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Assessment of a few trace elements (Zinc, Chromium, Cadmium, and Manganese) in patients with active tuberculosis receiving care at the Central Hospital in Benin City, Edo State

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Research Article

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ABSTRACT

Tuberculosis (TB) infection is on the rise worldwide and continues to be one of the leading causes of adult mortality in developing nations. The serum contents of several trace elements, including zinc (Zn), manganese (Mn), chromium (Cr), and cadmium (Cd), were assessed in 100 blood samples from 60 active tuberculosis patients (test subjects) and 40 people who seemed to be in good health (control). An Atomic Absorption Spectrophotometer was used to measure the elements' serum concentrations. The findings indicated that patients with TB had substantially ($P<0.05$) greater levels of Cd than the control group, but significantly ($P<0.05$) lower quantities of Zn, Mn, and Cr. Zn and Mn concentrations in TB patients did not change significantly ($P>0.05$) according to sex, however Cr and Cd concentrations did differ significantly ($P<0.05$) between the male and female participants. Age-dependent decreases in Cr and increases in Cd were seen in both genders, although there was no significant difference ($p<0.05$) in the amounts of Mn and Cd across the age groups examined. Our findings imply that whereas serum Cd levels are up in TB patients, Zn, Mn, and Cr concentrations are decreased.
Key words: Infectious disease, Serum concentration, Tuberculosis, Trace elements

INTRODUCTION

Mycobacterium tuberculosis is the most common strain of mycobacteria that causes tuberculosis (TB), a common infectious illness. Although it usually affects the lungs, this airborne illness may also affect other regions of the body (Garner et al., 2007). The majority of infections are asymptomatic (latent tuberculosis), and 10% of latent TB infections ultimately develop into active illness, which kills over 50% of individuals infected if treatment is not received (WHO, 2005). Fever, night sweats, weight loss, and a persistent cough with colored sputum are typical signs of an active TB infection. Numerous symptoms may result from infection of various organs (Khan et al., 2008).

A trace element is a dietary mineral required in trace amounts for an organism's healthy growth, development, and operation (Mills, 2005). Zinc, the second most prevalent trace element, functions in the body as a cofactor for one hundred different zinc-dependent enzymes, including carboxypeptidase, DNA polymerase, and alkaline phosphatase. The immune system, cell proliferation, collagen formation, wound healing, bone metabolism, reproduction, taste, smell, and vision are all primarily regulated by these enzymes. Red meat, fruits, vegetables, fish, and seafood are all part of a diet high in zinc (Lawn et al., 2005).

Humans also naturally contain manganese, although in extremely little levels. It is a strong antioxidant that actively searches for and neutralizes free radicals in the human body, preventing many of the potential risks they pose (Arnetz and Nicolich, 1999). It is an actual component of the manganese super oxide dismutase enzyme. Because it is essential for growth, metabolism, and the antioxidant system, it is also regarded as a significant metal for human health (Arnetz and Nicolich, 1999).

Humans need tiny quantities of chromium, although it's unclear how the mineral works in the body or how much is necessary for good health (Lettow, 2004). It is mostly present in two forms: 1) hexavalent (chromium 6+), a hazardous form resulting from industrial pollution, and 2) trivalent (chromium 3+), which is physiologically active and found in food. Insulin, a hormone essential to the body's metabolism and storage of

protein, fat, and carbohydrates, is known to be enhanced by chromium (Sharma, 2003). Chromium is known to activate some enzymes in vitro and enables insulin at intracellular locations, such as the ribosomes. The structure and metabolism of nucleic acids depend on chromium (Arnetz and Nicolich, 1999).

As a trace element, cadmium is thought to have no function in human nutrition or higher physiological processes (Schwartz and Levin, 2001). It is a byproduct of smelting zinc and certain lead ores, and it occurs naturally with zinc. Cadmium is a strong opponent of various important minerals, such as calcium, iron, copper, and zinc, and it is harmful in moderation (Lettow, 2004). Additionally, cadmium weakens the immune system, making the user more vulnerable to infectious illnesses like TB (Khan et al., 2008).

Numerous disorders have been thoroughly studied in relation to the biological function of trace elements, particularly zinc (Zn), manganese (Mn), and chromium (Cr). Therefore, the purpose of this research is to assess the serum levels of several trace elements (Zn, Mn, Cr, and Cd) in TB patients.

MATERIALS AND METHODS

Study Location: Central Hospital in Benin City, Edo State, Nigeria, served as the study's site. South-South Nigeria's Edo State is an inland state. Kogi State borders it on the north and east, Delta State borders it on the south, and Ondo State borders it on the west. The state's official language is English. Igarra, Edo, Esan, and Okpamheri are the state's principal tribal languages. Edo State's capital, Benin City, has 1,147,188 residents, while the state's population as of 2014 was expected to be 5 million (NPC, 2014).

