

A survey study on the relationship between helminthes infection and other microorganism infection

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Abstract

Parasitic helminthes infections take place mostly in regions where exposure to other pathogens is as well prevalent. A parasitic worm infestation may encourage infection with another microbe. There are many hypotheses and evidence for how this is done First, helminths naturally encourage a T-helper cell type 2 (Th2) immune response, relating cytokines for example interleukin IL-4, IL-5 and IL-13. seacond in cooperation Th2 and Treg responses have been proposed to decline the generation of protective Th1 or Th17 immunity against bacterial or viral pathogens.

Third helminth-modified intestinal metabolism promotes susceptibility to microbe coinfection. This search summarizes our recent understanding in what way the host's immune response to infection with various kinds of parasitic worm affect susceptibility to predisposition to infection with further microbes.

Keywords: Helminthes; Co-infection; Immunity; Survey

1. Introduction

Helminthes are enormous, multicellular parasitic microorganisms. Previous research indicates that roughly 33% of the worldwide human populace might be diseased with parasitic helminth, this causes significant general wellbeing concerns, particularly in locales using poor disinfection or restricted admittance to clean water suitable for use. Helminthes are usually categorized into the next groups: trematoda (flukes), for example *Fasciola hepatica* and *Schistosoma*; nematodes (roundworms), such as *Ascaris lumbricoides*; whipworms, *Trichuris trichiura*; hookworms, such as *Necator americanus*; and cestodes (tapeworms) (Allen, 2011). Many of parasitic helminthes cause persistent diseases. The host's immune system deals with parasitic worms completely differently from other microbes for example fungi, protozoa, bacteria and viruses. Helminths can be found essentially in tissues such as filaria or schistosomiasis, or alternatively in the lumen of the intestine, for example hookworms, in general in humans or experimental animals such as mice, the typical helminth-prompted type 2 immune response (Salgame *et al.* 2013). These persistent diseases are regularly related to evolution of mucosal and systemic T helper cell CD4+ type 2 (Th2) ,which play important role in immune responses. Globally, worms infestation is distinguished by amplified levels of cytokines like interleukin: IL-4, IL-5, IL-13, eosinophilia, creation of immunoglobulin E (IgE), and encouragement of alternatively activated macrophages . The alternatively activated macrophages are thought to assume a significant part in tissue destruction triggered through the helminthes infection (Jackson *et al.* 2009) .Numerous helminths look after themselves from host immunity via manipulating host immunoregulatory pathways which increase the activity of regulatory T cells (Treg), that motivate the discharge of regulatory cytokines such as transforming growth factor (TGF)and IL-10. This immunomodulation via helminths eventually leds to destruction of both Th1 and Th2 immune responses(Ezenwa and Jolles , 2011)

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Down-regulated proinflammatory response, active damage repair mechanisms and a well-structured progression of Th2 anti-helminthes effector responses may all be associated with helminth infection. Although exposure to helminthes in exposed human populations commonly starts in youth, delayed age-intensity peaks are a proof to the slow development of immunity Metenou (Dembele et al.2011)

There are many previous studies that showed that the immunosuppressive activities of helminthes infections possibly will make persons less responsive to microbial pathogens and to vaccination. This is a significant alarm for the reason that wherever helminthes infection is predominant, there are likewise risky microbial infectious agents, like virus, bacteria and parasites (Furze *et al.* 2006).

1.1. Trematodes (Flukes)

The class trematoda is the biggest group of platyhelminths. Chronic infections brought on by tissue-invasive trematodes , such as schistosomes are characterized by an immune response dominated by modifying cytokines (like IL-10). It has been demonstrated in the past that the IL-10- dominated environment by chronic helminth infection modifies the responses to vaccination and other pathogens, including *H. pylori* (Moss *et al.*1996). *M. tuberculosis*, *P. falciparum* and HIV (Downs *et al.* 2012).

1.1.1. Effects of trematodes on bacterial infections

Opisthorchis viverrini is a liver fluke, and infection with it leads to development progress of cholangiocarcinoma, a malignant tumour of the bile ducts. In (Thailand) where flukes are widespread, it was found that 66.7% of the patients who underwent previous studies who had cholangiocarcinoma were also infected with gram-negative *Helicobacter pylori*. This supports the theory that co-infection between *Helicobacter pylori* and *Opisthorchis viverrini* strongly helps increases intensity level of hepatocellular abnormalities significantly. In fact, hamsters infected with *O. viverrini* increased the severity of the hepatobiliary abnormalities in an experimental model (Dangtakot *et al.* 2017)

