Serum Albumin/Globulin ratio in Tuberculosis and HIV Patients any Relationship?

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Abstract

Background: Tuberculosis (TB) remains an important communicable disease all over the world. The serum protein levels in TB patients may be altered by low immunity, edema and decrease antioxidant activity. This study therefore evaluates the relationship between TB and serum proteins with emphasis on albumin/globulin ratio as an important component for treatment and management of TB. The study also aimed at comparing albumin/globulin ratio of tuberculosis patients, HIV patients, those on drugs and naive patients.

Materials and Method: A total of 120 participants (42 control and 78 patients) aged between 15-years-65 years and sex-matched attending Plateau State Specialist Hospital were enrolled. Total protein was estimated using Biuret method and albumin by Bromocresol green method, serum globulin value was obtained by subtracting albumin from total protein then albumin/globulin ratio was calculated. Screening for HIV antibody was done using Determine strip and confirmed with Unigold.

Results: Evaluated albumin/globulin ratio (1:4) was obtained in the TB case when compared to control group (p = 0.002). The albumin was significantly higher in study group compared to control (2.95 ± 0.86 and 2.75 ± 0.65 g/dl) while total protein and globulin was significantly lower (6.17 ± 1.66 and 6.76 ± 0.86 g/dl, p = 0.011 and 3.22 ± 1.9 and 3.97 ± 0.86 g/dl with p = 0.016. Patients seropositive for HIV antibody had a decrease in serum total protein, albumin and globulin but high albumin/globulin ratio. Total protein, albumin, globulin and albumin/globulin of TB patients not on drugs were elevated compared to those currently undergoing treatment. Age group < 30 years when compared with age group between 30-40 years showed significant low albumin and albumin/globulin ratio (2.74 ± 0.75 and 3.10 ± 0.72 g/dl, p = 0.025 and 0.97:1 ± 0.66 and 1.42:1 ± 1.47, p = 0.042).

Conclusion: Our work suggests that individuals < 30 years had hypoproteinaemia which maybe lead to low immunity. Our results also suggests that albumin/globulin ratio of TB patients on drugs were higher which may be due to hyperalbuminaemia observed in this group. For effective treatment and management of TB infected individuals, appropriate use of drugs, adherence to treatment plan, close monitoring of dietary intake is needful in building and improving immunity.

Keywords: Tuberculosis; HIV; Albumin total protein; Globulin

Introduction

Tuberculosis (TB) is a common and often deadly infectious disease caused by various strains of mycobacterium usually Mycobacterium Tuberculosis in humans [1]. It was originally referred to as Koch’s bacillus after Robert Koch who first identified it in 1882 in Berlin, Germany [2]. Mycobacterium tuberculosis is found in infected human and is transmitted to primates, dogs and other animals that are in close association with man. M. bovis is the causative agent of tuberculosis in cattle and is transmitted to man, primates, pigs and domestic animals [2]. TB usually attacks the lungs but can affect other parts of the body such as the lymph nodes, kidneys, bones, central nervous system, peritoneum, eye as well as the skin and spread through air when people who have the disease sneeze or spit [3]. When people with active pulmonary TB cough, sneeze, speak, sing, or spit, they expel infectious aerosol droplets 0.5 to 5.0 μm in diameter. A single sneeze can release up to 40,000 droplets [4]. Each one of these droplets may transmit the disease, since the infectious dose of tuberculosis is very low (the inhalation of fewer than 10 bacteria may cause an infection) [5].

People with prolonged, frequent, or close contact with people with TB are at particularly high risk of becoming infected, with an estimated 22% infection rate [6].

WHO estimates that 210,000 new cases of all forms of tuberculosis occurred in Nigeria in 2010 and more than 90% of new cases and deaths occurred in developing countries [7]. There are changes in levels of serum proteins in response to both acute and chronic infections. In air infection like Mycobacterium Tuberculosis, it is expected that changes in plasma protein levels will occur in patients. However, the change in level of each protein at any particular time usually reflects the net effect of the rate of synthesis and rate of catabolism as a result of host microbe interaction. In chronic infectious TB disease, the albumin shows a decrease while globulin content shows an increase.
an increase leading to low Albumin to Globulin (A/G) ratio and albumin to alpha-2 globulin ratios [8].

Plasma protein fractions are albumin, globulin and fibrinogen. Albumin is a small globular protein with molecular mass of 66.3 kDa. It is the most abundant protein, has no carbohydrate side chain but is highly soluble in water due to high negative charge at pH 7.4. Albumins are synthesized by hepatic parenchyma cells. It functions mainly for maintaining colloid osmotic pressure and also serves for transportation of large compounds such as free fatty acids, amino acids and drug [9].

