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Interleukin (IL)-1α, IL–7 and IL–13 Profile among individuals with *Schistosoma haematobium* infection in Ewan Community, Edo State, Nigeria

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ABSTRACT

Schistosomiasis is an endemic parasitic disease exclusively located in tropical Africa, Asia and North America. The infection processes and indeed the control of this infection partly require an understanding of cytokine immune responses to the disease. This study therefore aims at determining the profiles of cytokines (interleukins) (IL) (IL-1α, IL-7 and IL–13) among schistosomes positive individuals. The investigation was carried out in Ewan in Edo State, Nigeria. Sera from 35 seropositive subjects were categorized as lightly and heavily positive. Also, 16 of these 35 seropositive subjects demonstrated parasites in the blood and as a result were further grouped into lightly infected (n = 4) and heavily infected (n = 12) of schistosomiasis based on the demonstration of *Schistosoma haematobium* infection. Sera of seropositive subjects were subjected to IL-1α, IL-7 and IL-13 assays. In the serum, IL-1α levels were significantly higher among the heavily positive subjects than the control subjects ($p < 0.05$). Conversely, depressed level of IL-1α was seen for schistosomiasis lightly positive subjects ($p < 0.001$). IL-7 level was significantly lower in heavily positive individuals than control subjects and lightly positive IL-7 level was significantly depressed ($p < 0.05$). There was no significant difference in IL-13 levels among schistosomes infected individuals and their non-infected counterparts. The depressed levels of serum IL-1α and IL -7 should serve as markers for individuals with lightly positive schistosomiasis infection in Ewan, Edo State, Nigeria.

Keywords: Interleukins, profile, schistosomes, Ewan Community.

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INTRODUCTION

Urinary schistosomiasis caused by *Schistosoma haematobium* is one of the most common tropical diseases which poses serious health hazard due to its associated morbidities. Globally, over 153 million are infected with this parasitic infection (Imarenezor et al., 2013). In Nigeria, pockets of foci of infections have been documented in various parts of the country (Imarenezor et al., 2016). In developing nations, the true epidemiological picture appears difficult because of inadequate research in this direction despite its relevance in planning its control in any locality (Imarenezor et al., 2013). This problem is compounded by the poor habits of people in developing countries like Nigeria in visiting hospitals for treatment. Also self-medication is still practiced as manifested by anthelminthic abuse (Mill et al., 2000). This act is worsened by presence of inadequate health facilities. One of the consequences of the self-medication and anthelminthic abuse includes the suppression of the egg laying capacity of the worms (Weitzmann et al., 2000).The net effect is erroneous diagnosis using ova in urine in any locality (Imarenezor et al., 2016). This may also become evidence in sub clinical

cases and period of immaturity of the worms when they are yet to commence egg lying (Goerdt and Orfanos, 2009). Another obvious difficulty occurs during very low grade infections. Although the uses of serological diagnosis are available, poverty poses a major serious impediment to the applications of serology in the epidemiological work in these countries (Scharton-kersten and Sher, 2002). To this end, this paper tends to evaluate the relative importance of cytokines in the control of schistosomes and there divergent roles in immunopathology of this disease, there is paucity of information in relation to the status of IL-1α, Il-7 and IL-13 in schistosomes infected individuals in our locality. This investigation therefore seeks to determine the profile of these cytokines in schistosomes positive subjects in an endemic community like Ewan in Nigeria.

MATERIALS AND METHODS

This study was carried out in Ewan community in Akoko Edo Local Government Area, Edo State, Nigeria. The community lies between latitude 70° N and longitude 60° E with population of over 4,000 inhabitants. The people in the studied community are predominantly farmers.

Ethical considerations

Ethical clearance was obtained from the Edo State Ministry of Health and Ewan Health Centre. Before the commencement of the investigation, the nature, objectives and benefits of the investigation were thoroughly explained to inhabitants of these communities. Informed consents were obtained from 272 individuals who were screened for schistosomiasis infection.

Population recruited

Of the 272 individuals screened, sera of 35 seropositive subjects with *Schisotosoma haematobium* infection were evaluated for interleukins (IL-1α, IL-7 and IL-13) levels.

Staging of schistosomes

Sera obtained from venous blood were used to categorize the level of infection by double serial dilution as: lightly positive (1:2-1:4) (n=9) and heavily positive (≥1:32) (n = 14) according to the manufacturer's instruction (Instituut voor Tropische Geneeskunde, Antwerpen, Belgium). Of the 35 seropositive, 16 individuals demonstrated parasite in the examined blood.