Informed consent and ethical approval: The Ministry of Health in Edo State provided ethical permission for the sample collection. Prior to the blood sample being collected, each participant in the research gave their informed permission.

Sample size and collection: Central Hospital in Benin City, Edo State, served as the study's site. In all, one hundred (100) samples were utilized in this investigation. It included samples from forty (40) people who seemed to be in good health (control) and sixty (60) active TB patients (subjects) at Central Hospital Benin City. In order to measure the serum trace metals (Zn, Cr, Mn, and Cd), five milliliters of blood were drawn by venipuncture from fasting participants and placed in an unadorned container. After letting it stand for an hour to clot, it was centrifuged for ten minutes at 3000 g. After that, the serum was separated and kept at 40°C until it was needed for analysis.

Criteria for inclusion and exclusion: These individuals were chosen based on the following criteria: they had to be between the ages of 20 and 65, have sputum specimens that tested positive for acid-fast bacilli by microscopy, and exhibit radiographic and clinical abnormalities that were compatible with pulmonary TB. This research eliminated those participants who had previously had anti-TB therapy, were pregnant or nursing, were using immunosuppressive medications, or had other illnesses.

Sample Analysis: The Beck 20 (AAS) Atomic Absorption Spectrophotometer was used to assess the amounts of zinc, chromium, manganese, and cadmium in serum. The stock standard was diluted with deionized water and the necessary PPM for the standardization of the associated trace metals to create the working standard solution. After making sure the samples were well mixed, 2 milliliters of the thawed samples were transferred to a clean 10 milliliter centrifuge tube and diluted to 10 milliliters using 0.1M hydrochloric acid. After removing cellular debris by centrifuging the diluted serum sample at 3000 revolutions per minute, it was sucked straight into the burner for examination and data recording. Every analysis was done at the University College Hospital's Clinical Chemistry Laboratory in Ibadan, Oyo State, Nigeria.

The test's fundamental idea Using the direct approach outlined by Kaneko (1991), serum trace metals were measured using a flame Atomic Absorption Spectrophotometer (AAS). When the elements' atoms were inhaled into the AAS, they vaporized and absorbed light with the same wavelength as the metal's excited state, i.e., the vaporized ground state (unexcited) atom of a trace metal in the excited state. The trace metal content of the solution is directly correlated with the quantity of light absorbed.

Statistical analysis: Tables were used to display the findings. The data was shown as mean × standard deviation (S.D). One-way analysis of variance (ANOVA) and the student's t-test were used to compare test participants and control groups. At $p<0.05$, a significant difference was deemed to exist.

RESULTS

The average levels of zinc, manganese, chromium, and cadmium in the individuals and control are shown in Table 1. According to the data, the patient and control had mean zinc levels of 75.11±10.68 ug/dl and 88.34±10.21 ug/dl, respectively, and manganese levels of 3.61±0.45 ug/dl and 9.62±1.60 ug/dl. Similarly, the patients' and control's mean levels of chromium were 0.96±0.33 ug/dl and 1.14±0.19 ug/dl, respectively, while cadmium was 0.21±0.21 ug/dl and 0.15±0.31 ug/dl. When compared to the control, the participants' concentrations of zinc, chromium, and manganese were significantly lower ($p<0.05$), however their concentrations of cadmium were significantly higher ($p<0.05$).

The distribution of zinc, manganese, chromium, and cadmium in the male and female study participants is shown in Table 2. Males and females had mean zinc values of 72.81±12.32 ug/dl and 77.59±8.40 ug/dl, respectively, and manganese values of 3.51±0.51 ug/dl and 3.71±0.35 ug/dl. Despite the fact that the mean concentration of zinc and manganese was somewhat greater in females than in males, the findings indicated that there was no significant difference ($p>0.05$) between the male and female participants under study. However, cadmium in men (0.24±0.19) was substantially greater ($p<0.05$) than in females (0.18±0.12), while chromium in females (1.01±0.33) was significantly higher (p0.05) than in males (0.81±0.33).

The distribution of zinc, manganese, chromium, and cadmium among the subjects in the various age groups is shown in Table 3. The findings indicated that the levels of manganese and cadmium in the various age groups did not vary significantly ($p<0.05$). Additionally, there was no significant difference ($p<0.05$) in zinc and chromium levels between the ages of 36–50 and 51–65, however both men and females showed a significant rise ($p>0.05$) in zinc and chromium levels between the ages of 20–35. Zinc levels decreased as age increased in the various age categories for both men and females, accordingly. Additionally, the mean levels of manganese and chromium decreased somewhat with age in both male and female individuals, but the values were greater in females than in men. In a similar vein, cadmium levels rose with age and were greater in men than in women.

