Analysis of Serum Electrolytes Profile of Tuberculosis Patients in a Teaching Hospital

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Abstract:
Background: Tuberculosis is a contagious chronic disease caused by mycobacterium tuberculosis troubling millions of people worldwide. Although primarily known impact on respiratory system, tuberculosis can lead to systemic effects including serum electrolytes imbalances.

Objectives: Objective is to analyze serum electrolytes profile of tuberculosis patients.

Methods: The study is conducted on 169 patients of PTB in the department of pulmonology, Khyber teaching hospital, Peshawar from January 2011 to June 2017. The patients were going through anti-tubercular therapy. Demographics and laboratory tests were collected from the patient’s hospital profile and analysis was done through PSPP.Ink.

Results: The mean age was 46.29±19.91 years and 51.5% of the patients were female. The mean serum sodium and potassium concentrations were 133.31±7.93 mmol/L and 3.93±0.87 mmol/L respectively. Hyponatremia and hypokalemia prevalence were 56.2% and 28.4% respectively. There was no significant correlation between variables with no significant value of p.

Conclusion: There is decrease in the level of serum sodium and potassium concentrations in tuberculosis patients.

Keywords: Hyponatremia, Hypokalemia, Tuberculosis, Electrolyte analysis.

Introduction
Electrolytes are fundamental for the basic life functions. Essential electrolytes comprise of Na⁺, K⁺, Cl⁻, Ca²⁺, Mg²⁺ and others. Food and fluids we take are the sources of electrolytes. The electrolytes imbalance disturbs normal physiologies and can progress to serious life complexities. Sodium a basic ion is present in ECF (extracellular fluid), maintains ECF volume and also regulates cellular membrane potential. Sodium and potassium are exchanged across the cell membranes by active transport through ATPase pump. Kidneys are the site of Na⁺ regulation and in proximal tubule of nephron the major part of Na⁺ is reabsorbed. Sodium transport across is controlled by aldosterone and it occurs through sodium-chloride symporters. Hyponatremia is the most frequent and common electrolyte disorder among the imbalances. Serum Na⁺ level below 135 mmol/L is considered hyponatremia and manifestations associated with hyponatremia include nausea, confusion, disorientation, headaches and delirium. Serum Na⁺ level above 145 mmol/L is considered hypernatremia and manifestations include unrest, tachypnea and sleeplessness. Rapidly correcting Na⁺ imbalance could present with severe consequences like ODS (osmotic demyelination syndrome) and cerebral edema. Malnutrition and long-lasting alcohol abuse are some other variables that can contribute to ODS development. Hyponatremia is regarded a common electrolyte irregularity and in seriously ill hospitalized patient hyponatremia must be taken into consideration.
The frequency of mild hyponatremia is estimated as 15-30% and its severe form as 1-4% in hospitalized patients.

Hyponatremia generally occurs as a result of secondary water retention to mismatch of absorption of oral or intravenous water with water excretion. Noticeable depletion of circulating volume cause release of antidiuretic hormone (ADH) non-osmotically and the SIADH (syndrome of inappropriate ADH secretion) are the two disturbances in which antidiuretic hormone release is not subdued in spite of decrease in osmolality of plasma. Hyponatremia has two familiar causes. SIADH diagnosis is constituted by excluding other etiology of hyponatremia. SIADH is reported in many clinical scenarios like CNS disorders (stroke, trauma and demyelinating or inflammatory diseases), malignancies (mediastinal, extrathoracic and pulmonary tumors), pulmonary diseases (infections, positive-pressure ventilation and acute respiratory failure), drugs (phenothiazines, prostataglandin-synthesis inhibitors, desmopressin, tricyclic antidepressants and serotonin-reauptake inhibitors). Tuberculosis can induce hyponatremia by means of a number of mechanisms containing its local invasion to the adrenal glands, local invasion to pituitary gland or hypothalamus. Tuberculous meningitis and via pulmonary infection to secrete inappropriate antidiuretic hormone. K+ ion is present primarily inside the cell. ATPase pump is mainly accountable for homeostasis regulation between Na+ and K+ ions, which pumps in potassium to cell in exchange of sodium, which moves out. K+ filtration occurs at glomerulus and reabsorption of K+ takes place at PCT (proximal convoluted tubule) and LOH (loop of Henle). At distal convoluted tubule of nephron secretion of Potassium takes place and is increased by aldosterone hormone. Potassium is also secreted by potassium-chloride cotransporters and potassium channels present at the apical tubular membrane. Serum K+ level below 3.5 mmol/L is considered hypokalemia. Fatigue, muscle twitching and weakness are few features of hypokalemia. Hypokalemic paralysis is systemic fatigue of body that could be sporadic or hereditary either. Serum potassium concentration greater than 5.2 mmol/L is considered hyperkalemia. Muscle weakness, muscle cramps, arrhythmias, myoglobinuria and rhabdomyolysis are the clinical features of hyperkalemia. Potassium imbalances may be caused by kidneys to excrete potassium, the failure of mechanisms to move it from the circulation into the cells or combination of both factors.

