

## Comparative study of serum electrolytes & urea level in patient infected with pulmonary tuberculosis & HIV with respect to ATT

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### Abstract

**Objective:** To study the effect of Tuberculosis and Anti tubercular drugs on Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>, HCO<sub>3</sub><sup>-</sup> electrolytes, and urea level with respect to ATT. **Methods:** Patients were classified in to 4 groups, normal patients, new positive cases of M. tuberculosis patients without HIV, new positive cases of tuberculosis co-infected with HIV, positive cases of M. tuberculosis patients on anti tuberculous drugs, over a period of one year. Comparative study of serum electrolytes & urea levels was done in patient infected with pulmonary tuberculosis & HIV with respect to ATT. **Results:** In our study Pulmonary TB was more common in males and in the 2nd and 4th decade of life. In this study groups we observe that 72.7% patients were male. In our study, most of the cases were non-smokers. study suggests that the sodium value was significantly lower in new case TB patients. The mean sodium levels were significantly lower when TB patients on drugs compared to new case TB patients (P < 0.05). There was a significant decrease in potassium value of new case of TB patients when compared with control. There was a significantly lower mean value of chloride in new case of TB patients when compared with control (P < 0.05). There was no significant difference between new case TB patients and control in means of Serum Urea level (P > 0.05). **Conclusion:** Electrolyte and acid-base balance monitoring in patients with tuberculosis is recommended routinely. Serum sodium and Chloride further decreased in patients on Anti tubercular drugs. In Tuberculosis (TB) co-infected with HIV patients common electrolyte disturbances were decreased in serum sodium level and increase in potassium level. Close monitoring and aggressive management are mandatory in TB patients especially HIV co-infected patients as high incidence of electrolyte disturbances are common.

**Keywords:** Acid-Base Balance, Tuberculosis, Anti Tubercular Drugs, Electrolyte Disturbances, Aggressive Management.

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### Introduction

In spite of newer modalities for diagnosis and treatment of TB, unfortunately, millions of people are still suffering and dying from this disease. Electrolyte disturbances have been reported in tuberculosis (TB) infection. Tuberculosis is most common cause of death world over due to single infectious agent in adult and account for over a quarter of all avoidable death globally. India accounts for nearly one third of global burden of tuberculosis. Every year approximately 2.2 million persons developed tuberculosis of which about 1 million are new smear positive highly infectious cases and about 5 lac people die of tuberculosis every year [1,2].

In 2014, 9.6 million new cases of TB were reported to WHO, fewer than two thirds (63%) of the 9.6 million people estimated to have fallen sick with the disease. This means that worldwide, 37% of new cases went undiagnosed or were not reported. The quality of care for people in the latter category is unknown [3].

Of the 480 000 cases of multidrug-resistant TB (MDR-TB) estimated to have occurred in 2014, only about a quarter of these 123 000 were detected and reported. India and China had the largest number of cases (23% and 10% of the global total, respectively) [2]. Though India is the second-most populous country in the world one fourth of the global incident TB cases occurs in India annually. In 2012, out of the estimated global annual incidence of 9.6 million TB cases, 2.2 million cases were estimated to have occurred in India [3-5].

Factors contributing to the resurgence of tuberculosis in developing countries include co-infection with HIV; emergence of multiple resistant tuberculosis, inadequate treatment, poverty, malnutrition, overcrowding, armed conflict and increasing numbers of displaced persons. Diarrhoea, vomiting, and excessive sweating, are common features of HIV/AIDS and tuberculosis infections and have been described as possible cause of loss of water and electrolyte.

In view of this associated water, electrolyte and urea derangement and associated cytochemical changes in Tuberculosis, this study was designed to determine the effect of treatment on common electrolytes and urea status in patients with tuberculosis. Comparing electrolytes and urea values in controls with pulmonary tuberculosis patients not on treatment, comparing electrolytes and urea values in controls with pulmonary tuberculosis patients on treatment, and electrolytes and urea in pulmonary tuberculosis patient on treatment with those not on treatments could all contribute to the body of knowledge on electrolyte disturbances and urea levels associated with these diseases [6,7].

### Materials and methods

#### Source of data

This present study was conducted in the department of Respiratory Medicine, New Medical College and Hospital, Kota on the patients who were classified in to 4 groups, normal patients, new positive cases of M. tuberculosis patients without HIV, new positive cases of tuberculosis co-infected with HIV, positive cases of M. tuberculosis patients on anti tuberculous drugs, over a period of one year [2015 to 2016]

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**Study design**

Descriptive cross sectional study among 110 cases with various categories of TB and controls

**Study population**

Include 4 categories of patients

- Group 1: 50 normal patients without TB .
- Group 2: 20 new positive cases of M. tuberculosis patients without HIV.
- Group 3: 20 new positive cases of tuberculosis co-infected with HIV.
- Group 4: 20 positive cases of M. tuberculosis patients on anti tuberculous drugs for last 2 months.

