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Cytokine Analysis in Adults with Soil Transmitted Helminths Infection in Padang City and Detection of IgG4 from Ascariasis Infection

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A B S T R A C T

There are lots of worms that live in the dirt. All persons, including the elderly, are frequently discovered to have soil-transmitted helminths (STH). This is so that the parasite can influence how the immune system reacts by elevating IgG4 antibody levels. *A. lumbricoides* antigen-specific antibodies are found in blood samples using the ELISA method's IgG4 detection. STH infection compromises the human immune system, leading to elevated immunoglobulin E (IgE) levels, eosinophilia, and the generation of T-helper 2 (Th2) cells, particularly in response to variations in TNF- α and IL-4 levels. The ascariasis and STH are detected in this evaluation using the *A. lumbricoides* IgG ELISA Kit, TNF- α, and IL-4 ELISA Kit. The purpose of this research is to ascertain the incidence of STH in adults. There were 78 participants in this study; the most common age range was 46–55 years old (28 participants); the most prevalent sex was female (65 participants); 57 participants tested positive for IgG4; the majority of sufferers were in the 17–25 year age group (88.9%); and the majority were of the male sex (76.9%); the levels of TNF– α and IL–4 were checked, and they were found to be 18.9%. In this study, women between the ages of 46 and 55 make up the majority of the respondents. The majority of respondents were female and between the ages of 17 and 25, and less than half of them diagnosed ascariasis and STH.

Introduction

Soil-borne infection, also known as soil-transmitted helminth (STH), is the only common health problem that occurs in tropical countries (Incani *et al.,* 2017). This infection is spread by STH worm eggs that are found in contaminated human feces in areas with poor sanitation (Dunn *et al.,* 2016). This disease usually does not cause death, but it causes chronic infection and prolonged morbidity and disrupts a country's economic growth (Silver *et al.,* 2018). *A. lumbricoides* has the highest prevalence rate, with an estimated 807 million to 1.2 million people worldwide (CDC, 2020). West Sumatra has reached second place with an estimated prevalence

rate of 82.3% in a survey of 10 provinces in Indonesia regarding worm prevalence (Renanti and Rusjdi, 2015). A profile of the Padang City Health Office from 2012 to 2015 also revealed that the intensity of STH infection in the city of Padang is increasing, and the Koto Tangah Sub-District has become an area with a high prevalence in the last three years, with estimates of around 690, 663, and 341 cases from 2013 to 2015 (Nugraha *et al.,* 2019).

The worm *A. lumbricoides* is the STH group that causes the most infections in humans (Pilotte *et al.,* 2019). This is due to the ability of female worms to produce eggs in large numbers and under various environmental conditions, as well as their ability to prevent the transmission of infectious diseases from human to human (Al-Tameemi and Kanaan Kabakli, 2020). Although these worms are often seen in schoolchildren, parents can also catch the infection (Juhairiyah and Indriyati, 2016). Infections that affect the elderly often have chronic causes (Nurhayati and Irawati, 2020).

These worm parasites can manage the immune system's response to an attack. T Helper 2 is activated at the start of an infection by destroying the parasite (Chen *et al.,* 2012). In these parasites, the test will determine the response of the T regulator (Treg) by expressing several molecules to block the immune system response, the most prominent being interleukin 10. (IL-10) (Wiria *et al.,* 2012). IL-10 will work on B cells to increase the switch to IgG4 and block IgE, which is an intermediary in the allergic response to parasite antigens (Hairani, 2012). Elevated plasma IgG4 concentrations are associated with hyporesponsive and asymptomatic worm infections. This suggests that chronic worm infection occurs in humans with high IgG4 and low IgE levels. As a result, effector immunity does not function (Allen and Maizels, 2011).