Infection with *Fasciola hepatica* in the bile duct, on the other hand, was linked through the increased pathogenicity of a microbial co-infection in the bowel. *F.hepatica* is parasite of ruminant livestock that modulates the immune response of its host's and affect susceptibility to pathogenic bacterial such as *Escherichia coli* O157. Past study looked into whether *E. coli* O157 shedding is linked to *F. hepatica* infection in cattle (Howell *et al.*2018)

Mice infected with *S. mansoni* and *M. tuberculosis* or with *S. mansoni* and BCG32 had a greater bacterial load in their lungs than mice who were not infected with *S. mansoni*. Mice infected with something like *Nippostrongylus brasiliensis*, an intestinal helminth with a lung stage, had reduced protection to *M. tuberculosis* infection (Frantz *et al.* 2010 ; Potian *et al.*2011).

1.1.2. Effects of trematodes on viral infections

There are many previous studies that have touched upon that there is a relationship between parasitic worms and viruses, and among them the Egyptian study, that was carried out on Egyptian hepatitis C patients who had an additional infection with *Schistosoma mansoni*. The study documented that the cases that had a co-infection with *Schistosoma mansoni* showed a high concentration of HCV proteins in contrast to the cases that did not have a corporate infection with *Schistosoma mansoni*. On this basis they hypothesized that the immunological response to *Schistosoma mansoni* infectious disease may have increased the spread of hepatitis C virus and an amplified concentration of HCV proteins (Attallah *et al.* 2016)

1.1.3. Effects of trematodes on protozoa infections

Laboratory animals model have been used to investigate the relationship between trematodes and protozoa, and these studies have shown that the animals model infected with *S. mansoni* obstruct the initiation of a pro-inflammatory classically activated macrophage phenotype in the lungs of animals model that may promote subsequent infection with malaria. The malaria disease was too much for the coinfecting mouse to handle (Craig and Scott, 2017).

1.2. Cestodes (Tapeworm)

The cestodes sources of critical health complications and economic damages, especially in America, Africa and Asia for example *Echinococcus granulosus* (Manus, 2012).

Previous serological research displayed that 26 percent of people in widespread regions were seropositive for *E. granulosus* antigens, demonstrating that majority of individuals had been contracted the infection. With elevated levels

of antibodies, chiefly IgE, IgG1 and IgG4 (Gavidia et al. 2008) and chief Th2 cytokines, such as IL-4, IL-5, IL-6, and IL-1, (Zeng and Inohara, 2016). Cystic echinococcosis infection powerfully influences host immune responses and shows that the host immune response to cystic echinococcosis varies from a bacteria or virus infection (Casaravilla et al. 2014)

1.2.1. Effects of cestoda on other infections

The bowels microbiota plays a fundamental role in protecting human health, influencing metabolism, immunity, and the host's development and growth (Thaiss et al. 2016).

Previous studies have documented that cestoda infectious disease in the bowels prompted typical Th2 immune responses that could possibly regulator the microbiota in mice's bowels (Deepshika et al. 2017;

Guernier et al. 2017; Wegener et al. 2017). It is still uncertain either *E. granulosus* infection influences the bowels microbiota of humans or rodents only. Rats models show an vital part in studies of developing natural science and host specificity in echinococcosis (Nakaya et al. 2006; Elissondo et al. 2007).

Many experimental studies presented that the percentages of IgG, IgG1 and IgG2a antibodies against hydatid cystic echinococcosis antigens have correlation with the arrangement of different types of bacterial. Records of *Enterorhabdus*, and *Clostridium* genera were clearly associated to IgG1 and IgG2b levels, demonstrating that both these microbes possibly will be tolerated by Th2 antibodies or that Th2 may even be advantageous for those microbial genera. While, IgG2a, a Th1 related antibody, was connected with augmented number of *Barnesiella*, demonstrating Th1 has a part for increasing genus *Barnesiella*. Previous experimental information likewise exhibited that Th2 related immunoglobuline IgG1, IgG2b and IgG3 declined amounts of bacteria in the genus *Escherichia*, *Shigella*, *Ruminococcus*, *Ruminococcus* and *Intestinimonas* (Zhang et al. 2005; Bao et al. 2018).