**Ethical approval**

The study received approval of the ethics review committee of New Medical College and Hospital, Kota (Date:25/7/2016, Letter No:F.3()/Acad./Ethical comm./MCK/2016/421). Written informed consent was obtained from each subject after the study has been explained to them.

**Criteria of exclusion**

- Patients with symptoms of acute febrile illness like malaria fever, typhoid and dengue.
- Diabetes Mellitus,
- Severe malnutrition,
- Patients with intestinal infection which could lead to dysentery,
- Women using contraceptives,
- Patients on corticosteroid therapy,
- Pregnant women
- Patients with CLD and CKD

**Observation chart****Table 1: Age distribution of cases and controls**

S.N.	Age group	new cases of TB	TB & HIV	TB on drugs	control
1.	≤20	1	2	1	0
2.	21-30	5	4	7	1
3.	31-40	7	7	10	17
4	41-50	4	5	2	16
5.	>50	3	2	0	16
Total		20	20	20	50

Mean age of study groups and control in years

- New cases of TB : 37.60 ± 11.637
- TB & HIV : 37.30 ± 11.531
- TB on drugs : 36.35 ± 12.106
- Control : 41.20 ± 9.928

In our study we found a male predominance, majority of patients 72.7% were males.

**Table 2: Comparing parameters in control patients with cases (new tb cases, tb cases co-infection with hiv, tb cases on drug).**

Parameter	Controls n = 50 M ± SD	New TB cases n = 20 M ± SD	t- Value	P- Value	TB&HIV n = 20 M ± SD	t- Value	P- Value	TB on drugs n = 20 M ± SD	t- Value	P- Value
age	41.66±9.8 2	37.6±11.6 37	1.481	0.143	37.30±11. 53	1.596	0.115	36.35±12.10	1.91	0.06
Height(cm)	167.3±7.5	165.7±9.1 5	.756	0.452	166.15±8. 99	.547	0.586	166.25±8.77	.506	.616
Weight(kg)	54.66±7.1 7	43.7±5.42	6.186	0.000	40.3±4.32	8.347	0.000	43.2±6.049	6.298	0.000
BMI	19.55±2.4 3	15.97±2.2	5.703	0.000	14.64±1.5 5	8.342	0.000	15.638±1.95 2	6.398	0.000

In Table, the mean age and mean height for all the patients was not significantly different from those of the control patients. There was a significant decrease in weight (in kilograms) when TB-co-infection with HIV patients was compared with new cases of Tuberculosis (40.3 ± 4.32 vs 43.7±5.42; P < 0.05). There was no significant difference in the weight when new cases of tuberculosis were compared with TB patients on

drugs ( $P > 0.05$ ). BMI was significantly higher in controls when compared with new TB cases, TB co-infection with HIV patients and TB on drugs ( $19.55 \pm 2.43$  vs  $15.97 \pm 2.2$ ,  $14.64 \pm 1.55$  and  $15.638 \pm 1.952$ )  $\text{kg/m}^2$ .

**Table 3: Symptoms at presentation**

Symptoms	New cases of TB	TB & HIV	TB on drugs
Fever	20	10	2
Dyspnoea	5	2	5
Cough	20	18	8
Chest pain	2	4	1
Night sweats	1	5	2

All of the new cases of TB patients had fever and cough. Most of the TB & HIV patient have also presented with cough.

**Table 4: Duration of smoking (in pack years)**

Duration of smoking (in pack years)	New sputum positive	HIV & TB	TB on treatment	Control
$\leq 5$	17	19	19	44
5 – 10	2	0	1	6
$> 10$	1	1	0	0

**Table 5: Radiological findings**

	consolidation	Cavity	fibrosis	others
Control	0	0	0	0
New cases	14	9	0	3
TB&HIV	11	0	0	8
TB on drugs	11	6	1	7
Total	36	15	1	18

