Nutritional status and immunological profile in HIV infected patients with pulmonary tuberculosis involved in rural-urban migrants to Nairobi, Kenya

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Running headline:
HIV infected with pulmonary tuberculosis

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Abstract

Introduction: Rural-urban migration in general, significantly contributes to the increased incidence of HIV and tuberculosis, as well as poor nutritional status. We analysed the nutritional status and immunological profile in HIV positive patients with pulmonary tuberculosis and the association between nutritional status and the CD4 count.

Patients and methods: A retrospective analysis of 69 ART-naive subjects diagnosed with pulmonary tuberculosis was carried out. Subjects were diagnosed with active pulmonary tuberculosis through smear analysis and/or posteroanterior chest X-ray.

Results: Out of 28 (40.6%) and 41 (59.4%) subjects with smear positive and smear negative pulmonary tuberculosis, respectively, 18/9 (64.3% and 19.5%, resp.) had a CD4 count below 100 cells/μl, 9/21 (32.1% and 51.2%, resp.) had a CD4 between a 100-250, and 1/12 (3.6% and 29.3%, resp.) had a CD4 above 250 (p<0.05). Out of 28 (40.6%) and 41 (59.4%) subjects with smear positive and smear negative pulmonary tuberculosis, respectively, 15/15 (53.6% and 36.6%, resp.) had BMI<18.5, and 13/26 (46.4% and 63.4%, resp.) BMI 18.5-24.9 (p=0.36).

Discussion: No significant association between low BMI and smear positive/smear negative pulmonary tuberculosis was seen. Statistically significant association was found between low baseline CD4 count and smear positive pulmonary tuberculosis. This suggests that positivity of the sputum sample microscopy tends to be detected in patients with low CD4 counts, therefore in subjects with significantly impaired function of the immune system. Low socioeconomic status of the study population makes health care provision onerous; therefore there is an urgent need for development of simple and cheap diagnostic methods.
1. Introduction

Since 1984, when the first case of HIV in Kenya was reported, the number of cases has significantly increased and according to the 2012 KAIS report current prevalence of HIV in adults and adolescents in Nairobi country was 4.9%. (KAIS Report, 2012) According to the report of the World Health Organisation from 2014, Kenya belongs among the 22 high burden countries for TB and HIV/AIDS infections with an estimated incidence rate of HIV and TB co-infection of 109 (105112)/100000 population. (Global Tuberculosis Report, 2014) Coincidentally, in the last few years, reported cases of tuberculosis and HIV co-infection in Kenya have increased, which constitutes a serious public health concern.

Tuberculosis is the main cause of morbidity and mortality in people living with HIV/AIDS worldwide. (Reid & Shah (2009) Prevalence of tuberculosis in HIV infected patients possesses a dual epidemic concern especially in Sub-Saharan Africa. Tuberculosis is the most common opportunistic infection in HIV infected individuals, accounting for significant morbidity and mortality in this respective group of patients. Moreover, the diagnosis of HIV-associated TB is often challenging due to atypical clinical and radiographic manifestations, more frequent extrapulmonary disease, and higher rates of smear-negative pulmonary TB. (Gray et al. (2013)

The association between tuberculosis and malnutrition includes two major interactions: the effect of tuberculous infection on the nutritional status of the individual and the effect of malnutrition on the clinical manifestations of the tuberculosis resulting from impairment of the immune system. (Oliveira et al. (2014)

It is widely known that low socio-economic status significantly contributes to increased prevalence of tuberculosis in HIV infected individuals. In Nairobi, a large percentage of the population involved in rural-urban migration ends up living in informal settlements of large cities with poor health outcomes. Poor health outcomes that informal settlements’ residents exhibit at all stages of the life course are rooted in three key characteristics of slum settlements: poor environmental conditions, poor infrastructure, and limited access to services due to lack of income to pay for treatment and preventive services. (Zulu et al. (2011) Based on our experience, individuals migrating from rural to urban settings, due to above-mentioned factors, are often involved in illicit alcohol consumption, cigarette smoking, drug abuse and sexual promiscuity. All these factors together with generally poor living conditions play an important role in the development of pulmonary tuberculosis in an immunocompromised individual.

The objective of this study was to analyse the nutritional status and immunological profile in HIV positive patients with pulmonary tuberculosis involved in rural-urban migration to the capital city of Kenya, Nairobi; as well as to analyse the association between the nutritional status and the CD4 count at the diagnosis of pulmonary tuberculosis.

2. Patients and Methods

Study design

A retrospective analysis was carried out in the ART clinic of St. Raphael Clinic, Mihang’o, Nairobi, Kenya, from January 2013 till July 2015. St. Raphael Clinic is located on the outskirts of Nairobi, the capital city of Kenya that serves a large population of people with a low socio-economic status, who migrated from villages to the capital city. We retrospectively analysed 69 subjects, who attended our centre on an outpatient basis and presented with HIV/TB co-infection. All the subjects included in
the study were ART-naïve. No subject had a history of tuberculosis.

