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Hyponatremia in Pulmonary Tuberculosis and the Prevalence of Adrenal Insufficiency in the Hyponatremic Patients with Pulmonary Tuberculosis

[1]Tabitha Merium Sabu,[2]Mary John, [3]Neeru Mittal
[1]Senior Resident (Department of General Medicine),[2]Professor (Department of General Medicine), [3]Associate Professor(Department of Pulmonary Medicine), Christian Medical College, Ludhiana

Abstract:
Background: *Hyponatremia is a frequently encountered electrolyte disturbance in patients with Pulmonary Tuberculosis (PTB). The pathophysiological mechanism identified for hyponatremia in Pulmonary Tuberculosis include Adrenal Insufficiency and Syndrome of Inappropriate ADH secretion (SIADH). The symptoms of adrenal insufficiency are often merged with the symptoms of tuberculosis and hence adrenal insufficiency is often overlooked in these patients. Identifying adrenal insufficiency in patients of tuberculosis is a priority as these patients may progress to adrenal crisis which can be life threatening.*
Objective: *To evaluate the prevalence of adrenal insufficiency in hyponatremic patients with pulmonary tuberculosis*
Materials and Methods: *The study was conducted in the department of Medicine and Pulmonary Medicine, Christian Medical College and Hospital, Ludhiana over a period of one year. All patients diagnosed with pulmonary tuberculosis (PTB) meeting the inclusion criteria were included in the study. An ACTH stimulation test using synthetic ACTH (Acton Prolongatum) was performed on all the patients. A diagnosis of adrenal insufficiency was made when post ACTH cortisol was less than 18 ng/dl. The hyponatremic patients were identified and the prevalence of adrenal insufficiency in them was seen.*
Results: *A total of 84 patients diagnosed with pulmonary tuberculosis formed the study group. There were 45 (53.57%) females. The mean age of the study population was 49.4± 18.84 years. The mean sodium of the study group was 133.18 ± 6.48mEq/L. Majority of the patients, i.e 52 (61.90%) had hyponatremia and profound hyponatremia with serum sodium less than 125 mEq/L was present in 7 (8.33%) of the patients. Adrenal insufficiency was present in 7 (8.33%) of the patients of pulmonary tuberculosis. Amongst the 52 patients with hyponatremia, adrenal insufficiency was present in 5 (9.61%) of them.*
Conclusion: *Hyponatremia was present in majority of the patients of pulmonary tuberculosis. Amongst the patients of hyponatremia, adrenal insufficiency was present in 9.61% of them.*
Keywords: *Hyponatremia, Pulmonary Tuberculosis, Adrenal Insufficiency*

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I. Introduction

Hyponatremia is the most common electrolyte abnormality seen in hospitalized patients. It is defined as a serum sodium concentration of less than 135 mEq/L. (1,2)The estimated prevalence of hyponatremia ranges between 15 to 30 % of the hospital inpatients. Profound hyponatremia with a serum sodium of less than 125 mEq/L is present in around 1 to 6% of the hospital admissions. (2,3)It is being increasingly reported in neurological and neurosurgical diseases, lung disorders, heart failure, tuberculosis, hypothyroidism and in patients on diuretics.(1,4) Hyponatremia is associated with higher mortality, morbidity and hospital readmissions.(5) Symptomatic hyponatremia, which is one of the medical emergencies is being treated promptly though the cause of hyponatremia is often not effectively evaluated. Evaluating the cause is salient as this often leads diagnostic clue to other medical conditions.(2) Hyponatremia along with hypoglycemia and hyperkalemia are the biochemical abnormalities associated with adrenal insufficiency.(6)The diagnosis of adrenal insufficiency in tuberculosis is delayed as the symptoms of adrenal insufficiency including fever, weight loss, fatigue, vomiting, diarrhea are often merged with the symptoms of many other diseases including tuberculosis, gastrointestinal disorders and sepsis.(7). Physicians need to keep a high index of suspicion to identify adrenal insufficiency. Identifying a patient of adrenal insufficiency is very important as this can prevent an impending adrenal crisis and thereby decreasing mortality and morbidity of the tuberculosis patients.(8)

Aim: To determine the prevalence of adrenal insufficiency in the hyponatremic patients diagnosed with pulmonary tuberculosis.