Serum protein consists of albumin and globulins and its level in normal subjects vary from 6-8 g/dl. Normal range of albumin is 3.2-4.5 g/dl and globulin ranges from 2.3-3.5 g/dl [2]. Tuberculosis is one of the principal infectious causes of disease and death worldwide, yet there are very marked differences in the incidences from region to region roughly, one-third of the world’s population has been infected with Mycobacterium tuberculosis, and new infections occur at a rate of 90-95% of infections remain asymptomatic [11].

In 2007, an estimated 13.7 million people have active tuberculosis disease with 9.3 million new cases and 1.8 million deaths, while in 2010, there were an estimated 8.8 million new cases and 1.5 million associated deaths, mostly occurring in developing countries [12]. The annual incidence rates vary from country to country. At one extreme there is an incidence of disease of less than 5 per 100,000 per annum in the population of Western Europe [13]. Intermediate incidence of 50 - 100 per 100,000 and 100 - 200 per 100,000 were reported in Eastern Europe and the Indian subcontinent respectively. Africa has an annual incidence rate of 363 per 100,000 populations [14].

Nigeria has the fourth highest burden of tuberculosis in the world, with an annual incidence of 311 cases per 100,000 populations in 2006 [15], although tuberculosis is so prevalent that it has been declared a global emergency most people do not develop the disease after infection. The ratio of infection to the disease is about 10%. There is approximately about one third of the world population-two billion people have been infected with tubercle bacillus [16], but the great majority only has latent tuberculosis infection. In 2007, an estimated 13.7 million people had active tuberculosis disease with 9.3 million new cases and 1.8 million deaths, while in 2010, there were an estimated 8.8 million new cases and 1.5 million associated deaths, mostly occurring in developing countries [12]. The annual incidence rates vary from country to country. At one extreme there is an incidence of disease of less than 5 per 100,000 per annum in the population of Western Europe [13]. Intermediate incidence of 50 - 100 per 100,000 and 100 - 200 per 100,000 were reported in Eastern Europe and the Indian subcontinent respectively. Africa has an annual incidence rate of 363 per 100,000 populations [14].

There are a number of known factors that make people more susceptible to TB infection worldwide the most important of these are HIV/AIDS compromise the immune system. WHO, reported that approximately 11 million people around the globe are infected with both HIV and TB. Smoking more than 20 cigarettes a day also increases the risk of TB by two to four times [19].

Other disease states that increase the risk of developing tuberculosis are chronic liver disease, malnutrition and alcoholism [20]. Diets may also affect the risk. For example, among immigrant in London from the Indian subcontinent, vegetarians Hindu Asians were found to have an 8.5 fold increase risk of TB, compared to Muslim who eat meat and fish daily [21]. This increased risked could be caused by micronutrient deficiencies, possibly irons, Vitamin B12 or Vitamin D and an increased risk of contracting tuberculosis [22].

Also overcrowding may contribute to the spread of disease. Prisoners especially in poor countries are particularly vulnerable to infections such as HIV/AIDS and TB. TB out breaks have been reported in prisons is much higher than among the general population in some countries as much as 40 times higher due to overcrowding [23].

This work was therefore aimed at estimating albumin/globulin ratio in serum of tuberculosis patients, comparing the albumin/globulin ratio in tuberculosis patients on drugs, those not on drugs and determining the relationship between A/G ratio and TB disease.

Material and Method

The study was conducted on out patients in Plateau Specialist Hospital Jos, a total of 120 blood samples from subjects between the ages of 15 years - 65 years were analysed. 78 were from patients with confirmed pulmonary tuberculosis i.e. those on anti-tuberculosis drug treatment and those not on any anti-tuberculosis drug treatment while 42 were non tuberculosis individuals who served as control participants out of the 78 patients,64 were on TB treatment while remaining 14 were not on any form of TB treatment.

2ml of blood were collected using sterile syringes with minimum stasis by venepuncture and transferred into chemically cleaned, dried and labelled sample containers. The samples were also allowed to clot, then retracted and centrifuged at 3,000 rpm for 5 minutes. The serum was then transferred to clean and well label vials for further analysis. An inclusion criterion was based on patient age i.e. between 15 - 60 years and patients diagnosed for TB by using the revised National Tuberculosis Control Algorithm [24].

The Biuret test is a chemical test used for detecting the presence of peptide bonds. In the presence of peptides, a copper(II) ion forms violet-colored coordination complexes in an alkaline solution [25]. Several variants on the test have been developed, such as the BCA test and the modified Lowry test. The Biuret reaction was used to assess the concentration of proteins.

Serum Albumin was determined using the bromocresol green method based on the reaction of albumin with the dye bromocresol green to produce a coloured complex which was measured calorimetrically to give the concentration of the albumin [26].