**Table 6: Mean (x)  $\pm$  SD of the biochemical parameters in different subject groups**

Group	Na+ (mmol/L)	K+ (mmol/L)	Cl- (mmol/L)	HCO <sub>3</sub> - (mmol/L)	Urea (mg/dL)
Control	$139.16 \pm 2.73$	$3.86 \pm 0.29$	$102.90 \pm 3.15$	$22.86 \pm 1.78$	$32.36 \pm 5$
New cases	$134.95 \pm 3.486$	$3.69 \pm 0.28$	$98.10 \pm 3.597$	$22.8 \pm 1.79$	$32.45 \pm 6.91$
TB&HIV	$132.55 \pm 3.95$	$4.18 \pm 0.47$	$96.15 \pm 3.646$	$24.30 \pm 2.08$	$35.10 \pm 2.22$
TB on drugs	$132.70 \pm 3.585$	$4.07 \pm 0.20$	$96.70 \pm 4.725$	$24.3 \pm 2.05$	$32.45 \pm 4.59$

**Table 7: Comparing biochemical parameters in control patients with cases (new TB cases, TB cases on drug, TB cases co-infection with HIV).**

Parameter	Control n = 50 M $\pm$ S D	New TB cases n = 20 M $\pm$ SD	t- Value	P- Value	TB&HIV n = 20 M $\pm$ SD	t- Value	P- Value	TB on drugs n = 20 M $\pm$ SD	t- Value	P- Value
Na+	$139.16 \pm 2.73$	$134.95 \pm 3.486$	5.222	0.000	$132.55 \pm 3.95$	7.832	.000	$132.70 \pm 3.585$	7.968	0.000
K+	$3.86 \pm 0.29$	$3.69 \pm 0.28$	2.2	.031	$4.18 \pm 0.47$	3.38	.001	$4.07 \pm 0.20$	2.801	.007
Cl-	$102.90 \pm 3.15$	$98.10 \pm 3.597$	2.044	.045	$96.15 \pm 3.646$	7.739	0.00	$96.70 \pm 4.725$	0.414	0.680
HCO <sub>3</sub> -	$22.86 \pm 1.78$	$22.8 \pm 1.79$	0.127	.06	$24.30 \pm 2.08$	2.908	.005	$24.3 \pm 2.05$	2.92	0.005
S. urea	$32.36 \pm 5$	$30.45 \pm 4.95$	0.061	0.952	$35.1 \pm 2.22$	2.34	.022	$32.4 \pm 4.59$	0.069	0.945

In Table, the sodium value was significantly lower in all three study

### Results

- In our study Pulmonary TB was more common in males and in the 2nd and 4th decade of life. In this study groups we observe that 72.7% patients were male and only 27.2% patients were female.
- In our study, most of the study cases were non-smokers. In our study groups we observe that 68.3% patients were non-smokers and only 31.6% patients were smokers.
- This study suggests that the sodium value was significantly lower in new case TB patients. The mean sodium levels were significantly lower when TB patients on drugs compared to new case TB patients ( $132.70 \pm 3.585$  vs  $134.95 \pm 3.486$ ;  $P < 0.05$ ).
- There was a significant decrease in potassium value of new case of TB patients when compared with control ( $3.69 \pm 0.28$  vs  $3.86 \pm 0.29$   $\text{mmol/L}$ ;  $P < 0.05$ ).

- There was a significantly lower mean value of chloride in new case of TB patients when compared with control ( $98.10 \pm 3.597$  vs  $102.90 \pm 3.15$   $\text{mmol/L}$ ;  $P < 0.05$ ).
- There was no significant difference between new case TB patients and control in means of Serum Urea level ( $30.45 \pm 4.95$  vs  $32.36 \pm 5$   $\text{mmol/L}$ ;  $P > 0.05$ ).

### Statistical analysis

Data was compiled using MS excel 2007 and analysis was done with the help of Epi-Info 7 software. Frequency and percentage were calculated & statistical test (Chi Square) was applied wherever applicable;  $p < 0.05$  was taken as statistically significant.

### Discussion

This is a descriptive cross sectional study done in the Department of Respiratory Medicine, New Medical College Hospital, Kota during period Aug. 2015 to July 2016. Patients are classified in to 4 groups, normal patients, new positive cases of M. tuberculosis patients

without HIV, new positive cases of tuberculosis co-infected with HIV, positive cases of *M. tuberculosis* patients on anti tubercular drugs. The aim of the study was to study the imbalance of Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>, HCO<sub>3</sub><sup>-</sup> electrolytes, and urea level among patients in different study groups.

In a study similar to ours, Folaranmi OM et al did comparative study of plasma electrolytes (Na, K, Cl, and HCO<sub>3</sub>) and urea levels in HIV/AIDS and pulmonary tuberculosis infected subjects. John Kennedy N et al did a comparative study of serum electrolyte and urea in type ii diabetes and mycobacterium tuberculosis patients in Owerri Nigeria and their results were similar to ours[8,9].