II. Materials and Method

This study was conducted in the department of General Medicine and Pulmonary Medicine at Christian Medical College and Hospital, Ludhiana over a period of one year. All patients diagnosed with pulmonary tuberculosis were included in the study after an informed consent. Patients of diagnosed primary adrenal insufficiency, patients on steroids, critically ill patients who required immediate steroid replacement and patients of HIV-Tuberculosis co infection were excluded from the study.

Adrenal insufficiency was diagnosed by short synacthen test (SST) using the synthetic ACTH called Acton Prolongatum. A fasting blood sample for basal cortisol was collected in the morning and intramuscular synthetic ACTH was given. A post ACTH blood sample was collected 60 minutes after that. All patients with post ACTH cortisol of less than18 ng/dl were diagnosed with adrenal insufficiency. Serum sodium was determined in all the patients of pulmonary tuberculosis and the hyponatremic patients were identified.The prevalence of adrenal insufficiency in the hyponatremic patients was determined. The prevalence of adrenal insufficiency in pulmonary tuberculosis patients was also seen.

Study Design: Prospective observational study.
Inclusion criteria:
1. All patients of pulmonary tuberculosis above 18 years of age

Exclusion criteria:
1. Patients of HIV-Tuberculosis co-infection
2. Patients of diagnosed primary adrenal insufficiency
3. Critically ill patients of suspected adrenal insufficiency requiring urgent steroid supplementation
4. Patients already on steroid**s**

Statistical analysis: Categorical variables were presented in number and percentage and continuous variables were presented as mean ± SD. Statiscal analysis was done using SPSS version 21.0

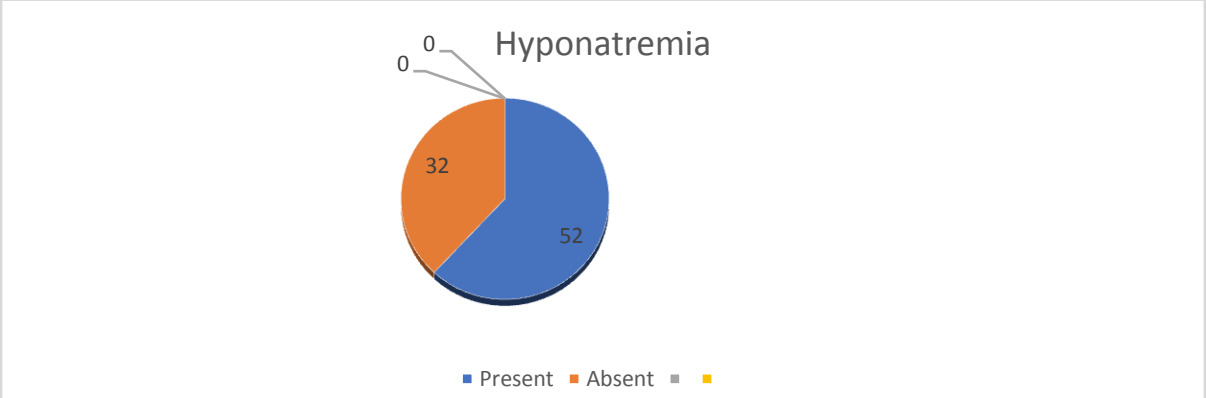
III. Results

A total of 84 patients diagnosed with pulmonary tuberculosis formed the study group. There were 45 (53.57%) females. The mean age of the study population was 49.4± 18.84 years. The mean sodium of the study group was 133.18 ±6.48mEq/L. Majority of the patients, i.e 52 (61.90%) had hyponatremia (Table 1 and Figure 1) and profound hyponatremia with serum sodium less than 125 mEq/L was present in 7 (8.33%) of the patients.

