Short communication

Pro-inflammatory Cytokine Profile of Pulmonary Tuberculosis Patients in Central Hospital, Agbor Nigeria

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Abstract

Background: The aim is to determine the pattern of cytokines secretion by assessing interleukins (IL-1, IL-6, and tumor necrosis factor-alpha (TNF-α) in pulmonary tuberculosis patients. **Materials and Methods:** A cross-sectional study was conducted on 146 consecutive (54 males and 92 females) sputum positive for tuberculosis and 38 apparently healthy age- and sex-matched sputum negative for tuberculosis as control were recruited between May 2016 and June 2017. A volume of 5 mL of blood samples was collected for the determination of serum IL-1, IL-6 and TNF-α using the ELISA method. **Results:** There was a higher cytokine mean ± standard error of the mean for tuberculosis subjects (95.77 ± 6.68 pg/mL; 107.54 ± 14.76 pg/mL, 122.09 ± 16.55 pg/ml) and controls (79.88 ± 3.53 pg/ml; 78.35 ± 6.82 pg/ml; 94.11 ± 14.08 pg/ml) for interleukin-1, interleukin-6, and TNF-α, respectively, when compared. There was strong correlation between mean values of IL-6 and TNF-α (r = 0.72315, $P < 0.05$). There was significance difference ($P < 0.05$) observed in the mean serum concentrations of cytokines among the genders ($P < 0.05$). **Conclusion:** The study revealed that IL-1, IL-6, TNF-α are important biological markers for tuberculosis disease.

Keywords: Biomarkers, cytokine, Nigeria, proinflammatory, tuberculosis

Introduction

Mycobacterium tuberculosis (Mtb) infection is contracted by inhalation of the microorganism in infected droplets containing the microorganism. Not all that are exposed to Mtb develops clinical signs and symptoms suggestive of the disease, suggesting that the human body exhibits immune responses which are sufficient to naturally control the infective process. The development into a clinically active disease occurs only in a small proportion of individuals who harbor latent infection.[1] Pathogenesis of Mtb involves cell-mediated immune response, which can be studied with the use of peripheral blood and cells harvested from the lungs. A substantial humoral response to Mtb occurs, although the significance of this response in terms of control of the disease is unknown.[2] Immune response to Mtb is important in the control of the disease and how the cells of the immune system help in the elimination or development of clinically active disease conditions.[3] Cytokines are secreted by T helper cells against the infectious agents are of critical importance for the outcome of many diseases. Tumour necrosis factor-alpha (TNF-α) as well as the reactive nitrogen production by macrophages early in tuberculosis infection had been found to be critical for protection against tuberculosis.[4] Several cytokines have been suggested to be involved in tuberculosis pathogenesis; hence, they are considered biomarkers for tuberculosis.[5,6] The present study was conducted to determine the serum level of interleukin-1 (IL-1), IL-6, and TNF-α in tuberculosis and determine their significance as biomarkers.

Materials and Methods

Study population

A cross-sectional study was conducted on 146 consecutive patients attending Central Hospital Agbor who tested sputum positive for tuberculosis using GeneXpert technologies from May

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2016 to June 2017 and 38 apparently healthy subjects as controls. Ethical Clearance was obtained from Delta State Ministry of Health, Asaba and Central Hospital, Agbor, for the study.

Specimen collection and Analysis

Five milliliters of venous blood was collected asceptically into a plain vacutainer tubes and allowed to clot, separated and kept frozen until analysis. Serum IL-1β, IL-6, and TNF-α were evaluated by the ELISA method (Elabscience, Houston, USA.) following the manufacturer's instructions.

Data analysis

Statistical data were analyzed using the IBM Corp. Statistical Package for Social Sciences (SPSS) Version 21. Armonk, NY, USA. Student *t*-test and Pearson's correlation were used with a $P < 0.05$ considered significant.

Results

Figure 1 shows the mean ± standard error of the mean (SEM) gender distribution of cytokine concentration among the study population. There was a statistically significance difference ($P < 0.05$) in the mean serum concentrations of cytokines among the genders. Female TB subjects have a higher mean concentration of TNF-α and IL-6, whereas the male TB subjects had higher mean levels of IL-1 when compared.