**Study subjects**

The analysis included 69 adult subjects who were diagnosed with active pulmonary tuberculosis. Out of 69 patients, 37 were females and 32 were males. The mean age of the cohort of TB/HIV coinfected subjects was $36.7 \pm 8.1$ years. All the HIV positive subjects presented with at least three symptoms of active pulmonary tuberculosis were diagnosed with active pulmonary tuberculosis through smear analysis and/or posteroanterior chest X-ray.

**Study methods and procedures**

All subjects included in the study underwent an examination with conventional light microscopy of Ziehl-Neelsen-stained smears prepared directly from two samples of sputum (spot sample and morning sample). Two trained microscopists read all the prepared samples. Based on the presence or non-presence of acid-fast stained bacilli the samples were either positive or negative, respectively.

The smear negative subjects underwent additional screening procedure, i.e. posteroanterior chest X-ray. A trained physician according to the Guidelines for Management of Tuberculosis and Leprosy in Kenya, June 2014, interpreted each chest X-ray. All the patients included in the cohort underwent blood sampling for baseline CD4 count analysis (using a flow cytometry) and weight and height measurements for calculation of BMI. The subjects were stratified according to the baseline CD4 count in three groups: a CD4 count <100 cells/μl, a CD4 count between 100-250 cells/μl, and a CD4 count >250 cells/μl. According to the baseline BMI the subjects were stratified into three groups: underweight BMI <18.5 kg/m², normal weight BMI 18.5-24.9 kg/m², and overweight BMI ≥25.0 kg/m². Median baseline CD4 count was $133 \pm 164.58$ cells/μl. Median baseline BMI was $19.0 \pm 2.7$ kg/m².

**3. Results**

Out of 69 analysed HIV positive ART-naïve subjects diagnosed with pulmonary tuberculosis, 28 (40.6%) had smear positive pulmonary tuberculosis and 41 (59.4%) smear negative pulmonary tuberculosis.

In the 28 smear positive subjects, 15 (53.6%) were underweight (BMI<18.5) and 13 (46.4%) had normal weight (BMI 18.5-24.9) ($p=0.36$). No subject with smear positive pulmonary tuberculosis, however, was found to be overweight. In 41 subjects with smear negative pulmonary tuberculosis, 15 (36.6%) subjects were underweight and 26 (63.4%) subjects had normal weight ($p=0.47$). No subject in both the sub-subsets was found to be overweight. (Fig. 1)

Baseline CD4 count analysis was performed in each subject. Out of 28 subjects with smear positive pulmonary tuberculosis 18 (64.3%) had their initial CD4 count lower than 100 cells/μl, 9 (32.1%) had a CD4 count in the range of 100-250, and 1 (3.6%) had a CD4 count above 250 ($p<0.05$). Out of 41 subjects with smear negative pulmonary tuberculosis, 8 (19.5%) had their CD4 count lower than 100 cells/μl, 21 (51.2%) had a CD4 count in the range of 100-250 and 12 (29.3%) had CD4 count above 250 ($p<0.05$). (Fig. 1)

Among the 28 subjects with smear positive pulmonary tuberculosis, 15 subjects had BMI below 18.5 kg/m² and 13 subjects had BMI in between 18.5 and 24.9 kg/m². Among the 15 subjects, 7 subjects (46.7%) had baseline CD4 counts below 100 cells/μl, 6 (40.0%) had baseline CD4 counts between 100-250 cells/μl, and 2 (13.3%) had CD4 counts above 250 cells/μl. Among the 13 subjects with BMI in the range from 18.5 to 24.9 kg/m², 7 subjects (53.8%) had
baseline CD4 counts below 100 cells/μl, 3 (23.1%) had baseline CD4 counts between 100-250 cells/μl, and 3 (23.1%) had CD4 counts above 250 cells/μl. \((p=0.68)\) (Fig. 2)

Among the 41 subjects with smear negative pulmonary tuberculosis, 15 subjects had BMI below 18.5 kg/m\(^2\) and 26 subjects had BMI in between 18.5 and 24.9 kg/m\(^2\). Among the 15 subjects, 6 subjects (40.0%) had baseline CD4 counts below 100 cells/μl, 5 (33.3%) had baseline CD4 counts between 100-250 cells/μl, and 4 (26.7%) had CD4 counts above 250 cells/μl. Among the 26 subjects with BMI in the range from 18.5 to 24.9 kg/m\(^2\), 7 subjects (26.9%) had baseline CD4 counts below 100 cells/μl, 11 (42.3%) had baseline CD4 counts between 100-250 cells/μl, and 8 (30.8%) had CD4 counts above 250 cells/μl. \((p=0.71)\) (Fig. 3)

