 (27%) and 110 (73%) of the 150 participants were women. This observation was consistent with research conducted by Khan et al.[7], Mukherjee et al. [69.3% males, male to female ratio 2.25:1], and Bokam et al. [72.2% male majority][2]. The Revised National Tuberculosis Programme (RNTCP) also revealed the higher male prevalence[19]. However, a study by Jafari et al. revealed that compared to females, males had lower rates of tuberculosis (45.5%)[18]. TB notification rates have been found to be similar in both sexes till puberty, followed by a continuing widening of the gap between male and female cases. In males,

the TB prevalence was found to be higher with increase in age. This difference is most marked in the age group beyond 60 years [20]. Of the 150 patients, 114 (76%) had hyponatremia, or serum sodium levels less than 135 mmol/l; of these, 26% were female and 74% were male. According to our study, 61% of patients with PTB had hyponatremia, as reported by Bokam et al.[2]. Only 9% of the patients in our study had severe hyponatremia, while the majority of patients (39%) had mild hyponatremia. Many cases of electrolyte imbalances arise during clinical practice; however, hyponatremia is the most common, with a prevalence of up to 15% in the general hospital population. Hyponatremia most commonly occurs as syndrome of inappropriate anti diuretic hormone secretion (SIADH) [6].

The average serum sodium levels across all participants in our study were  $130.91 \pm 4.59$ . Compared to other age groups, patients over 60 had mean serum sodium levels that were lower. Elderly patients are more likely to experience hyponatremia, and this is primarily due to degenerate physiology, co-morbid conditions, and

polypharmacy involvement. Due to inadequate fluid therapy and dehydration, elderly patients are particularly vulnerable to hyponatremia [21].

Males in our study had mean serum sodium levels of  $130.84 \pm 4.57$  and females had mean serum sodium levels of  $131.13 \pm 4.70$ , suggesting that males had lower sodium levels than females. Similar to our findings, Borkam et al. study also revealed that males had mean serum sodium levels that were lower ( $132.9 \pm 5.8$  mmol/L) than females ( $133.3 \pm 5.6$  mmol/L)[2]. In contrast to our research, Khan et al. found that males had mean serum sodium levels of  $136.03 \pm 6.5$  compared to females' levels of  $135.00 \pm 6.5$  [7].

In our study, the majority of patients, or 39.33%, had mild hyponatremia (serum sodium 130-134 mmol/l), followed by moderate hyponatremia (27.33%) and severe hyponatremia (serum sodium <125 mmol/l) nearly 9.33% of the patients.

Seventy-two (63%) of the 114 hyponatremia patients had AFB-positive sputum. At  $p < 0.001$ , this was statistically significant. Sputum AFB was positive in 46% of patients with mild hyponatremia, 83% of patients with moderate hyponatremia (serum sodium 125-129 mmol/l), and 79% of patients with severe hyponatremia (serum sodium <124 mmol/l). With the exception of 4 out of 14 patients who had severe hyponatremia and needed vasopressor support for hypotension, the majority of patients did not exhibit any symptoms. Studies showed that patients with chronic hyponatremia are often asymptomatic irrespective of the degree of hyponatremia. Symptoms may only occur if there is acute exacerbation of hyponatremia, or if serum sodium falls below 110 mmol/l [22]. In this study there were no patients with serum sodium values less than 118 mmol/l.

50 patients (33.33%) out of 150 had diabetes as a co-morbidity. 38 (76%) of the 50 patients with pulmonary tuberculosis and diabetes also had hyponatremia. This indicates that patients with diabetes have a higher prevalence of hyponatremia. Nevertheless, this did not reach statistical significance ( $p=0.88$ ). Studies have indicated that diabetes mellitus poses a significant risk of developing tuberculosis. Moreover, tuberculosis may exacerbate glycemic control in diabetics and cause glucose intolerance [23]. Hyponatremia is one of the numerous electrolyte abnormalities that diabetic patients commonly experience. Because glucose is an osmotically active substance, there is an increase in the movement of water out of the cells in the case of hyperglycemia, which leads to a dilution of serum sodium levels [24].

Twenty (13.33%) of the 150 patients had retroviral illness. Fifteen (75%) of the twenty patients with PTB and HIV had hyponatremia. According to a previous study, TB is the most common

opportunistic infection among those living in north Karnataka, and HIV prevalence is also high there. From the latent form of TB, nearly 12 to 20 times as many HIV-positive individuals are at risk of developing active TB [25].

### Conclusion

Because hyponatremia can have serious consequences and may indicate an underlying medical condition, it is crucial to identify it. Because early detection and treatment of an underlying electrolyte abnormality may reduce tuberculosis-related mortality and morbidity as well as shorten hospital stays, patients with PTB must be evaluated for hyponatremia.