Figure 2 shows the mean ± SEM of cytokine concentration among the study population among age groups. There was a statistically significance difference ($P < 0.05$) in the mean serum concentrations of IL-1 among the age groups. However, age group 0–15 years had the highest mean ± SEM serum concentration of IL-1 (138.80 ± 60.50) and TNF-α (166.18 ± 81.04); while the age group 61–75 years recorded the highest values for IL-6 (117.13 ± 31.23). There was no significance ($P > 0.05$) in IL-6 and TNF-α in the study population when compared.

Figure 3 is the bar chart of the profile of the mean serum cytokines of TB subjects and controls. There was significantly higher ($P < 0.05$) serum concentration of IL-1 (95.77 ± 6.78); IL-6 (107.54 ± 14.76) and TNF-α (122.09 ± 16.55) in TB subjects when compared with controls (79.88 ± 3.53; 78.35 ± 6.82; 94.11 ± 14.08).

There was a very strong significant correlation between IL-6 and TNF-α ($r = 0.73215$; $P < 0.05$) as shown in Figure 4.

Discussion

Cytokines regulate the cellular immune response and offer protection against infectious diseases such as Mtb infection. IL-1 was observed to be significantly higher ($P < 0.05$) in tuberculosis subjects (95.77 ± 6.78 pg/ml) when compared with control individuals (79.88 ± 3.53). This is in tandem with an earlier study,[8] which reported IL-1 as a pivotal cytokine in defense against tuberculosis. This finding probably suggests that IL-1 has an elaborate time of clinical manifestation of tuberculosis, thereby have higher serum concentrations before the commencement of treatment. IL-1 released by macrophages are actively involved the regulation of immunity at the site of infection.[8] Furthermore, the increased IL-1 in the tuberculosis subjects may likely be associated with the role they play in the formation of IL-1 granuloma, as reported by previous authors.[9] Male Mtb subjects had significantly higher IL-1 when compared with female Mtb subjects. This is in agreement with a previous study,[10] which reported similar results. This may be attributed to the activities of estrogen in female subjects.

IL-6 enhances the growth of the invading mycobacteria inside monocytes;[11,12] hence, IL-6 is critical for the development of resistance in tuberculosis infection.[13] This study observed significantly higher IL-6 levels Mtb subjects. This finding is in agreement Correia *et al*.[14] which reported that IL-6 is activated in response to host defense against Mtb. Wong *et al*.[15] in their study suggested that the ability to diagnose tuberculosis using IL-6 and TNF-α are known to have significantly higher concentration than nontuberculosis patients. In this study, there was a strong significant correlation

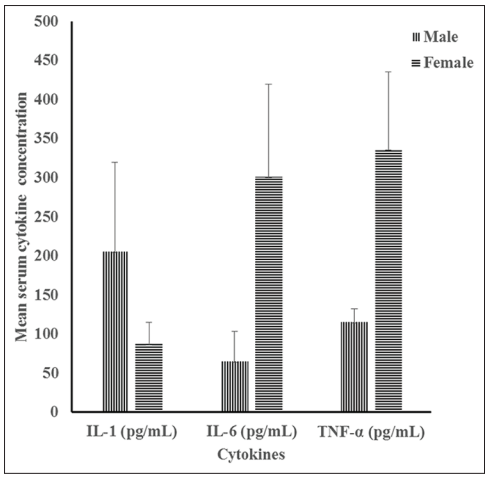

Figure 1: Bar chart of mean ± SEM of serum concentration of cytokines among study population based on gender

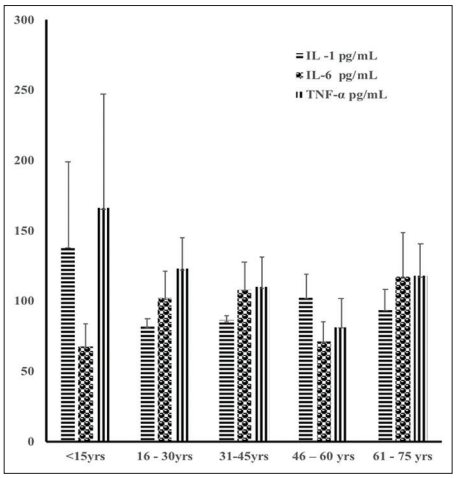

Figure 2: Bar chart of the mean serum concentrations of cytokines of age groups in the study population