Exclusion criteria

Individuals with Hepatitis B, HIV or sickle cell anemia were excluded from the study.

Interleukin assay

Sera were obtained from 35 schistosomes positive subjects and then assayed for IL-1α, IL-7 and IL-13 using standard enzyme linked Immunosorbent assay (ELISA) according to the manufacturer's instruction (Abcam Plc, United kingdom). Also, interleukin evaluation was carried out on 10 individuals who are seronegative for schistosome infection and other aforementioned diseases as control group.

Data analysis

Data obtained were analysed using Welch t-test and Tukey-analysis of variance (ANOVA).

RESULTS

Figure 1 shows IL-1α profile among categories of seropositive human subjects. The differences in the levels of IL-1α for lightly positive compared with the control subjects were not significant. Serum IL-1a levels were significantly higher in heavily positive subjects than control subjects ($P < 0.05$). The serum IL-1α concentrations for the categories of seropositive subjects were not significant.

Table 1 presents the IL-1α, IL-7 and IL-13 concentrations in serum of subjects with light and heavy stages of infection. The difference in serum IL-1α concentrations between light and heavy stages of infection was statistically significant ($p < 0.001$). The levels of IL-7 for lightly positive subjects were not significant ($p > 0.05$). However, IL-7 level in heavily positive subjects was significantly lower than the control subjects ($p < 0.001$). There was no significant difference in the IL-7 concentration of seropositive subjects ($p > 0.01$) (Figure 2). The mean difference in serum IL-7 concentrations between lightly positive and heavily positive infection were statistically significant ($p < 0.05$). The mean differences of IL-13 levels compared with schistosomes negative volunteers were not significant ($p > 0.05$) (Figure 3). The differences in the levels of IL-13 among the categories of seropositive subjects were also not significant ($p > 0.01$). This suggests that IL-1a may be implicated in the immunopathogenesis of *Schistosoma haematobium* infection.

The authors reported unaltered IL-13 levels in seropositive and serum IL-13 levels in the lightly and heavily positive of *Schistosoma haematobium* infected human subjects.

DISCUSSION

Our data demonstrated elevated level of serum IL-1α among the strongly seropositive volunteers. Similarly, serum IL-1α levels of schistosomes in heavily positive patients were increased compared to lightly positive. The elevated levels of serum IL-1α supports the report of (Kovacs et al., 2008) in which derived variant surface glycoprotein (VSG) from *S. haematobium* elicit IL-1α. This suggests that IL-1α may be implicated in the immunopathogenesis of schistosomes infection. We also