Table 1: Mean value of zinc, manganese, chromium and cadmium in subjects studied and control

Parameters	Subjects (n=60) Mean ± S.D	Control (n=40) Mean ± S.D	F Value	P Value
Zinc (ug/dl)	75.11Ä10.68	88.34 Å 10.21	0.246	0.002*
Manganese (ug/dl)	3.61Ä0.45	9.62 Å 1.60	0.186	0.001*
Chromium (ug/dl)	0.96 Å 0.33	1.14 Å 0.19	0.215	0.004*
Cadmium (ug/dl)	0.21 Å 0.12	0.15 Å 0.13	0.134	0.001*

*The mean difference is significant at p-value<0.05. Values are inMean Å Standard Deviation

Table 2: Distribution of zinc, manganese, chromium and cadmium in male and female subjects studied

Parameters	Male Mean ± S.D (n=26)	Female Mean ± S.D (n=34)	F Value	P Value
Zinc (ug/dl)	72.81 Å 12.32	77.59 Å 8.40	0.823	0.344
Manganese (ug/dl)	3.51 Å 0.51	3.71 Å 0.35	1.182	0.621
Chromium (ug/dl)	0.81 Å 0.33	1.01 Å 0.33	0.317	0.004*
Cadmium (ug/dl)	0.24 Å 0.19	0.18 Å 0.12	0.203	0.002*

*The mean difference is significant at p-value<0.05. Values are as MeanÅS.D

Table 3: Distribution of zinc, manganese, chromium and cadmium in subjects studied in the different age groups

Parameters	Male 20-35 years (n=14) 36-50 years (n=8) 51-65 years (n=4) Mean ± S.D	Female 20-35 years (n=22) 36-50 years (n=10) 51-65 years (n=2) Mean ± S.D	F Value	P Value
Zinc (ug/dl) 20-35 years	75.05 Å 11.10	69.25 Å 6.45	0.312	0.003*
36-50 years	72.08 Å 11.57	68.34 Å 8.21	0.895	0.331
51-65 years	70.49 Å 6.56	66.65 Å 6.88	1.603	0.521
Manganese (ug/dl)				
20-35 years	3.69 Å 0.48	3.23 Å 0.45	0.775	0.571
36-50 years	3.58 Å 0.48	3.01 Å 0.32	0.627	0.364
51-65 years	2.56 Å 0.50	2.67 Å 0.53	1.110	0.765
Chromium (ug/dl)				
20-35 years	1.11 Å 0.20	0.91 Å 0.48	0.405	0.003*
36-50 years	0.88 Å 0.33	0.81 Å 0.20	1.205	0.737
51-65 years	0.84 Å 0.44	0.78 Å 0.22	0.694	0.383
Cadmium (ug/dl)				
20-35 years	0.24 Å 0.13	0.18 Å 0.12	0.585	0.271
36-50 years	0.28 Å 0.14	0.26 Å 0.15	0.872	0.441
51-65 years	0.30 Å 0.15	0.28 Å 0.24	1.067	0.650

*The mean difference is significant at p-value<0.05. Values are as Mean Å Standard Deviation

DISCUSSION

According to reports from India (Ahmad et al., 1985), Indonesia (Karyadi et al., 2000), Africa (Ciftci et al., 2003), and Northern Nigeria (Koyanagi et al., 2004), serum samples from TB patients had lower zinc concentrations (75.11±10.68ug/dl) than those from seemingly healthy controls (88.34 Å 10.21ug/dl). Redistribution of zinc from serum to other organs (Cousins and Leinart, 1988) or a decrease in zinc-carrier proteins and/or an increase in metallothionein production—a protein that carries zinc to the liver—were likely the causes of the loss (Gabay and Kushner, 1999). It is important to note that low zinc levels in TB patients may indicate a significant correlation between hypozincaemia and reduced immune response and degree of malnutrition, as previously shown in TB patients (Graham et al., 1991).

It has been shown that zinc deficiency reduces peripheral mononuclear cells' production of gamma interferon (IFN-) and tumor necrosis factor-α (TNF-) (Beck et al., 1997). Additionally, a mutation in the gene encoding for the IFN-receptor led to an increased susceptibility to mycobacterial infections (Newport et al., 1996), and anti-TNF-administration to patients may cause reactivation of TB (Mayordomo et al., 2002). Thus, it is plausible that zinc deficiency plays a role in TB activation. Interestingly, adult TB patients who take zinc supplements (Pant et al., 1987) or zinc and vitamin A supplements may have a quicker resolution of chest X-ray pathology (Karyadi et al., 2002) and a quicker clearance of acid fast bacilli from sputum.