### References

1. Global Tuberculosis Report 2018. Available from URL- [https://www.who.int/tb/publications/global\\_report/en](https://www.who.int/tb/publications/global_report/en). Last accessed 2019 on March 1.
2. Bokam BR, Badikillaya VU. Prevalence of hyponatremia in pulmonary tuberculosis - A pilot study from a tertiary care center in south India. *Int J Med Sci Public Health* 2017; 6(1):75-79.
3. Saeed BO, Beaumont D, Handley GH, Weaver JU. Severe hyponatraemia: Investigation and management in a district general hospital. *J Clin Pathol* 2002; 55(12):893-896.
4. Ellison DH, Berl T. Clinical practice. The syndrome of inappropriate antidiuresis. *Engl J Med* 2007; 356(20):2064-2072.
5. Spasovski G, Vanholder R, Allolio B, Annane D, Ball S, Bichet D, et al. Clinical practice guideline on diagnosis and treatment of hyponatremia. *Intensive Care Med* 2014; 40:320-331.
6. Huda MSB, Boyd A, Skagen K, Wile D, Van Heyningen C, Watson I, et al. Investigation and management of severe hyponatraemia in a hospital setting. *Postgrad Med J* 2006; 82(965):216-219.
7. Khan K, Rasool N, Mustafa F, Tariq R. Hyponatremia Due to Pulmonary Tuberculosis in Indian Population. *Int J Sci Study* 2017; 5(5):98-101.
8. Jacobi J, Schnellhardt S, Kulschewski A, Amann KU, Kuefner MA, Eckardt KU, et al. An unusual case of hyponatremia. *Nephrol Dial Transplant* 2010; 25(3):998-1001.
9. Kinjo T, Higuchi D, Oshiro Y, Nakamatsu Y, Fujita K, Nakamoto A, et al. Addison's disease due to Tuberculosis that required differentiation from SIADH. *J Infect Chemother* 2009; 15(4):239-242.
10. Lam KS, Sham MM, Tam SC, Ng MM, Ma HT. Hypopituitarism after tuberculous meningitis in childhood. *Ann Intern Med* 1993; 118(9):701-706.

11. Berger SA, Edberg SC, David G. Infectious disease in the sellaturcica. *Rev Infect Dis* 1986; 8(5):747–755.
12. Nagotkar L, Shanbag P, Dasarwar N. Cerebral salt wasting syndrome following neurosurgical intervention in tuberculous meningitis. *Indian Pediatr* 2008; 45(7):598–601.
13. Dass R, Nagaraj R, Murlidharan J, Singhi S. hyponatremia and hypovolemic shock with tuberculous meningitis. *Indian J Pediatr* 2003; 70(12):995–997.
14. Anderson NE, Somaratne J, Mason DF, Holland D, Thomas MG. Neurological and systemic complications of tuberculous meningitis and its treatment at Auckland City hospital, New Zealand. *J Clin Neurosci* 2010; 17(9):1114–1118.
15. Lee P, Ho KK. Hyponatremia in pulmonary TB: evidence of ectopic antidiuretic hormone production. *Chest* 2010; 137(1):207–208.
16. Vorherr H, Massry SG, Fallet R, Kaplan I, Kleeman CR. Antidiuretic principle in tuberculous lung tissue of a patient with Pulmonary Tuberculosis and hyponatremia. *Ann Intern Med* 1970; 72(3):383–387.
17. Schorn D. Inappropriate antidiuretic hormone secretion. Two cases presenting with Pulmonary Tuberculosis. *S Afr Med J* 1974; 48(27):1161–1162.
18. Jonaidi Jafari N, Izadi M, Sarrafzadeh F, Heidari A, Ranjbar R, Saburi A. Hyponatremia Due to Pulmonary Tuberculosis: Review of 200 Cases. *Nephrourol Mon* 2012; 5(1):687–691.
19. Directorate General of Health Services. Ministry of Health and Family Welfare. New Delhi, India. Revised National Tuberculosis Control Programme. Technical Guidelines for Tuberculosis Control, 2005.
20. Mukherjee A, Sarkar A, Saha I, Chowdhury R. Gender differences in notification rates, clinical forms and treatment outcome of tuberculosis patients under the RNTCP. *Lung India* 2012; 29(2):120–122.
21. Soiza R, Cumming K, Clarke J, Wood K, Myint P. Hyponatremia: Special considerations in Older Patients. *J Clin Med* 2014; 3(3):944–958.
22. Biswas M, Davies JS. Hyponatraemia in clinical practice. *Postgrad Med J* 2007; 83(980):373–378.
23. Dooley KE, Chaisson RE. Tuberculosis and diabetes mellitus: convergence of two epidemics. *Lancet Infectious Disease*. 2009;9(12):737–46.
24. Liamis G. Diabetes mellitus and electrolyte disorders. *World J Clin Cases* 2014; 2(10):488–496.
25. Banandur P, Rajaram SP, Mahagaonkar SB, Bradley J, Ramesh BM, Washington RG, et al. Heterogeneity of the HIV epidemic in the general population of Karnataka state, south India. *BMC Public Health* 2011; 11(Suppl 6):S13.