Globulin concentration was obtained by subtracting values of total serum protein from that of serum albumin. The normal reference value being 2.3-3.5 g/dl.
The value for Globulin/Albumin ratio was obtained by dividing albumin value by globulin value. Normal reference value 1.2:1 - 2:1.

Results

The demographic characteristics of the study participants are shown as comprising a total of 120 participants (42 in the control group and 78 in the Tuberculosis (TB) group). The control group consisted of 27 (64.3%) males and 15 (35.7%) females while the TB group consisted of 46 (59%) males and 32 (41%) females. They were grouped based on their ages as < 30, 30-40 and > 40 years. In the control group, 26 (61.9%) were < 30 years, 9 (21.4%) between 30-40 years and 7 (16.7%) > 40 years, while the TB group were 31 (39.74%), 27 (34.62%) and 20 (25.64%) with the age group as < 30, 30-40 and > 40 respectively. The mean standard deviation based on age in the control and TB groups were 30.71 ± 10.43 and 34.05 ± 11.85 respectively and p value 0.89, 0.2116, 0.666 and 0.78. The mean and standard deviation values of newly diagnosed and those on treatment (old) they were shown to have 6.60 ± 1.37 and 6.07 ± 1.71 g/dl, 2.67 ± 0.96 g/dl, 3.44 ± 2.29 g/dl and 1.52:1 ± 1.89 g/dl respectively while those negative for HIV antibody had 6.18 ± 1.68 g/dl, 3.01 ± 0.84 g/dl, 3.16 ± 1.81 g/dl and 1.37:1 ± 1.18 g/dl respectively with p values of 0.89, 0.2116, 0.666 and 0.78.

Table 1: Demographic characteristics of the study participants.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control group N (%)</th>
<th>TB group N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>27 (64.3)</td>
<td>46 (59)</td>
</tr>
<tr>
<td>Female</td>
<td>15 (35.7)</td>
<td>32 (41)</td>
</tr>
<tr>
<td>Age groups (in years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30</td>
<td>20 (61.9)</td>
<td>31 (39.74)</td>
</tr>
<tr>
<td>30-40</td>
<td>9 (21.4)</td>
<td>27 (34.62)</td>
</tr>
<tr>
<td>&gt;40</td>
<td>7 (16.7)</td>
<td>20 (25.64)</td>
</tr>
<tr>
<td>Mean</td>
<td>30.71 ± 10.43</td>
<td>34.05 ± 11.85</td>
</tr>
</tbody>
</table>

Table 2: Characteristics of the TB study participants.

The TB subjects who were positive for HIV antibody had total protein, albumin, globulin and albumin/globulin ratio values as 6.11 ± 1.64 g/dl, 2.67 ± 0.96 g/dl, 3.44 ± 2.29 g/dl and 1.52:1 ± 1.89 g/dl respectively while those negative for HIV antibody had 6.18 ± 1.68 g/dl, 3.01 ± 0.84 g/dl, 3.16 ± 1.81 g/dl and 1.37:1 ± 1.18 g/dl respectively with p values of 0.89, 0.2116, 0.666 and 0.78.

Discussion

Our study population consisted of a total of 120 participants (42 in the control group and 78 in the tuberculosis (TB) group). The TB
group had 46 (59%) male and 32 (41%) females while the control group was comprised of healthy individuals matched for age and sex. Those < 30 years had the highest number of participants for both test and control groups 31 (39.74%) and 26 (61.9%), followed by group 30 - 40 years 9 (21.4%) and 27 (34.6%) in the control and TB group respectively. This agrees with previous reports from developing countries where about 80% of TB affected individuals were below 30 years [27,28], as compared with reports from developed countries where majority of affected population were above age 50 years. This variation may be due to reactivation from primary or secondary infections caused by co-infection or inexperience in diagnosis and therapeutics approach by health personnel or lack of laboratory facilities as noted by [29].

The mean total protein and globulin was significantly lower in the TB patients when compared to the control group: 6.17 ± 1.66 and 6.76 ± 1.66 g/dl (p = 0.011), 3.22 ± 1.90 and 3.97 ± 0.86 g/dl (p = 0.016) respectively, this might have been caused by anorexia, mal-absorption and impaired cell mediated immunity as noted by Narwadiya [30]. The elevated mean value for albumin/globulin ratio was 1.4 for TB patient, when compared with control subject; at value 0.002 was obtained which is significantly low. In contrast, the mean albumin of 2.95 ± 0.86 g/dl in TB case was higher than in control group which was 2.75 ± 0.65 g/dl with p value 0.149. No significant difference was observed at p > 0.05. This is in line with the work of Damburame et al. whose work showed a decrease in total protein among people with TB.