According to the study's findings, TB patients' serum manganese levels were significantly lower than those of the control group. This outcome is consistent with earlier research conducted in Northern Nigeria (Koyanagi et al., 2004), Africa (Ciftciet al., 2003), Indonesia (Karyadi et al., 2000), and India (Ahmad et al., 1985). Manganese is important in neurological function and stimulates enzymes linked to protein synthesis and fatty acid metabolism. Superoxide dismutase (SOD), an antioxidant that aids in preventing damage from free radicals, contains manganese (Mn). Because oxidative stress and free radical production are characteristics of

TB patients (Newport et al., 1996), high Mn levels are necessary for SOD to develop and operate properly in TB patients in order to neutralize the created free radicals. Therefore, manganese status has a special impact on the structure and function of the mitochondria (Wilson et al., 1997).
Interestingly, the majority of these enzymes are unaffected by manganese shortage, most likely because magnesium can often replace manganese. Manganese is necessary for healthy bone development in mammals.

CNS control, reproduction, and lipid metabolism. Because of its impact on the metabolism of biogenic amines, manganese plays a significant part in the brain's regular operation. The correlation between catecholamine and manganese concentrations in the brain may be caused by this mechanism. The proper use of manganese in the human body is thought to sometimes be hampered by calcium and iron. Deficiency symptoms may include weakness, intense cramping, sweating, rapid heartbeats, and eye issues. Severe deficiencies may lead to osteoporosis, cardiac problems, pancreatic damage, infertility in women, and an increased risk of infectious diseases (Soeters, 2005).

Additionally, this research demonstrates that the mean chromium content in healthy controls (1.14±0.19ug/dl) is higher than that of TB patients (0.96±0.33ug/dl). Other studies (Graham et al., 1991; Gabay and Kushner, 1999; Koyanagi et al., 2004) are consistent with this result. Chromium's primary physiological function is as an insulin cofactor. Chromium enhances the effects of both endogenous and exogenous insulin in its organic form, most likely via increasing the insulin's adhesion to cell membranes. The glucose tolerance factor (GTF), also known as the dinicotinic acid-glutathione complex, contains the organic form. The metal component of GTF is chromium; when combined with insulin, GTF influences the metabolism of triglycerides, glucose, and cholesterol. Chromium is thus necessary for protein synthesis, amino acid transport, glycogen production, and glucose tolerance. Additionally, chromium has a role in the activation of a number of enzymes.
In addition to being a necessary micronutrient for Mycobacterium TB and its host, chromium is also needed for the production of several vitamins. According to a recent research, coordination complexes of chromium and other metals with the pyrophosphate ligand were used to create a new anti-tuberculosis therapy using metal-based medications. According to this research, these metals are crucial for managing TB infection because of their strong potency and significant selectivity against M. tuberculosis (Gabay and Kushner, 1999). Nevertheless, scientists still don't fully understand how chromium affects TB.
Older adults often have greater blood levels of cadmium (Cd), which reflects both current and cumulative exposures (Soeters, 2005). This is consistent with the study's results, which showed that the individuals' mean concentration of cadmium (Cd) rose with age and was substantially greater (0.21±0.21ug/dl) than that of the control group (0.15±0.31ug/dl). These variations in exposure to trace elements may raise the risk of tuberculosis, which rises with age. The current research, which found that people with TB had lower levels of zinc and manganese and higher levels of cadmium, supports this. Because Cd impacts the immune system, elevated levels of Cd in our TB participants are thus associated to the formation and progression of TB. This suggests that high Cd may be involved in the pathogenesis of TB.

Additionally, lung emphysema and bone disorders (osteomalacia and osteoporosis) may result from prolonged exposure to cadmium. Additionally, diarrhea, severe vomiting and stomach pains, bone fractures, reproductive failure and possibly infertility, damage to the central nervous system, immune system damage, psychological disorders, DNA damage or the development of cancer, and increased susceptibility to tuberculosis infection, as demonstrated in this study due to immune system damage, are all consequences of cadmium toxicity (Paton et al., 2004).

CONCLUSION

The study's findings demonstrated that although the individuals' serum concentrations of cadmium were greater than those of the control, those of zinc, manganese, and chromium were much lower. Serum samples from TB patients showed a drop in zinc, manganese, and chromium, which was most likely caused by inflammatory

processes. Additionally, prior deficits that increased susceptibility to infection may be the cause of the low qantities of zinc, chromium, and manganese seen in this research.

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