### Serum Sodium

In our study the sodium value was significantly lower in new case TB patients, TB co-infection with HIV patients and TB patients on drugs when compared with controls (134.95± 3.486, 132.55±3.95, 132.70±3.585 vs 139.16 ±2.73) mmol/L. The mean sodium value was significantly decreased when patient started anti tubercular drugs when compared to new case TB patients (132.70±3.585 vs 134.95±3.486; P < 0.05). There was a significant difference in sodium level between new case TB patients and patient co infected with HIV. Junaidi et al. found that serum sodium was higher than expected in non-tubercular patients. The prevalence of hyponatremia and

hypocalcaemia obtained as 51% and 29%. Chung and hubbard have noted that nearly 11% of patients with active TB (pulmonary or non-pulmonary) are affected with hyponatremia, and it is apparent that the main cause of serum sodium depletion in these patients is SIADH. Bryant et al. has suggested the syndrome of inappropriate secretion of antidiuretic hormone for patients with an infectious pulmonary disease such as PTB. Olalekan AW et al. reported that the mean sodium level in HIV co-infected with TB was significantly low when compared with new cases of pulmonary Tuberculosis (140.55±8.07 Vs 142.10±6.68 meq/l). A study by Folaranmi OM et al. shows that mean sodium level in Tuberculosis patients is significantly high compared with HIV patients (147.0±6.8 Vs 125.8±5.8 meq/l). The lower significant plasma level of sodium found in TB co infections with HIV patients than the new cases pulmonary tuberculosis patients is consistent with the finding of U. Siddiqui et al. This can be attributed to the loss of Na<sup>+</sup> through diarrhoea presented by most of AIDS infected patients. AJ Cusano et al. also said that Defective renal sodium conservation due to HIV infection of the kidney itself can cause hyponatremia. At the same time, decreased Na<sup>+</sup> observed in patients on drug than new cases pulmonary TB patients could be due to the fact that in patients on drug experience vomiting. This is one of the major adverse reactions of some anti TB drugs especially Pyrazinamide[8-12].

### Serum Potassium

**Table 8: Comparison of K<sup>+</sup> in present study with other studies in different study groups.**

Groups	O.M. Folaranmi et al	A.W. Olalekan, F.A et al	S.N.Bhagyamma et al	Present study
Control	4.3 ± 0.7	3.17 ± 0.31	3.79±0.27	3.86±0.29
New TB cases	2.53 ± 0.52	3.07 ± 0.42	3.39±0.20	3.69±0.28
TB with HIV	4.9 ± 0.82	3.66 ± 0.42	4.10±0.49	4.18±0.47
TB on drugs	-	3.75 ± 0.15	-	4.07±0.20

It was found that the mean K<sup>+</sup> level in patients with TB co infections with HIV patients was significantly higher than those of the new cases pulmonary tuberculosis patients and the control patients. The above observation can be attributed to the facts that in HIV/AIDS infection, there is the killing of cells by virus, high grade pyrexia/fever (causing the destruction of cells) and therefore leading to the influx of K<sup>+</sup> from the cells to the plasma. Folaranmi OM et al 2004 also showed similar results in his study. He found that the mean value of potassium in HIV co-infected with TB and new cases of TB patients (4.9±0.82 Vs 2.53±0.52 meq/l). M.F. Kalin et al found that the major causes for increased potassium levels HIV/AIDS infection include adrenal insufficiency and hyporeninemic hypoaldosteronism. M.J. Choi et al found that administration of trimethoprim or pentamidine is also a reason for increased potassium levels in HIV/AIDS infection. The mean K<sup>+</sup> value of patients on drug was significantly higher compared to the new TB cases and control; this may be due to Rifampicin (less often than twice weekly) which cause flu like syndrome characterized by fever and anaemia leading to hyperkalemia. In this study, the level of K<sup>+</sup> was significantly lower in pulmonary tuberculosis patients when compared to the normal patients. This agreed with another study. In the stress situation due to severe/chronic illness there is increased catabolism of protein leading to the movement of K<sup>+</sup> from the intercellular compartment to the plasma and consequently excreted in the urine, sweat and vomitus without any compensatory replacement through food due to anorexia a common feature of pulmonary tuberculosis[8-12].

