Original article:

Intestinal Parasitic Infections and Eosinophilia: A Cross-sectional Study among Primary School-aged Children in Medan, Indonesia

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Abstract:

Background: Intestinal parasitic infections (IPIs) and its implication, such as malnutrition, growth stunting, anemia, and concentration impairment, still become a global burden. The primary immune cell that firstly involved in counteracting parasitic invasion is eosinophil. Therefore, higher levels of eosinophils could be suspected of having a parasitic infection.

Objective: Our study aimed to reveal the prevalence of IPIs and its correlation with eosinophilia.

Material and Methods: The study was located in two different public primary schools, Public Primary School 060925 Harjosari 1, Amplas, Medan, Indonesia and Public Primary School 101747 Hamparan Perak, Deli Serdang, Indonesia which enrolled 132 primary school children aged 8-12 years graded III-VI, consisting of 22 males and 110 females, who had met the inclusion criteria between May and October 2016. Parasitology examination was carried out at the Department of Parasitology, Faculty of Medicine, Universitas Sumatera Utara using Kato-Katz, Lugol, trichrome, and modified acid-fast stain.

Results: The study found intestinal protozoa infections were the most common IPIs in the population, Giardia lamblia as the most prevalent species (37.1%), while hookworm with the fewest findings (2.8%). Additionally, the statistical analysis proved a significant correlation between IPIs and eosinophilia (p-value 0.021; 95% CI 1.13-5.58).

Conclusion: eosinophilia patients with profound clinical manifestation should be further assessed to be considered for the administration of anti-parasitic medication.

Keywords: Parasites, helminthiasis, eosinophils, protozoa

Introduction

Intestinal parasitic infections (IPIs) are parasitic infections caused by helminthic and protozoal manifestations, and it remains a neglected health problem for developing countries, particularly Indonesia. IPIs could clinically produce mild diarrhea in humans or severe debilitating symptoms and long-term complications. Chronic infection of the organism frequently leads to malnutrition, growth stunting, and cognitive impairment among children.1 IPIs are separated into two different groups, Soil-transmitted Helminth (STHs) and intestinal protozoa infections, based on its etiologic agent. Giardia lamblia, Cryptosporidium parvum, and Entamoeba histolytica are the most common intestinal protozoa infection. Ascaris lumbricoides, Trichuris trichiura, and hookworm are the most prevalent STH. The prevalence of IPIs is varied, higher in developing regions ranging from 34.2-65.5% in Ethiopia,1 31% in Indonesia4, and 65-90.4% in Sudan.5 6 The initiation of immune response starts as early...
as the organism firstly invaded the outer barrier of the intestinal mucosa. The recognition and effector immune cell spends for at least hours or days, but eosinophil acts a pivotal role in primary response for parasitic invasion concurrent with the other active immune reaction. Eosinophil counts for 2-3% of the total leukocytes in human; it will fully function after the exposure of specific virulence factor followed by a cytotoxic effect in the mucosal environment. Therefore, It will elevate or so-called ‘eosinophilia’ as a result of parasitic invasion or emerging autoimmune disease. Neglecting eosinophilia patients could cause significant implication towards the patient quality of life. There must be a thorough anamnesis and precise information relating to existing risk factors and previous illnesses which supported by physical and laboratory examination.\(^7\)

The major inducer for eosinophil proliferation is interleukin-5 (IL-5), which produced as a response of parasitic infections. IL-5 plays an essential role as the eosinophil activator after its secretion from the activated T-helper 2 (Th2) which exposed to intestinal parasites.\(^8\) The primary objective of the study was to identify the species of human intestinal parasitic infections (IPIs) among primary school-aged children and assessed the correlation between the prevalence of IPIs and eosinophilia. The findings of the study would strengthen the evidence of the association between eosinophilia and parasitic intestinal infections that help the clinician to determine the diagnosis.

**Materials and Methods**

**Study location and population**

We conducted the cross-sectional study in Medan, Indonesia which is located along the northeastern coast of Sumatera Island with a coordinate of 3°35′ N 98°40′ E. There were approximately 2,097,610 people in the city based on the 2010 census. The regional climate is known as tropical rainforest climate with no significant dry season and average temperatures 27°C (81°F) throughout the year which is very supportive for the parasitic proliferation and development.

There were 132 school-aged children, 22 males and 110 females, from two different public primary schools, Public Primary School 060925 Harjosari 1, Medan and Public Primary School 101747 Hamparan Perak, Deli Serdang, Indonesia who enrolled into the study between May and October 2016. The study location was selected as the matter of its densely populated characteristic with poor hygiene and sanitation environment. The guardian’s consent is the main inclusion criteria for the children while the other obligatory criteria, including aged 8-12 years, graded III-VI, no consumption of anti-helminthic drug for the past six months, and no history of immunological disorder (allergy, asthma, atopic dermatitis, rheumatic disease, immunodeficiency, malignancies, other infectious disease or hemophilia).