There are two types of immune responses associated with STH infection: acute and chronic responses. Acute immunity is one of the immune responses that works when STH first infects humans. When an acute response is unable to eliminate STH, a chronic response is the next best thing (Gazzinelli-Guimaraes, 2018). The current immune response is characterized by increased levels of Th2-related cytokines interleukin-4 (IL-4), interleukin-5 (IL-5), interleukin-13 (IL-13), and eosinophils. This immune response manifests itself as long-term STH and substance-induced tubular paralysis. The two factors mentioned above cause T-helper 2 (Th2) to become more active and able to respond to the immune response triggered by T-helper 1 (Th1) and activate the T-regulator. Treg cells will suppress a stronger immune response so that the human body will be more susceptible to the effects of STH which allows parasites to multiply in the tubules of the human body (Gazzinelli-Guimaraes, 2018). The conventional method of diagnosing ascariasis is through the detection of *A. lumbricoides* eggs in feces (Vlaminck *et al.,* 2016). This test is relatively safe and easy to prepare, with a low false-positive rate. The disadvantages of this method are that it has a high variation in EPG values based on repeated stool sampling with a non-random distribution of eggs (in the same stool) and daily fluctuations in egg detection (based on different stools from the same person), as well as potential errors in stool pot labeling. High variation, accompanied by the use of small stool volumes (usually 41.7 mg), causes this detection to have limited sensitivity in areas with low infection intensity (Lamberton *et al.,* 2015). Microscopic examination is indeed simpler, more affordable, and faster in estimating the level of infection and STH intensity, but any negative findings cannot ensure 100% infection-freeness because only a few of the total larvae that migrate throughout the body will return and multiply in the small intestine (Vlaminck *et al.,* 2016).

Another test that can be used to diagnose ascariasis is a serological examination using the IgG4 ELISA method. This method is sensitive and specific for parasite serodiagnosis, which has recently been developed and used in research (Vlaminck *et al.,* 2016). This was the main finding of Gowon *et al.,* (2018) who used microscopy technology to detect ascariasis and IgG4 more positively than IgG4. In contrast to other studies that mostly use a microscope, the detection of IgG4 levels consistently produces significant prevalence data in terms of the presence of parasites in the target population (Gowon *et al.,* 2018). Furthermore (Naglaa, 2016) conducted a study in Egypt on the effect of *Ascaris lumbricoides* infection on cytokines, specifically IL-4, IL-5, and TNF- α. The findings revealed a link between *A. lumbricoides* infection and levels of IL-4, IL-5, and TNF- α.

Materials and Methods

Research Design

This research uses a descriptive method with a cross-sectional design that takes place from July 2021 to May 2022 in one of the urban villages in Padang City, namely

Pasie Nan Tigo Village. This study used venous blood samples to detect IgG4, TNF- α, and IL-4 levels in participants. The reagent used was adapted to the research by (Gowon *et al.,* 2018) namely the IgG *Ascaris lumbricoides* ELISA kit (Abcam Scientist Inc., USA) with type ab108707, Anti-*Ascaris lumbricoides* IgG Human ELISA Kit, which is a special kit for examining IgG4 levels in *A. lumbricoides* infection, and the ELISA kit (Abcam Scientist Inc., USA) for TNF- α and IL-4, which is a special kit for examination for TNF- α and IL-4 (Gowon *et al.,* 2018).

Sampling

This study's sample consisted of 17-year-old adult men and women who agreed to become research subjects by signing an informed consent form. Subjects who had taken deworming medication within the previous 6 months of the study's start date were excluded. The sampling technique used was multistage random sampling with a minimum number of samples through a categorical descriptive study formula, namely 78 respondents for the examination of IgG4 levels and 24 respondents for TNF- α and IL-4 levels.

Data Analysis

The data analysis performed was a univariate data analysis to find frequency distribution data.

Results and Discussion

Examination of STH-infected Stool Distribution

The prevalence of a single *T. trichiura* infection was found to be higher (87.5%) than 12.5%. This is because *T. trichiura* is more difficult to treat than other types of STH, where if it is usually infected by two other worms (*A. lumbricoides* and hookworms), it heals immediately after taking the medicine. However, in *T. trichiura* worm infections, you have to take the medication three days in a row before you can show improvement (Hotez *et al.,* 2007) because most drugs available on the market today have low effectiveness against this type of worm (Uneke, 2010).

Distribution of respondents who detected ascariasis with IgG4

The results showed that of the 78 respondents who were examined for IgG4 levels using the ELISA method, there were 57 respondents (73.1%) who were positive for IgG4 and 21 respondents (26.4%) who were negative for IgG4.