4. Discussion

In the analysed cohort of HIV positive subjects involved in rural-urban migration, no significant association between low BMI and smear positive/smear negative pulmonary tuberculosis was seen. No subject with pulmonary tuberculosis irrespective of smear positivity, was found to have BMI of 25.0 and above. No significant differences in baseline BMI values were found in the two sub-sets of subjects. (Fig. 1)

Statistically significant were the findings in the cohort of subjects with smear positive pulmonary tuberculosis, 18/28 subjects (64.3%) had a baseline CD4 count below 100 cells/μl, 9/28 (31.1%) subjects had a baseline CD4 count in the range of 100-250, and 1/28 (3.6%) had a CD4 count above 250 cells/μl \((p<0.05)\). On the other hand, in the cohort of subjects with smear negative pulmonary tuberculosis, 8/41 subjects (19.5%) had a baseline CD4 count below 100 cells/μl, 21/41 (51.2%) subjects had a baseline CD4 count in the range of 100-250, and 12/41 (29.3%) had a CD4 count above 250 cells/μl \((p<0.05)\). This suggest that positivity of the sputum sample microscopy tends to be detected in patients with low CD4 counts; in other words in subjects with a significantly impaired immune system.

One of the limitations of the study was definitely a lack of diagnostic means. Only recently, the GeneXpert and mycobacterial culture became available for all the patients infected with HIV with suspected tuberculosis. However, mycobacterial culture is not suitable for immediate diagnosis, due to the fact that it is too slow and too complex to be used in resource-poor settings. Chest radiography itself, especially in HIV positive patients, also has its important shortcomings, one of them being low specificity. In a study performed in Kenya, the number of patients labelled as having TB using CXR with a negative culture that were placed in treatment was rather high: 22% among all suspects (smear positive and smear negative) and 45% among smear-negative suspects. (Cleeff et al. (2005))

Individuals involved in rural-urban migration to the capital city Nairobi, Kenya, due to low socioeconomic status associated with poor health outcomes, belong to a group of vulnerable individuals. They often seek health care professionals when their health condition has already significantly deteriorated, as our study demonstrated by the low baseline CD4 count. In addition, the scarcity of diagnostic methods available in resource-poor settings significantly restricts the provision of health care services. There is an urgent need for development of simpler, cheaper, and more sensitive diagnostics for tuberculosis for use in resource-poor settings.
**Figure 1** – Distribution of BMI and CD4 values in the cohort.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Smear positive PTB (n=28)</th>
<th>Smear negative PTB (n=41)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)⁺</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight</td>
<td>15 (53.6%)</td>
<td>15 (36.6%)</td>
<td></td>
</tr>
<tr>
<td>Normal weight</td>
<td>13 (46.4%)</td>
<td>26 (63.4%)</td>
<td>0.16</td>
</tr>
<tr>
<td>Overweight</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>CD4 (cells/μl)  &lt;100</td>
<td>18</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>100-250</td>
<td>9</td>
<td>21</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>&gt;250</td>
<td>1</td>
<td>12</td>
<td></td>
</tr>
</tbody>
</table>

⁺ Underweight defined as BMI <18.5 kg/m², normal weight BMI 18.5-24.9 kg/m², overweight BMI ≥25.0 kg/m².

**Figure 2** – Association between baseline BMI and CD4 count in smear positive subjects.

<table>
<thead>
<tr>
<th>Baseline CD4 count* (n=28)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100</td>
<td></td>
</tr>
<tr>
<td>100-250</td>
<td></td>
</tr>
<tr>
<td>&gt;250</td>
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</table>

<table>
<thead>
<tr>
<th>BMI</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>7 (7/7)</td>
</tr>
<tr>
<td>Normal weight</td>
<td>7 (7/3)</td>
</tr>
<tr>
<td>Overweight</td>
<td>0 (0/0)</td>
</tr>
</tbody>
</table>

* CD4 count expressed in cells/μl.

**Figure 3** – Association between baseline BMI and CD4 count in smear negative subjects.

<table>
<thead>
<tr>
<th>Baseline CD4 count* (n=41)</th>
<th>p value</th>
</tr>
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<tbody>
<tr>
<td>&lt;100</td>
<td></td>
</tr>
<tr>
<td>100-250</td>
<td></td>
</tr>
<tr>
<td>&gt;250</td>
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</table>

<table>
<thead>
<tr>
<th>BMI</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>6 (6/5)</td>
</tr>
<tr>
<td>Normal weight</td>
<td>7 (7/11)</td>
</tr>
<tr>
<td>Overweight</td>
<td>0 (0/0)</td>
</tr>
</tbody>
</table>

* CD4 count expressed in cells/μl.

**References:**


