Serum ferritin and other iron parameters in patients with pulmonary tuberculosis

Sir,

Defect in iron metabolism has been a well-known physiological factor not only in infections but also in many situations of inflammation, malignancy and tissue injuries. Hematological and iron-related measurements in active pulmonary tuberculosis have been carried out in which anemia occurring in patients was unrelated to iron deficient erythropoiesis. Lee associated anemia occurring in chronic disorders characteristically as due to the disturbance of iron metabolism.[1] This disturbance of iron metabolism is manifested by low serum iron concentration, low levels of total iron binding capacity of transferrin (TIBC), reduced transferrin saturation (TS), raised serum ferritin and increased iron stores. Reduced supply of iron to the normoblasts results in hypochromic and microcytic erythropoiesis. Pulmonary tuberculosis (PTB) is seen in both male and female Saudi adults. There is scarcity of information on the effect of PTB on iron metabolism at diagnosis and following management of patients. This study was undertaken to fill this gap. Fifty Saudi patients (30 men and 20 women) diagnosed as suffering from pulmonary tuberculosis were studied. In males, the age ranged from 22 years to 70 years (mean 42 years) and in females, from age 23 years to 65 years with a mean of 38 years. Out of 30 males, 3 were taxi drivers and the rest were unemployed. In females, 18 were housewives and 2 were students. All the patients were seen at the chest clinic, at Saharee Hospital, Riyadh where they were hospitalized for 6 weeks or more and given full courses of antituberculous therapy. Laboratory investigations were performed at diagnosis and 6 weeks after therapy. Ten ml of fresh blood specimen was taken from each patient between 8 am and 10 am. Three ml (anticoagulated) was used for full blood count; serum separated from 4 ml of clotted blood was used to measure iron parameters. The last 3 ml was used to determine the erythrocyte sedimentation rate. Serum iron was measured by ferroxine method using the BM/Hitachi 717, the TIBC and TS were determined firstly by measuring transferrin, which was carried out by the Cobas Mira Plus Analyser. Thereafter, the TIBC and TS were calculated. Serum ferritin levels were measured by Ciba-Cornings Automated Chemiluminescence System (ACS: 180) employing a 2 side chemilumminometric (sandwich) immunoassay. The data analysis was conducted separately for each sex using the student t-test assuming equal variances and the non-parametric (Wilcoxon S) Z-tests were used to determine the statistical significance between the mean values. A p value of <0.05 was considered significant. Values for serum iron, total iron binding capacity of transferrin, saturation fractions and serum ferritin in the male and female groups at diagnosis and after treatment are shown in **Tables 1 and 2**. The serum iron in the males increased from the initial (pre-treatment) value of 7.53 umol/L to 11.03 umol/L after treatment. Similarly, in the female group, the serum iron value

Table 1 - Values of serum ferritin, serum iron, total iron binding capacity, transferrin saturation before treatment.

Parameter	Male (N=30)				Female (N=20)			
	Mean	Median	SD	Range	Mean	Median	SD	Range
Serum Iron (umol/L)	7.53	5	7.03	1-31	5.55	5.50	3.03	1-11
TIBC (umol/L)	46.18	45.55	10.95	26.1-69	44.12	41.95	10.77	72-287
Transferrin Saturation Fraction ug/L	15.49	11.74	12.13	3.17-6.36	12.69	13.13	6.66	3.03-25.64
Serum Ferritin Ug/L	363.56	259.0	381.95	6-1770	235.95	226.0	481.42	16-593

TIBC - total iron binding capacity; N - number; SD - standard deviation

Table 2 - Values of serum ferritin, serum iron, total iron binding capacity, transferrin saturation after treatment.

Parameter	Male (N=30)				Female (N=20)			
	Mean	Median	SD	Range	Mean	Median	SD	Range
Serum Iron (umol/L)	11.03	9.50	7.09	2-34	8.55	9	4.44	2-17
TIBC (umol/L)	50.83	48.50	8.55	41-68	52.80	51.50	5.98	37-63
Transferrin Saturation Fraction ug/L	21.32	20.60	11.86	4.87-45.94	16.28	16.61	8.11	3.57-30.35
Serum Ferritin Ug/L	219.80	157.50	171.68	18-677	153.41	102.50	145.90	8-433

TIBC - Total iron binding capacity; N - number; SD - standard deviation

increased from the pre-treatment of 5.55 umol/L to 8.55 umol/l after treatment. The increases were statistically significant ($p<0.007$). Similar rises were seen in the TIBC values and in the transferrin saturation fraction after treatment. In the males, the TIBC increased from 46.18 umol/l to 50.83 umol/L and in the females from 44.12 umol/L to 52.80 umol/L. Transferrin saturation increased in value from 15.49 to 21.32 in the males and 12.69 to 16.28 in the females.

Serum ferritin. The mean serum ferritin value in the males before treatment was 363.56 ug/L (range 6-1770 ug/L) and in the females 235.95 ug/L (range 16-593 ug/L). These values were reduced significantly ($p<0.0004$) post-treatment. In the males it was reduced to 219.80 ug/L (range 18-677 ug/L) and in the females to 153.42 ug/L (range 8-433ug/L) **(Tables 1 & 2)**. Iron metabolic disorders accompanied by chronic infections have been of interest for some time. Defect in iron metabolism occurs, not only in infections but also in many situations in which inflammation, malignancy and tissue injuries occur.[1] The disturbance of iron metabolism is manifested by hypoferremia, hypotransferrinemia, reduced percentage trasferrin saturation, raised serum ferritin and increased iron stores.[2] All of these abnormalities were found in this study. Bayne et al followed 7 patients with PTB for 3 months and reported decreases in the serum ferritin levels.[3] Morris et al found increased iron stores in 81% of their patients with pulmonary tuberculosis.[4] Elevated serum ferritin was recorded in the patients. Lombard and Mansvelt reported increased iron stores in 3 out of 24 patients (13%).[5] The report of only 13% of patients with PTB having increased iron storage will seem low. This is contrary to the finding that all patients had increased serum ferritin values pre-treatment. However, the low incidence of iron storage reprted by Lombard and Mansvelt[5] may be explained by the reported poor nutritional status in the patients, with 60% having megaloblastic changes of folate deficiency in the bone marrow and 40% having associated anemia.[5] In this study, there are abnormalities in iron metabolism. The infection was complicated in all patients by hypoferremia, hypotransferinemia, and raised serum ferritin and reduced transferrin saturation. Raised serum ferritin in PTB is attributed to 2 factors: Firstly, monocytes and macrophages produce serum ferritin. In PTB, there is monocytosis. Monocytosis was seen in this study. Secondly, serum ferritin is a C-reactive protein that increases in inflammatory conditions, and in favor of this was a positive correlation between serum ferritin and C-reactive protein which, is a well-known acute phase reactant. This positive correlation continues to be maintained by following the treatment of the chronic condition and after 6 weeks to 3 months, concentration of both proteins are reduced. Measurement of C-reactive protein was however, not carried out in this study. In conclusion, in this study the significant fall in serum ferritin level was sequel to the decrease seen in the monocyte count following antituberculous therapy. Indeed, the fall of serum

ferritin value post treatment and the increases recorded in other serum iron parameters are significant signs of successful therapeutic response to the treatment of the disease.

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