Based on this study, the number of respondents who were positive for IgG4 was 57 (73.1%), while 21 other respondents (26.9%) were negative for IgG4. Data from other researchers who were part of the umbrella study of this study found that only 17 (21.8%) adult respondents in Pasie Nan Tigo Village were infected with STH worms through microscopic examination. This concluded that the IgG4 ELISA method could detect *A. lumbricoides* more accurately (Gowon *et al.,* 2018).

Detection of ascariasis by finding *A. lumbricoides* eggs or DNA in feces is lacking in terms of accuracy in estimating the true prevalence. This method has limited sensitivity for recent infections and does not detect infections with immature stages of the parasite.

This concludes that the absence of *A. lumbricoides* eggs in the feces does not necessarily prove that there was no recent infection or exposure to the larval stage. Giving mass treatment to a community also causes a decrease in the antibody level of that community, making this technique usable for assessing the effect of new Ascaris infection control measures on endemic populations (Vlaminck *et al.,* 2016).

An ELISA test with specific IgG4 can be used to detect specific antibodies to *A. lumbricoides* worm antigens present in blood samples. This method can detect the presence of *A. lumbricoides* worms more accurately than microscopic techniques, thereby showing an overview of the existence of this worm parasite in a target population (Vlaminck *et al.,* 2016; Gowon *et al.,* 2018).

TNF- α and IL-4 level distribution in the STH-infected group

The average TNF- α and IL-4 levels in the STH group were dominated by *Trichuris trichuria* (87.5%), followed by *Ascaris lumbricoides* (12.5%).

Based on this study, the number of respondents who were positive for *T. trichiura* was 21 (87.5%), while those who were positive for *A. lumbricoides* were 3 (12.5%).

Because Immunity to nematode worm infection is one of the infections that activates the humoral response, which is characterized by an increase in the levels of IL-4, IL-5, interleukin-10 (IL-10), and interleukin-13 (IL-13).

Figure.1 *Ascaris lumbricoides* **Figure.2** *Trichuris trichiuria*

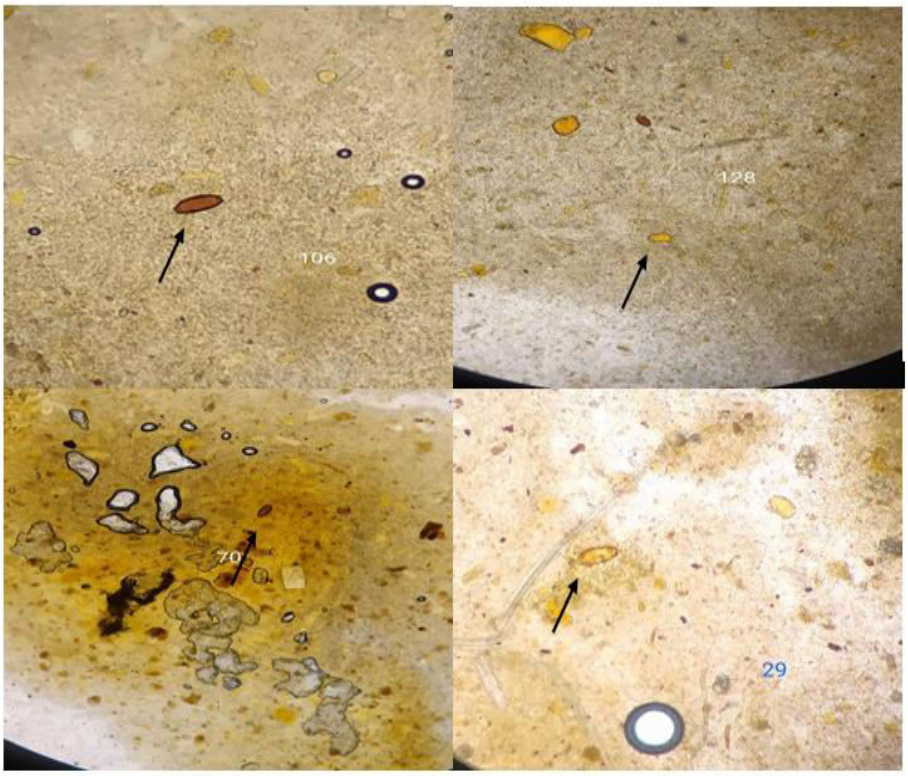


Figure.3 Shows the distribution of respondents with ascariasis detected with IgG4**.**