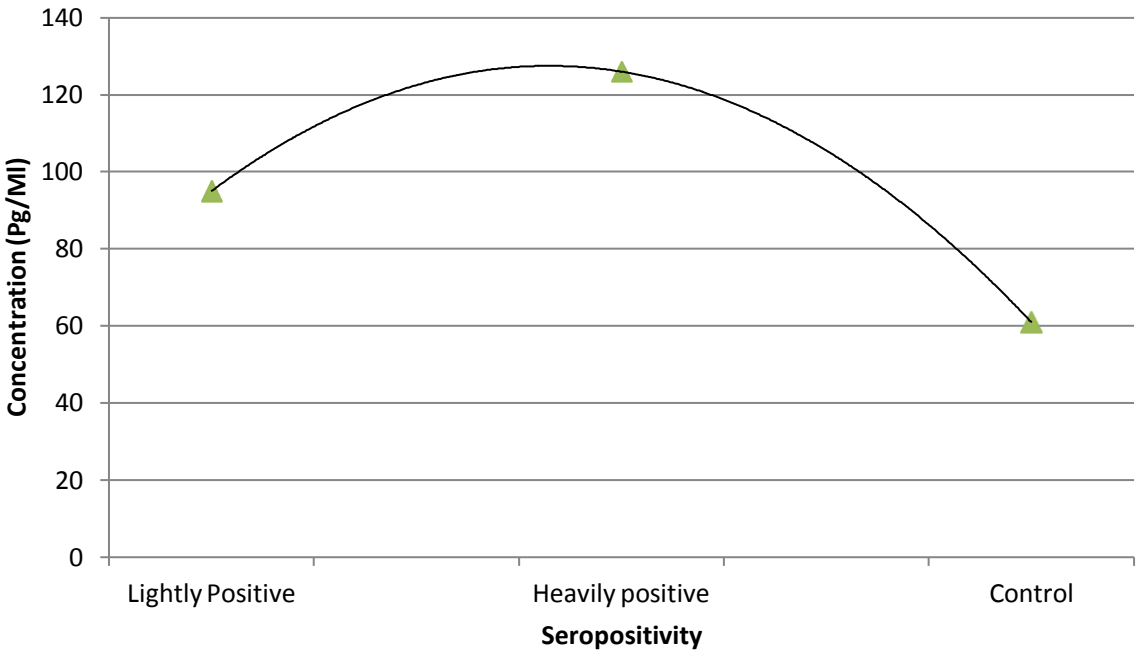

Figure 1. IL-1α profile among categories of seropositive.

Table 1. IL-1α, IL-7 and IL-13 Profile in serum of individuals infected lightly and heavily with schisotosomes.

Parameter	Lightly infected n = 4	Heavily infected n = 12	Mean difference	t-value	Control
Mean serum IL-1α (pg/ml)	95.41 ± 11.51	125.95 ± 9.66	95% CI: 17.36 to 42.6	5.15	60.84 ± 31.32
Mean serum IL-7 (pg/ml)	135.98 ± 4.43	122.30 ± 6.29	95% CI: -19.86 to -7.69	4.93	159.64 ± 77.73
Mean serum IL -13 (pg/ml)	62.01 ± 4.10	65.57 ± 4.22	95% CI: -1.98 to 7.06	1.32	50.0 ± 15.47

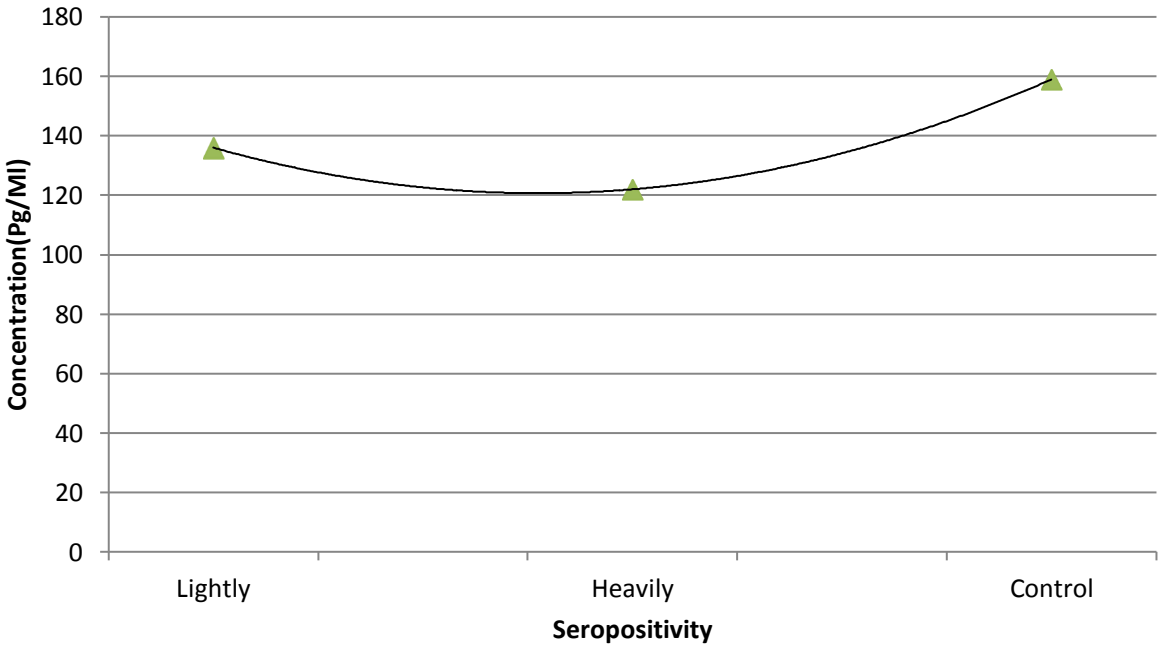

Figure 2. IL-7 profile among categories of seropositive.

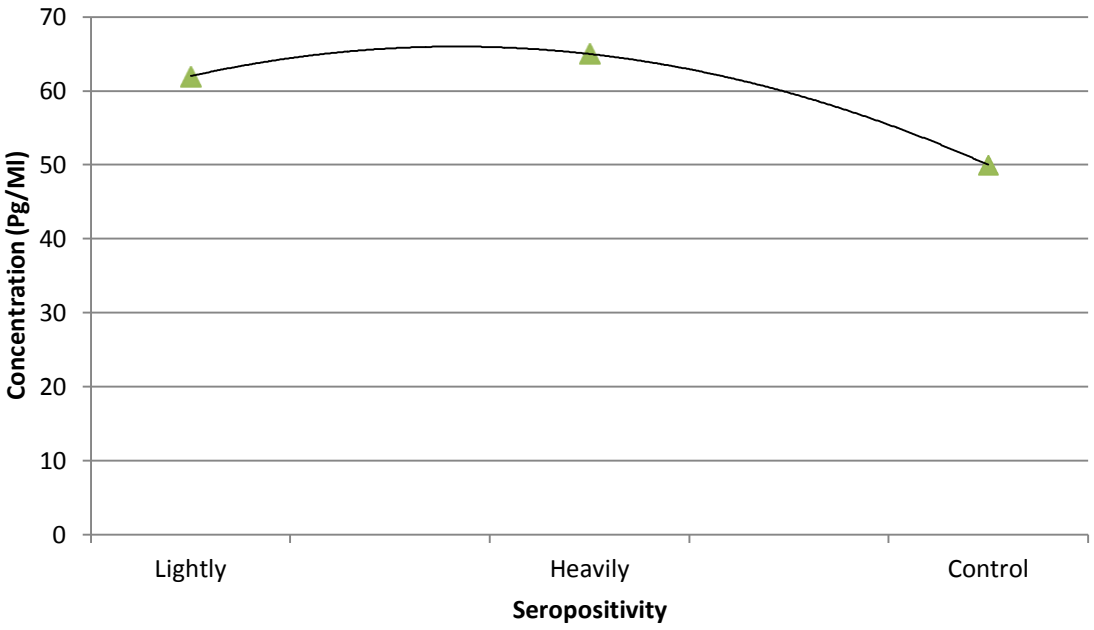

Figure 3. IL-13 profile among categories of seropositive.

observed that the profile of IL-13, an anti-inflammatory cytokine was unaltered in the serum of heavily positive individuals. This data therefore suggests that the imbalance between IL-13 and IL-1α could be due to the inability of IL-13 to immunomodulate IL-1α in schistosomes heavily positive subjects. This partly contradicts the hypothesis of a switch from dominant type I to a predominant type II cytokine (Goerdt and Orfanos, 2009). The authors observed depressed levels of IL-7 with severity of infection. These findings contradict the report that human chronic schistosomiasis was associated with elevated IL-7 production (Schopf et al., 2008). It has been documented that natural killer cells are recognized as major effectors of innate resistance to protozoan infections through the control of the growth of this pathogens by indirectly producing cytokines (Imarenezor et al., 2016). In a report, by Mukodzi et al. (2002), IL-7 deficient patients were observed to be deficient of T and natural killer (NK) cells. This study therefore suggests that depressed IL-7 concentration with disease progression may be associated with the pathogenic conditions in schistosomes positive patients which could be due to a regulatory role of anti-inflammatory cytokine in the serum as documented by (Landmark *et al*., 2007). We therefore suggest that IL-13 is not a mediator to host immune response of schistosomes infection. This observation is in consonance with the report that IL-13 in schistosomes susceptible mice was not the main trigger of alternative macrophages because IL-13 signalling occurred independently of an anti-inflammatory cytokine (IL-4), corroborating the natural propensity of animals to develop alternatively activated macrophages (Hestdal et al., 1992; Mills et al., 2000). The clearance of schistosome parasites through innate immunity involves macrophage/monocyte phagocyte system (Imarenezor et al., 2016).

Conclusion

This investigation showed elevated IL-1α among the heavily positive volunteers. Conversely, depressed levels of IL-7 were observed in heavily positive volunteers. These data suggests that IL-1a and IL-7 could be major mediators in the immunopathology of *S. haematobium* infection. Additionally, we propose that depressed levels of IL-7 should serve as a marker of schistosomes diagnosis in heavily positive subjects in our locality.

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