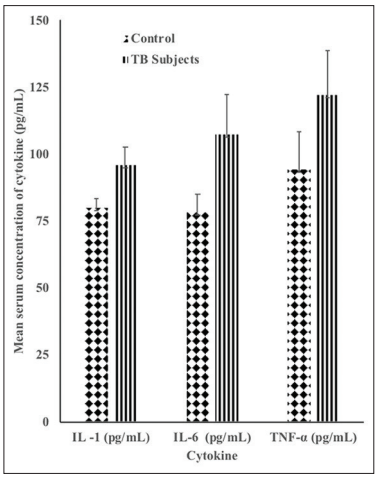

Figure 3: Bar chart of the mean serum concentrations of cytokines in the tuberculosis subjects and the healthy controls

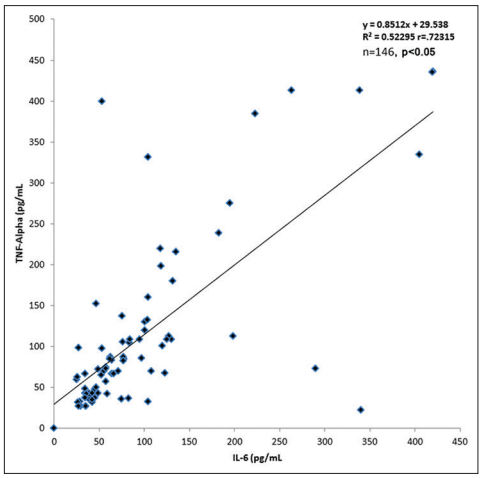

Figure 4: Relationship between circulating concentration of interleukin-6 and tumor necrosis factor-alpha in tuberculosis subjects

between IL-6 and TNF-α (r = 0.732, P < 0.05. IL-6 was significantly higher (P < 0.05) in female tuberculosis subjects than male tuberculosis subjects when compared. TNF-α, an important pro-inflammatory cytokine, plays a critical role in the pathogenesis of diseases, especially in the initiation of inflammation at the site of infection.[16-18] TNF-α has been found to enhances cell to cell communication in tuberculosis.[19] The results of this study show that TNF-α has the highest value in picogram per milliliter among the studied cytokine. The high mean serum concentration of TNF-α was observed in drug naïve tuberculosis subjects (122.09 ± 16.55 pg/ml) compared with healthy controls (94.11 ± 14.08 pg/ml) is consistent with the baseline values obtained by Deveci *et al*.[20] in their study on patients in active tuberculosis treatment and Pereira *et al*.[21] Hence, serum concentrations of TNF-α mirrored the extent of the severity of tuberculosis. TNF-α receptors are essential for the reactive nitrogen production by macrophages in early tuberculosis infection.[22] The finding of higher serum levels of TNF-α in active TB patients than the controls agrees with those of Shameem *et al*.[23] Thus, TNF-α may be used as an early marker of drug sensitivity in patients preparatory for TB treatment because TNF-α is produced at the site of disease in TB patients. Previous authors reported that TNF-α in plasma is closely associated with clinical deterioration in tuberculosis infection.[24] Activated macrophages and T-lymphocytes are the major TNF-α-producing cell which are required to increase the ability of macrophages to stimulates apoptosis and phagocytose the mycobacteria with the macrophages.[25,26] TNF-α was observed to be significantly higher in female tuberculosis subjects than male tuberculosis subjects. This is in tandem with the previous report by earlier authors.[10]

Conclusion

This study has observed that there is a strong correlation in the use of pro-inflammatory cytokines as a biomarker in the diagnosis, monitoring, and management of tuberculosis. Further research on these and more cytokines in order to determine their specific roles in diagnosis treatment and management of tuberculosis infection is strong advised.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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