Table 5: Comparison of serum protein of TB patients based on age group < 30 and > 30.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD (g/dl)</th>
<th>Age category</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>&lt;30</td>
</tr>
<tr>
<td>Total protein</td>
<td>6.32 ± 1.24</td>
<td>6.50 ± 1.27</td>
</tr>
<tr>
<td>Albumin</td>
<td>2.74 ± 0.75</td>
<td>3.10 ± 0.72</td>
</tr>
<tr>
<td>Globulin</td>
<td>3.55 ± 1.50</td>
<td>3.40 ± 1.58</td>
</tr>
<tr>
<td>Albumin/globulin ratio</td>
<td>0.97:1 ± 0.66</td>
<td>1.42:1 ± 1.47</td>
</tr>
</tbody>
</table>

Table 4: Comparison of serum protein of TB patients based on treatment regimen.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD (g/dl)</th>
<th>Phase of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Intensive</td>
</tr>
<tr>
<td>Total protein</td>
<td>6.20 ± 1.46</td>
<td>5.97 ± 1.91</td>
</tr>
<tr>
<td>Albumin</td>
<td>2.84 ± 0.99</td>
<td>2.89 ± 0.59</td>
</tr>
<tr>
<td>Globulin</td>
<td>3.36 ± 1.80</td>
<td>3.07 ± 2.01</td>
</tr>
<tr>
<td>Albumin/globulin ratio</td>
<td>1.25:1 ± 1.19</td>
<td>1.40:1 ± 1.14</td>
</tr>
</tbody>
</table>

Table 3: Comparison of serum protein of subjects based on sex in the control group with TB group.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD (g/dl)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total protein</td>
<td>6.64 ± 0.90</td>
<td>0.374</td>
</tr>
<tr>
<td>Albumin</td>
<td>2.61 ± 0.65</td>
<td>0.014</td>
</tr>
<tr>
<td>Globulin</td>
<td>3.95 ± 0.85</td>
<td>0.103</td>
</tr>
<tr>
<td>Albumin/globulin ratio</td>
<td>0.70:1 ± 0.26</td>
<td>0.006</td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total protein</td>
<td>6.98 ± 0.79</td>
<td>0.002</td>
</tr>
<tr>
<td>Albumin</td>
<td>2.98 ± 0.58</td>
<td>0.48</td>
</tr>
<tr>
<td>Globulin</td>
<td>3.99 ± 0.88</td>
<td>0.028</td>
</tr>
<tr>
<td>Albumin/globulin ratio</td>
<td>0.79:1 ± 0.27</td>
<td>0.23</td>
</tr>
</tbody>
</table>

Table 4: Comparison of serum protein of TB patients based on treatment regimen.

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and globulin in individuals on intensive phase and increased albumin/globulin ratio in those on continuation phase of treatment [32].

From the results obtained, it is evident that total protein, albumin and albumin/globulin ratio concentration are higher in age group > 30 years as compared to age category < 30 years where albumin and albumin/globulin ratio was significantly increase (p values 0.025 and 0.042) whereas total protein of age group < 30 years had no significant difference while globulin concentration were lower when compared to age group < 30 years which showed no significant difference. The variation may be due to socioeconomic status of the various aged groups.

Albumin concentration and albumin/globulin ratio was lower at age < 30 years when compared to age > 40 whereas total protein and globulin mean value are higher on comparison with age > 40 years. All had p values that showed no significant difference. Albumin/globulin ratio level is usually affected in tuberculosis disease this might be due to association of immunoglobulin and cellular immunity in the process.

Conclusion

Our findings show that albumin/globulin ratio, total protein and globulin had significant difference in TB patients compared to the control group. Males with TB had a significant high serum albumin and albumin globulin ratio compared with those in the control group also female with TB cases had significant low serum total protein and globulin but albumin/globulin ratio was significantly high.

This study shows serum protein of newly diagnosed patients was higher than those on treatment. Conversely, there was increase in serum total protein and globulin of individuals on intensive phase treatment for TB. It was observed that aged group > 30 years had significant high albumin, albumin/globulin ratio though total protein was elevated in relation to aged < 30 years.

For effective treatment of individuals with tuberculosis in addition to the use of appropriate anti-tubercular drugs, patients must adhere to treatment and employ frantic effort in the control of associated diseases (co-infection) such as HIV. Since nutritional status influences cellular immunity of the body system, the public should be enlightened on the need to pay close attention on dietary intake that are necessary for maintaining and improving the immune system. Physicians should also be guided on the use of drugs which may serve for boosting the protein level, since proteins are involved in transportation of drugs and building of immune system.

Limitations

Additional work should be done on a larger population of both HIV and TB patients over a longer period on different drug regimen.

References

12. World Health Organization (2011) "The sixteenth global report on tuberculosis".