1.3. Nematode (roundworm)

Nematode parasites establish some of the significant dangers to health hazards, spreading diseases with minor economical ramification around the planet (Ing, et al. 2000). Infections with filarial nematodes are a significant issue of public health in tropical nations. In vitro, *Wuchereria bancrofti* has been appeared to down regulate the creation of malaria-specific IFN- γ , furthest probable via the actions of IL-10 (Molyneux et al. 2003), however, these information don't prevent helminthes from promoting the association of other regulatory processes. Depletion of CD4⁺ CD25⁺ Tregs was appeared to restore a downregulated malaria- and bacillus Calmette-Guérin- specific T cell proliferative response, as well as IFN- γ production, in recent study in Indonesia (George, et al. 2015).

1.3.1. Effects of nematode on bacterial infections

Nematode infections and tuberculosis are two of the most important health care problems global and share a great deal of geographical overlap. In animal models of co-infection, *Strongyloides* has been exposed to modify the protective Th17 cytokine responses. Both Th1 and Th17 responses have been exposed to be vital in the initiation and maintenance of protective immune responses in mice models of tuberculosis infection, as well as in human tuberculosis control. Thus, infection with the *Strongyloides* worm makes experimental animals more susceptible to bacterial infection. Co-infections with distinct parasitic helminthes have been exposed to exacerbate susceptibility to salmonellosis. Mice infection with gastrointestinal helminth (*Heligmosomoides polygyrus*) has also been demonstrated to promote *Salmonella enterica* and *Typhimurium* pathogenesis (Su et al. 2014; Barr et al. 2010).

Experimentally infection by hookworm (*Necator americanus*) generate appeared to produce not just a local TH2 and regulatory T cell (Treg cell) response characterized by IL-10 and transforming growth factor- β (TGF- β), yet additionally a parallel systemic response (Elias et al. 2006; Tristão et al. 2002).

Indicating that lung responses to *M. tuberculosis* as well as gut responses induced by helminth may have an impact on the outcome of concurrent infections in different locations. Numerous clinical investigations have given proof that helminthes affect the host vulnerability to tuberculosis. In previous Ethiopia studies, an important relationship was established in the middle of tuberculosis and bowel helminth infection. Remarkably, the relationship amplified through the amount of simultaneously infecting helminth species. Additional research likewise establish that patients with pulmonary tuberculosis had a greater rate of helminth infection than in a control group. Those with helminth-coinfected tuberculosis have a lower IFN- γ response and prominent IL-10 response than patients with tuberculosis only. Mice coinfecting with filarial had a higher bacterial load (Pearlman et al. 1993).

1.3.2. Effects of nematode on protozoa infections

Co-infections protozoa with helminths possibly will have an important influence on the pathogenesis and predisposition of malaria .The onset malaria-driven Th1 cytokine responses was slowed in experimental model infected by *Nippostrongylus brasiliensis* two weeks earlier following infection by *Plasmodium berghei malaria*, changing the activating phenotype of the macrophages in the lung. Infections with helminth may lead to stimulate the secretion of IL10 via regulatory T cells, which possibly will lead to reduction in the expression of pro-inflammatory cytokines for example IL12 and IFN γ . In the meantime IFN γ plays a vital role in protecting against *Plasmodium falciparum* infection, it is reasonable to believe that helminthes infection may influence the development of an anti-inflammatory cytokine , in turn may exacerbate malaria pathogenicity (Ing et al.2000).

Table 1 Association between helminthes infections other microorganism infections

Categories	Basic results
Association between helminthes and virus	Trichinella spiralis associated with mouse norovirus (MNV)
	<i>schistosoma. mansoni</i> associated with Hepatitis C Virus (HCV)
	Soil-transmitted helminth (<i>N. americanus</i> , <i>Ancylostoma duodenale</i> , <i>Ascaris lumbricoides</i> , <i>Trichuris trichiura</i> and <i>Strongyloides stercoralis</i>) associated with Virus (<i>astrovirus</i> , <i>adenovirus</i> , <i>norovirus</i> , <i>norovirus</i> , <i>rotavirus</i> , or <i>sapovirus</i>)
Association between helminthes and bacteria	<i>Heligmosomoides polygyrus</i> associated with <i>Salmonella enterica</i>
	<i>Fasciola hepatica</i> associated with <i>Escherichia coli</i> O157
	<i>Strongyloides stercoralis</i> associated with <i>Mycobacterium tuberculosis</i>
	<i>Wuchereria bancrofti</i> associated with <i>Mycobacterium tuberculosis</i>
	Soil-transmitted helminth (<i>N. americanus</i> , <i>Ancylostoma duodenale</i> , <i>Ascaris lumbricoides</i> , <i>Trichuris trichiura</i> and <i>Strongyloides stercoralis</i>) associated with (<i>Aeromonas</i> , <i>Clostridium difcile</i> , <i>Campylobacter jejuni</i> , <i>Shigella spp</i> , <i>Salmonella enterica</i> , <i>Enteroinvasive E. coli</i>)
Association between helminthes and other helminthes	<i>Taenia saginata</i> associated with <i>Clonorchis sinensis</i>

1.4. Immunological links between helminthes and other infection.

An extensive literature on the relationship between helminthes and other co-infection has been published over the past 20 years .Following is summary some of this evidence, arranged in chronological orders

Midway through 1992, a team from United States of America (USA)reported that mice infected with *Schistosoma mansoni* show severely reduced CD8+ class I major histocompatibility complex (MHC)-restricted cytotoxic T-lymphocyte (CTL) function versus virus, as well as the predictable shift in cytokine pattern, and concurrently have reduced ability to clear the recombinant vaccinia virus infection. These findings indicate that natural immune protection against viral infections may possiblydiminished by helminth infections (Actor et al. 1993). In the year 1999, a group from Ireland showed that *Bordetella pertussis*-infected or immunized rodents can induce a Th1 response prompted in rodents with *F. hepatica* infection. Over and above inhibition the production of IFN-g and IL-2, *F. hepatica* infection likewise delayed removal of the bacteria from the lungs after *B. pertussis* defiance (Brady et al. 1999).

Schistosoma mansoni infection in rodents may impair the animals capacity to regulate *Mycobacterium bovis* infection and the immune response to mycobacterial antigens, according to 2005 study from Stockholm team In early 2013 s, a group from Stanford University reported that bladder contact to *S. haematobium* eggs elicits interleukin-4 (IL-4) manufacture and makes model mice vulnerable to bacterial urinary tract infections (UTI) .Also, when comparing mice that were exposed to a single infection from bacteria with mice that were suffering from a joint infection (worms and bacteria), they found a significant decrease in the number of killer T cells (Reese et al. 2014). Helminth infection reactivates latent γ -herpesvirus via cytokine competition at a viral promoter. Science, 345(6196), 573-577.

In 2013 Su *et al* suggested that decreased neutrophil recruitment is chief provider to the enhanced severity of *Salmonella enterocolitis* related to helminth coinfection

Previous studies in 2013, have documented that helminths can modify innate immune response to bacterial enteropathogens through invigorating regulatory cytokines (such as IL-10), antagonizing proinflammatory factors that could prompt severity of intestinal inflammation (such as keratinocyte-derived chemokine and macrophage inflammatory protein 2), obstructing elimination of pathogens, and decreasing accessibility of specific cytokines to pathogen. In 2014, study by Reese *et al* founded that helminth infection, differentiate through the incitement of the cytokine interleukin-4 and stimulation the transcription of herpesvirus infection *in vivo*. IL-4 motivated viral replication and obstructed the antiviral effect of interferon- γ (IFN γ) (Salgame *et al.* 2013)

In 2017, Reynolds *et al* reported that *elgimosomoides polygyrus* infection may possibly disorder the bowels metabolism through changing the arrangement of the microbiota, so modifying the abundance of microbiota. This, in turn, may lead to infection with salmonella bacteria or affect its virulence (Reynolds *et al.* 2017).

Improved penetrability of the intestinal barrier caused by helminthes infections might encourage the infiltration of bacterial endotoxins. Since they create chemical and physical barriers that shield the gut epithelia from attacking microbes, intestinal epithelial cells are very important for maintaining the homeostasis of intestines. One mechanism by which soil transmitted helminth infection may increase the likelihood of concurrent bacterial infection is that helminthes infection causes abdominal barrier failure and amplified "leakiness" of the intestinal epithelium [Chard *et al.* 2019].

In 2018 a group from china discovered that mice infected with *E. granulosus* were associated with an increased incidence rate with 2 types of bowel microbiota (*Parabacteroides* and *Eisenbergiella*), bacterial configuration of main types had favourable associations with IgG1 and IgG2b in *E. granulosus* infected rodents. The augmentation of genus parabacteroides in hydatid disease might be related through hepatic modification (biotin, lipid metabolism, and tryptophan metabolism (Bao *et al.*, 2018).

2. Conclusion

In conclusion, some helminthic illnesses, particularly in underdeveloped nations, are regarded as public health issues. Helminthic have evolved techniques to alter their host's immunity. While significant efforts have been made to comprehend the effects that host micro biome changes have on helminthic fitness and survival that may lead to infection with other microorganisms.

Compliance with ethical standards

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Disclosure of conflict of interest

The study's authors affirm that there were no financial or commercial ties that might be viewed as having a potential conflict of interest.

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