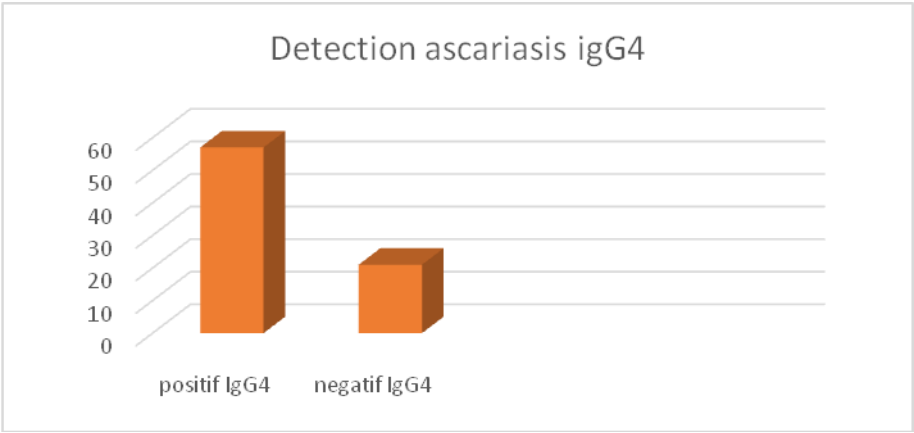
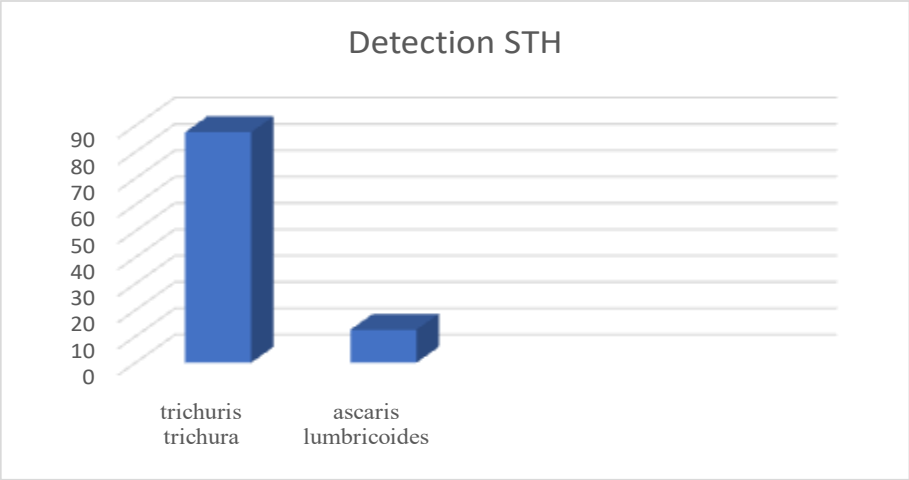


Figure.4 STH Type Frequency Distribution



These cytokines will cause the activation of T-helper (Th) towards T-helper 2 (Th2) to activate the humoral immune response, which will produce more IL-4 from these cytokines, IL-4 referred to as the prototype Th2 cytokines, which cause a humoral predominance by suppressing the cellular immune response, so that levels should increase far above normal in helminthic infections (Min, 2004).

Based on the results of the research that has been done, it can be concluded that the majority of the research respondents were in the age group of 46–55 years and were female.

More than half of the total respondents detected ascariasis based on the IgG4 ELISA, TNF- α, and IL-4 ELISA methods with sufferers. The majority are males between the ages of 17 and 25.

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Author Contributions

Nuzulia Irawati: Investigation, formal analysis, writing—original draft. Yanti Rahayu: Validation, methodology, writing—reviewing. Randi Septiah Hendri:—Formal analysis, writing—review and editing.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical Approval Not applicable.

Consent to Participate Not applicable.

Consent to Publish Not applicable.

Conflict of Interest The authors declare no competing interests.

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