A rare entity called severe hypokalemia is a known sign of miliary or disseminated TB and its relation is understood poorly. Potassium imbalance may occur during tuberculosis and antitubercular drugs usage. Certain antitubercular drugs, specifically some second-line drugs that are used in the treatment of drug-resistant TB, can have negative effects on electrolyte balance and kidneys. CI- is present in ECF and its serum levels are regulated predominantly by the kidneys. Cl- filtered by glomerulus of nephrons, is mostly reabsorbed by both PCT (proximal convoluted tubule) and DCT (distal convoluted tubule) by active and passive transport. PCT has major part in the reabsorption of Cl-. Low chloride levels in the blood by the level of 96 mmol/L is known as hypochloremia and hyperchloremia refers to high chloride levels in the blood above the level of 106 mmol/L. Chloride imbalance often occurs in association with other electrolytes. Patients with chronic or subacute tuberculosis may present with nocturnal sweating, pyrexia, shivering, and dysfunction of one or more organs. Tuberculosis could be linked with Electrolytes disturbances.

Aim of study was to find the frequency of electrolyte imbalances in tuberculosis patients.

**Methodology**

**Study design and Participants**

Patients with the diagnosis of tuberculosis who were admitted to ward of pulmonology, Khyber teaching hospital, Peshawar Pakistan from January 2011 to June 2014 were evaluated prospectively. Demographic and characteristic laboratory tests were recorded from the hospital records of patients’ charts. The patients who’s demographic and laboratory characteristics tests were not present were excluded from the studies. All the remaining 169 patients were added in the research.

**Statistics**

Data was assembled to analyze the laboratory characteristics tests of tuberculosis patients who present with electrolyte imbalance or not. The data was compared and analyzed by the use of PSPP software. The significant consideration for P value was less than 0.05. Data was analyzed and written with the help of mean, percentage and standard deviation. Tests were performed to check the distribution of quantitative data. The variables were mostly abnormally distributed and Kruskal–Wallis, spearman correlation and Mann–Whitney U tests were performed.

**Results**

The mean age was 46.29±19.91 and 51.5% of the patients were female. The mean serum Na+ concentration was 133.31±7.93 mmol/L. The mean serum potassium and chloride concentrations were 3.93±0.87 mmol/L and 100.40±8.51 mmol/L respectively. Analyzing the sodium level 56.2% of patients showed hyponatremia, 41.4% were normal and 2.4% showed hypernatremia.
Analyzing the potassium level, 28.4% of patients showed hypokalemia, 66.9% were normal and 4.7% showed hyperkalemia. Analyzing the chloride level, 24.9% of patients showed hypochloremia, 55% were normal and 20.1% showed hyperchloremia. There was no significant correlation between variables with no significant value of p.

Table 1: Frequency of electrolytes level in different age groups

<table>
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<th>Age</th>
<th>Sodium level</th>
<th>Chloride level</th>
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<td>3</td>
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<tr>
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<td>9</td>
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</tr>
<tr>
<td>Total</td>
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<td>4</td>
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</table>

Table 2: Frequency of electrolytes level in different gender

<table>
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</tr>
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</table>

Discussion:
According to the findings of our study, the frequency of hyponatremia, hypokalemia and hypochloremia come out as 56.2%, 28.4% and 24.9% respectively. Additionally, prevalence of hypernatremia, hyperkalemia and hyperchloremia obtained as 2.4%, 4.7% and 21.1% respectively. 24.9% hypochloremia and 21.1% hyperchloremia prevalence cannot be ignored in our studies as no considerable amount of data available related to chloride abnormalities in tuberculosis patients. The variables age and gender were seen having no relation with the electrolyte imbalances in tuberculosis patients. There was no significant relation between one electrolyte imbalance with another.