Table 1: Serum Sodium

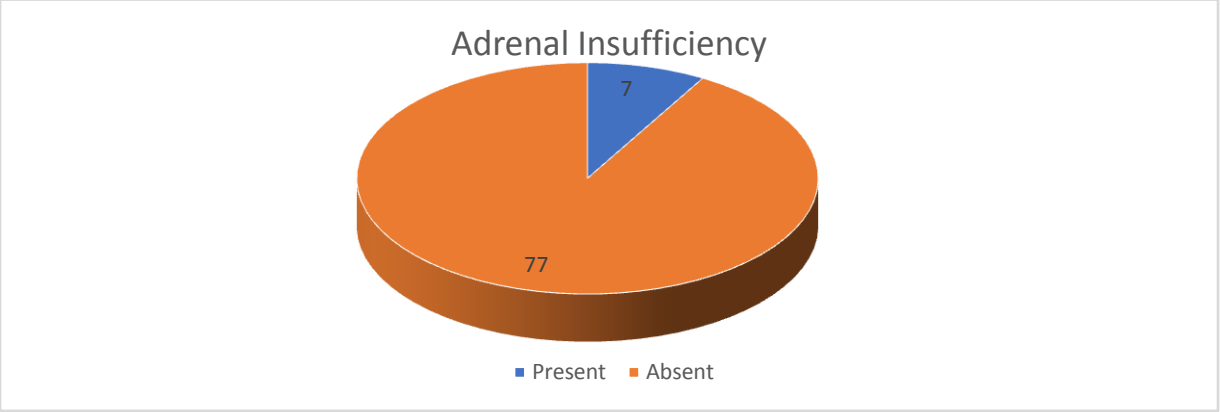
Serum Sodium (mEq/L)	Number (84)	Percentage
<125	7	8.33
125-129	14	16.67
130-134	31	36.90
135-144	30	35.71
≥145	2	2.38

Figure 1: Hyponatremia



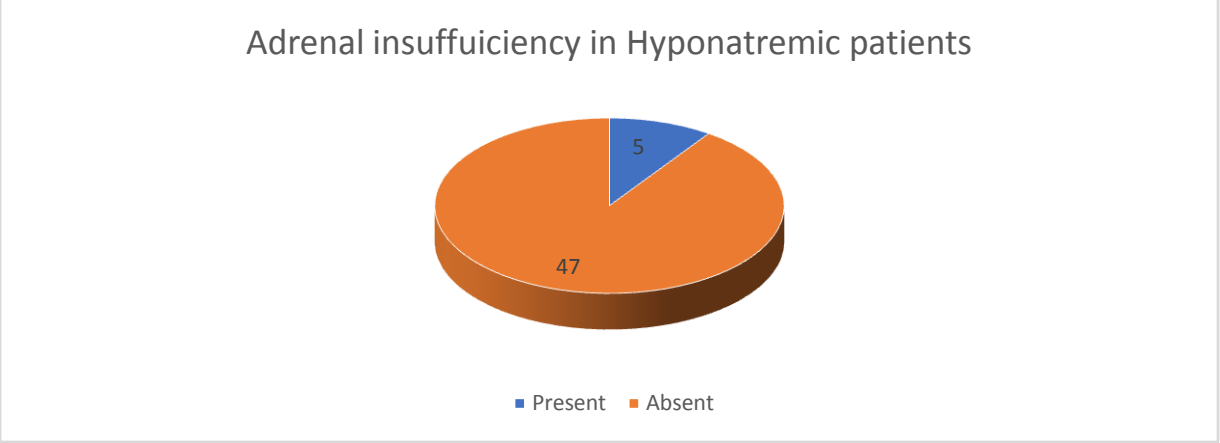
The mean basal cortisol of the study group was 14.62 ± 9.14 ng/dL. The mean post ACTH cortisol was 35.65 ± 14.52ng/dL. Adrenal insufficiency was present in 7 (8.33%) of the patients of pulmonary tuberculosis (Figure 2)