There was a significantly lower mean value of chloride in new case of TB patients when compared with control (101.20±3.12 vs 102.90±3.15 mmol/L; P < 0.05). There was no significant mean value of chloride in control when compared with TB patients on drugs (102.90±3.15 vs 102.55±3.30 mmol/L; P < 0.05). However, the mean value of chloride was significantly higher in new case TB patients when compared with TB co-infection with HIV (101.20±3.12 vs 96.15±3.646 mmol/L; P < 0.05). The mean value of chloride gave the same pattern as the level of Na<sup>+</sup> in the patients because Na<sup>+</sup> is always (in most cases) in association with Cl<sup>-</sup>, therefore the same reason for the level of Na<sup>+</sup> in the patients also holds for this[8-12].

The significantly lower bicarbonate level in the pulmonary tuberculosis patients than the HIV/AIDS and the normal subjects can be attributed to the body's compensatory mechanism to maintain electrochemical neutrality due to the plasma levels of Na<sup>+</sup> and especially chloride. The mean value of S.urea level was significantly higher in TB co-infection with HIV patients when compared with control (35.1±2.22 vs 32.4±4.59 mmol/L; P < 0.05). Mayne PD said that the significantly lower level of urea found in pulmonary tuberculosis patients than the HIV/AIDS co infection can be attributed to excessive loss of fluid through diarrhoea manifested by 21 (70%) of the HIV/AIDS patients[13,14].

Kaur J et al did an observational study on evaluation of serum electrolyte status among newly diagnosed cases of pulmonary tuberculosis. The present observational cross-sectional study was conducted on a sample of 60 newly diagnosed cases of pulmonary tuberculosis. This study focused on serum sodium, potassium and calcium levels in the patients under study and was the main outcome of this study. Hyponatremia was observed in 30 (50%) cases, hypokalemia was observed in 27 (45%) and hypocalcemia constituted 21 (35%) among the patients diagnosed with pulmonary tuberculosis. It was concluded that screening for serum electrolytes in pulmonary tuberculosis is essential. Early diagnosis and prompt management of these abnormalities are critical. Correction of these electrolyte imbalance could improve outcome of patient.[15,16] Vijayaraj R et al in a similar study did Comparative study of Clinico-Bacterio-Radiological Profile and Treatment Outcome of Smokers and Nonsmokers Suffering from Pulmonary Tuberculosis. It was seen cavitation was more among smokers, More number of advanced severity cases were present in smokers and more number of defaulters and less number of cured in smokers were present with a statistically significant with p-value less than 0.05. Smoking cessation programmes need to be targeted at tuberculosis patients both by clinicians specializing in tuberculosis and by national tuberculosis control initiatives. The effectiveness of such programmes in reducing smoking among tuberculosis patients and improving tuberculosis treatment outcomes also need to be assessed.

Kassu A et al in a similar study like us studied alterations in serum levels of trace elements in tuberculosis and HIV infections. Serum levels of copper, zinc, selenium and iron were determined using an inductively coupled plasma mass spectrometer. Compared with the control group, the concentrations of iron, zinc and selenium were significantly lower ( $P<0.05$ ) while that of copper and copper/zinc ratio was significantly higher ( $P<0.05$ ) in the serum of TB patients. TB patients with HIV coinfection had significantly lower serum zinc and selenium concentrations and significantly higher copper/zinc ratio compared to that in TB patients without HIV coinfection ( $P<0.05$ ). The results indicate that TB patients have altered profile of trace elements in their sera. This warrants the need for further investigations so that strategies for trace elements supplementation can be planned in addition to their potential as diagnostic parameters in monitoring responses to anti-TB chemotherapy. Patil L et al did an observational study on effect of antitubercular treatment on serum electrolyte and bicarbonate among pulmonary tuberculosis patients in tertiary care Hospital.

Biadola AP et al did a single center study in Brazil on routine laboratory parameters of newly diagnosed pulmonary tuberculosis patients. Objective was to evaluate the severity of tuberculosis and its association with laboratory tests before antituberculosis treatment. The evaluation of the severity showed a predominance of smear AFB (+), fever associated with other symptoms and infiltrative tuberculosis. It was concluded that the evaluation of electrolytes could contribute to clinical behavior; and non-segmented neutrophils are associated with a worse clinical prognosis in patients with tuberculosis.

#### Conclusion

Thus, we conclude that the Electrolyte and acid-base balance monitoring in patients with tuberculosis is recommended routinely. Serum sodium and Chloride further decreased in patients on Anti tubercular drugs. In Tuberculosis (TB) co-infected with HIV patients common electrolyte disturbances were decreased in serum sodium level and increase in potassium level.

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