In previous studies of hyponatremia prevalence among admitted patients, particularly the inpatients of respiratory wards, was documented in a range of (2.48%-40%)\(^{21}\). Hyponatremia prevalence of 51% was reported by Jonaidi Jafari N during his hyponatremia prevalence studies in tuberculosis patients\(^{6}\). Moreover, hyponatremia should be noticed in cerebral, endocrine, pulmonary and neoplastic pathologies. Frequency of severe hyponatremia evaluated as 1.1% in inpatients and in that study, tuberculosis was the most common (24%) underlying condition\(^{22}\). In our study frequency of severe hyponatremia was reported as 7.7% (<120mmol/L).
In 1969, Chung has documented, that approximately in
11% patients, hyponatremia was noted having active
Tuberculosis, and the primary evident cause was SI-
ADH23. A case of Primary tuberculosis reported by
Vorherr et al. having hyponatremia and antidiuretic
agents were found in infected lung tissues30. SIADH
has been suggested by Bryant et al. in patients having
pulmonary infections like Primary tuberculosis34. Two
cases of Primary tuberculosis reported by Schorn et al.
and found an abnormal inappropriate ADH level as a
rational mechanism of action25. A 74-year-old woman
reported by Cockcroft et al. having miliary tubercu-
losis and severe hyponatremia due to syndrome of
inappropriate ADH secretion (SIADH)10. Usalan et al.
documented a tuberculosis case and lethargy was re-
vealed due to hyponatremia evidently from SIADH27.
Lastly, Lee documented a case of primarily tuberculo-
sis having refractory hyponatremia due to syndrome of
inappropriate ADH secretion (SIADH)15.
SIADH has been noted in infectious disorders like tu-
berculosis. Weiss et al., in one of the first reports, doc-
umented hyponatremia in patients with primary tuber-
culosis as a result of SIADH15. It was then acknowl-
edged that hyponatremia along with increase in level
of antidiuretic hormone in tuberculosis is a strong in-
cicator for ectopic antidiuretic hormone production.
Couple of studies illustrated that antidiuretic hormone
level was unnoticeable following complete antituber-
cular therapy. Reports of SIADH linked with pulmo-
nary, CNS-related and miliary tuberculosis are noted.
At first presentation more than 60% patients may dis-
play with SIADH or hyponatremia in tubercular menin-
gitis. A number of infectious diseases are related with
SIADH19.
Nakashita et al. documented a SIADH case induced in a
patient of tuberculosis by ethionamide use and pro-
posed that drugs of TB to be taken into consideration
as likely reason of SIADH but study conclusion showed
that incidence of hyponatremia in those patients who
have taken maximum doses of ethionamide was no
higher than who taken lesser doses10.
The other mechanism, as involvement of endocrine
system by tuberculosis can prompt hyponatremia and
is important to be taken into account in patients with
primary tuberculosis. Tuberculosis was shown to in-
volve the suprarenal glands (adrenal glands) directly
and this association led to subclinical or overt hypo-
natremia and adrenal insufficiency. Tuberculosis bacilli
may also involve the pituitary gland as in childhood
years after tubercular meningitis treatment in 20% of
the cases hypopituitarism has been reported. The ap-
peared reason was tubercular lesions impressing the
pituitary stalk, hypophysis cerebri (hypothalamus),
and directly or indirectly, itself the hypophysis
(pituitary gland)31.

Hyponatremia induced by primary tuberculosis is usu-
ally mild to moderate, self-limited and asymptomatic.
Most of SIADH cases are reversible with effective pri-
mary tuberculosis therapy. Without enough attention
by physician SIADH could be overlooked. Conversely
TB patients of hyponatremia were more likely at risk
of increased mortality.
Moreover, occurrence of hyponatremia in AIDS pa-
tients with tuberculosis is higher. Smith et al. showed
that hyponatremia was found in 60% patients of AIDS
diagnosed with generalized tuberculosis, however half
of these patients of disseminated tuberculosis after
death were only diagnosed. The positive HIV patients
were overruled in our study, and can be the logic of
the variations between others and our findings6.

Hypokalemia was noted among the patients of tuber-
culosis in our study of electrolyte imbalances and no
enough research was found on hypokalemia during
tuberculosis. 31.3% hyponatremia was noted by Sonya
Shin MD during her research on tuberculosis patients
taking treatment for MDR-TB (multi-drug resistant
tuberculosis)32. MDR-TB patients medicated with in-
jectable agents or tablets and the commonly negative
reaction found is hypokalemia. Amikacin, rifampicin,
and viomycin-pyrazinamide are considered to be
linked with electrolytes imbalance, comprising
hypokalemia33.

Baskaran et al.,10 documented that Hypomagnesemia
contributing to hypokalemia and hypocalcemia, taking
place in patients with PTB as a major abnormality and
getting worse by streptomycin use24. Capreomycin
and Amikacin are aminoglycoside antibiotics35. It has
been documented that the use of amikacin and capre-
omy cin results in increase renal wasting of electrolyte
including magnesium, potassium and calcium35. Elec-
trolyte imbalances especially hypokalemia is linked
with several notable morbidities such as seizures, tet-
any, and cardiac arrhythmia35. Because of this, potassi-
um level in serum is one of the most notable parame-
ters regarding the safety of patients33.

Conclusion:
Study is conducted on tuberculosis patients admitted
to a teaching hospital and deals with serum electro-
ytes profile analysis. Study shows prevalence of hypo-
natremia (56.2%) and hypokalemia (28.4%) in tuber-
culosis patients receiving antitubercular therapy.

Ethical approval and consent
The study was approved by the institutional board of studies and informed consent was obtained from each participant included in the study.

Acknowledgment
The Authors admire all the participants.

Disclosure
The authors report no conflicts of interest.

Author’s contributions
RU was involved in the execution of the project. NM designed, executed the study. FU helped in organization of data. FJ supervised the study and wrote the manuscript. All named authors have read and approved the final version of the manuscript.

Data availability
Available from the corresponding author on reasonable request.

References