Figure 2: Adrenal Insufficiency in Pulmonary Tuberculosis patients



Amongst the 52 patients with hyponatremia, adrenal insufficiency was present in 5 (9.61%) of them (Figure 3)

Figure 3: Adrenal insufficiency in hyponatremic patients with Pulmonary Tuberculosis



The mean sodium of the patients with adrenal insufficiency was 134.29 ± 6.1 mEq/L. The mean sodium of patients with normal adrenal reserve was 133.08 ± 6.54 mEq/L

IV. Discussion:

Studies on the biochemical profile of the tuberculosis patients had found hyponatremia in pulmonary tuberculosis(9) and extra pulmonary tuberculosis.(2) A combination of pathophysiological mechanisms like Syndrome of Inappropriate ADH secretion (SIADH) and Adrenal Insufficiency are responsible for the hyponatremia in Pulmonary tuberculosis.(10) Adrenal insufficiency causes hyponatremia as a result of glucocorticoid deficiency which in turn causes increased ADH secretion as cortisol which acts as a physiological inhibitor of ADH is deficient. An ADH independent mechanism also can occur by the upregulation of the Na-K-2Cl co-transporter.(11)

Adrenal insufficiency has been documented in pulmonary, extra pulmonary and disseminated tuberculosis. This can be as a result of the direct infection and involvement of the gland (12) or can be a functional defect which can happen in any infection or chronic stress event, without anatomical involvement of the gland.(13) Any infection or stress leading to higher levels of inflammatory cytokines thus can cause decreased production of cortisol by the adrenal medulla.(13) Adrenal insufficiency of variable degrees has been documented in pulmonary and extra pulmonary tuberculosis.(12,14,15). However, adrenal insufficiency still remains as a underdiagnosed entity and there is a delay in diagnosing the same.(7) This may be even more overlooked in tuberculosis patients as the symptoms of a compromised adrenal gland overlap with the symptoms of tuberculosis.

In this study on 84 patients with pulmonary tuberculosis, hyponatremia was present in 52 (61.90%) of the patients. The mean sodium of the study group was 133.18 ± 6.48 mEq/L. This result was similar to the one obtained by the study done by Jonaidi Jafari N et al on patients of pulmonary tuberculosis where the mean sodium was 134.54 ± 4.95 mEq/L and hyponatremia was present in 51% of the patients.(10) In the study by Barnes et al in patients with active tuberculosis, hyponatremia was present in 41% of the patients.(14)

Adrenal insufficiency was present in 7 (8.33%) of the patients of pulmonary tuberculosis. This was similar to the result of the study by Barnes et al, where 6.67% of the PTB patients had adrenal insufficiency(14). The previous studies on adrenal insufficiency in tuberculosis showed a wide spectrum from a normal adrenal function to presence of adrenal insufficiency in up to 50% of the patients of adrenal insufficiency.(12)Zargar et al found that 32.14% of PTB patients had adrenal insufficiency.(15) However, Gulmez et al in his study on pulmonary tuberculosis patients in Turkey found normal adrenal function in the patients of pulmonary tuberculosis. (16)

The study by Barnes et al did not show any significant difference in the serum sodium of the patients with adrenal insufficiency and normal adrenal reserve group. (14)This was similar to our finding were the mean sodium of adrenal insufficiency group was 134.29 ± 6.1mEq/L and of patients with normal adrenal reserve was 133.08 ± 6.54mEq/L. In our study, amongst the 52 patients with hyponatremia, adrenal insufficiency was present in 5 (9.61%) of them.

The other causes of hyponatremia was not evaluated in the study, but we kept a high possibility that it can be due to reasons other than a compromised adrenal function.

V. Conclusion

In this study we concluded that hyponatremia is found in majority of the patients of pulmonary tuberculosis and adrenal insufficiency was present in 9.61% of the patients of hyponatremia. Prompt identification and treatment initiation is needed in these patients to prevent an impending adrenal crisis.

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