There was a brief oral explanation to all guardians who gave permissions for the children enrollment of the study as well as filling the short questionnaire for any previous or existing illnesses. One small plastic fecal container labeled with the children’s name was given to the guardian for the fecal sample examination in the Department of Parasitology, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia.

**Parasitological examination and eosinophil count**

The parasitological examination for helminthic and protozoal species includes Kato-Katz, as its sensitivity reached 74-95% when used in places with high infection rate\(^9\), Lugol, trichrome staining, and modified acid-fast staining or Kinyoun-gabbet for *Cryptosporidium sp.* infections\(^10\). In addition, eosinophil count was based on traditional technique using an improved Neubauer counting method and peripheral blood smear, calculating the absolute value in 1 mm\(^3\) per high-power field, under a light microscope. Blood was obtained from venous sampling via venipuncture to cubital vein as much as 3 ml which directly mixed in a tube containing EDTA. The interpretation for eosinophil count has two different categories, normal (1-6%) and eosinophilia (>6%).

**Data Analysis and study approval**

All data were doubled-checked in Microsoft Excel before the final analysis using Statistical Package for Social Sciences 21 (SPSS Inc. version 21).
Subsequently, the correlation between eosinophilia and IPIs were demonstrated using p-value < 0.05 which extracted from the Spearman correlation test and presented the data into a single table. The study has also obtained approval from the Medical Ethics Committee, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia.

**Results**

A total of 35 children were positive for IPIs consisting of 10 samples (28.5%) for Soil-transmitted helminths (STHs) and 25 samples (71.5%) for intestinal protozoa infections. The variation was demonstrated in Table 1 with *Giardia lamblia* as the prevalent species followed by *Entamoeba coli*; it showed that protozoal infection still predominated the infected children in the study. The prevalence of intestinal protozoa infections outnumbered STH findings among the population (71.4% versus 28.6%). Meanwhile, eosinophils were calculated under routine microscopic examination and produced the results demonstrated in Table 1 and Table 2. The study also obtained a significant correlation between IPIs and eosinophilia (p-value=0.021) and the higher median value of eosinophil levels among IPI-infected children was evident.

**Table 1.** Intestinal Parasitic Infection (IPI) species and effect on eosinophil levels

<table>
<thead>
<tr>
<th>IPIs species</th>
<th>n=35</th>
<th>%</th>
<th>Eosinophil levels (Median±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascaris lumbricoides</td>
<td>4</td>
<td>11.4</td>
<td>6.05 ± 2.21</td>
</tr>
<tr>
<td>Hookworm</td>
<td>1</td>
<td>2.8</td>
<td>2.5± 0.00</td>
</tr>
<tr>
<td>Trichuris trichiura</td>
<td>5</td>
<td>14.2</td>
<td>6.7 ± 3.2</td>
</tr>
<tr>
<td>Giardia lamblia</td>
<td>13</td>
<td>37.1</td>
<td>4.7 ± 7.14</td>
</tr>
<tr>
<td>Entamoeba coli</td>
<td>8</td>
<td>22.8</td>
<td>3.7 ± 2.82</td>
</tr>
<tr>
<td>Iodoamoeubabuschii</td>
<td>3</td>
<td>8.5</td>
<td>3.1 ± 1.78</td>
</tr>
<tr>
<td>G.lamblia&amp;I. butschii</td>
<td>1</td>
<td>2.8</td>
<td>2.8± 0.00</td>
</tr>
</tbody>
</table>

**Table 2.** Correlation between Intestinal Parasitic Infections (IPIs) and eosinophil levels among school-aged children

<table>
<thead>
<tr>
<th>Variable</th>
<th>n=132</th>
<th>%</th>
<th>Eosinophil levels (Median±SD)</th>
<th>r</th>
<th>p-value</th>
<th>PR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPIs (n=132)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>35</td>
<td>26.5</td>
<td>4.50 ± 5.36</td>
<td>0.197</td>
<td>0.021</td>
<td>2.51 (1.13-5.58)</td>
</tr>
<tr>
<td>No</td>
<td>97</td>
<td>73.5</td>
<td>3.60 ± 3.41</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Discussions**

The study result demonstrated the infection rate for 26.5% of 135 children which proved on findings of the parasitological examination. They were positive for seven distinct parasitological species with specific pathogenesis and virulence factors. The high-prevalent of IPIs among children gave the evidence that the infection remains a neglected tropical infectious disease among population whereas children are significantly affected by the infection. Several implications related to IPIs were emphasized from recent studies particularly in densely populated areas and associated with poor sanitation, inadequate access to clean water, lack of proper hygiene and sanitation knowledge. Poverty can also lead to an increase in the prevalence of IPIs as well as slow socioeconomic status that vulnerably suffer from a vicious circle of re-infection, leading to the higher morbidity. In the previous study, it was found that 40% of children in a similar location infected with STH and more than one-third of children were categorized as underweight. Underweight is noticeable as one of the clinical implications relating to chronic parasitic infection because it affects micronutrient absorption and ultimately increases the prevalence of malnutrition in the infected population.

Our study showed that intestinal protozoa infections are prevalent among children. *Giardia lamblia* appeared as the frequent infections of all IPIs (37.1 %) while the second most frequent was *Entamoeba coli* (22.8%). Similarly, Mehraj et al. and Chaudhry et al. conducted two different studies in Pakistan discovered that intestinal protozoa infection were highly prevalent, while *Giardia lamblia* became the main species found in the survey study. *Giardia lamblia* (also known as *G.duodenalis* and *G.intestinalis*) is a common intestinal protozoal species which infected 280 million people each year worldwide. *G.lamblia* has potential to cause persistent and recurrent infections as it is ubiquitous organism which also related to several clinical implications including worsening bowel permeability, growth impairment, wasting, and cognitive impairment.

Meanwhile, STH infections are also strongly associated with poor knowledge of proper behavior related to defecation process, hand washing, and the exposure with infected soil with fertilized eggs and larvae. Additionally, the infection burden is also highly associated with the environment as well as become a modifiable risk factor causing IPIs. Behavior, genetically susceptible, inadequate health care, and malnutrition are also increase the susceptibility of an individual infected with IPIs. Several studies conducted in different locations suggested that school-aged children.
suffered the most from various complications of the infection, such as significant iron deficiency anemia which may lead to decreased concentration, physical and cognitive development that are finally reducing school performance.19

Blood component builds human immune system to serve as natural resources in eradicating foreign antigen invasion, including lymphocytes, neutrophils, monocyte, and eosinophils. Eosinophilia can occur as a result of two pathological conditions, infectious and non-infectious process that is hard to distinguish each of two clinical entities. The clinician should consider the type of patient, concurrent symptoms, eosinophilia duration, and the severity of eosinophilia to strengthen the clinical evidence relating to the suspected diagnosis. Acute presentation of eosinophilia could represent autoimmune disease, acute schistosomiasis, or coccidiomycosis infection. Helminthiasis also appears with eosinophilia, notably coinciding with larval migration through tissue.

Based on our study, there was a significant correlation between IPIs and eosinophilia (p-value < 0.021). Ustun et al. also found similar result suggesting that eosinophil levels were higher among IPIs than in the control group (7.0% versus 6.5%) but not statistically significant.20 The study also observed higher levels of IL-5 in the group which was positive for a protozoal infection and statistically significant proven (p-value < 0.05). Kaminsky et al. conducted a study to observe IPIs and eosinophilia among HIV positive population; they found that STHs were highly prevalent among the people and correlated with eosinophilia (p-value < 0.05).21 Al-Mozan et al. examined the alteration of the blood component in IPIs patients, and concluded the findings ranges from the increase and decrease of each blood component still following the particular parasitic species.22 Higher levels of eosinophils emerged in mixed infection (6%) as well as *Hymenolepsis nana* and protozoa infections. In our study, it was found that single infection of soil-transmitted helminths (STHs), such as *T. trichiura* and *A. lumbricoides* samples, had higher eosinophils levels (median 6.7% and 6.05% respectively) compared to other IPIs and the lowest was found in hookworm and mixed infection (*G. lamblia* and *I. butschii*), with the median of 2.5% and 2.8%.

**Conclusions**

Intestinal Parasitic Infections (IPIs) are described as one of neglected tropical infectious disease as it is relentlessly producing clinical implications in the general population, mainly in school-aged children. The study findings could add evidence of eosinophilia individuals who suffered from a parasitic infection that directly could help the clinician to narrow the differential diagnosis. Furthermore, the presence of eosinophilia among high-risk patients will lead to further examination, including fecal examination, or even the administration of anthelmintic and antiprotozoal medications. Additionally, further study is also needed to determine the level of eosinophil threshold that can be used as a marker of infection with larger sample size.

**Conflict of interest declaration:** There was no conflict of interest

**Ethical clearance:** The study has been approve by the ethical medical research committee, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

**Author’s contribution:** First and Second author has involved in whole stages of publication process while the rest contributed for data analysis until manuscript preparation.
References: