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INTESTINAL PARASITIC REDUCE COVID-19

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ABSTRACT

Background: The Corona virus has a wide range of clinical manifestations and severity, including some factors that contribute to an increased risk of developing severe corona, such as cardiovascular disease, obesity, chronic lung disease and diabetes. **Body**: Parasite-driven immunomodulatory responses may mute hyper-inflammation associated with severe COVID-19. The researchers were collected Fecal samples from 136 immunocompromised patients (52 females and 84 males), aged 2 to 69 years. Specimens were fixed with 10% formalin for 30 min (2-3 g fecal-1) and then concentrated by a formalin-ether sedimentation technique. Samples were examined as wet saline mounts and in iodine preparation for detection of protozoan oocysts, cysts, helminthic eggs and larvae. Permanent stained smears were performed for intestinal coccidian parasites by the modified Ziehl-Neelsen technique and the modified trichrome stain. Intestinal parasites were detected in 54 (39.7%) most of them (25.7%) were with diarrhea. Patients co-infected with parasites had lower odds of developing severe COVID-19, with an adjusted odds ratio (aOR) of 0.23 (95% CI 0.17–0.30; p<0.0001) for all parasites, aOR 0.37 ([95% CI 0.26–0.51]; p<0.0001) for protozoa, and aOR 0.26 ([95% CI 0.19–0.35]; p<0.0001) for helminths. When stratified by species, co-infection with Entamoeba spp., Hymenolepis nana, Schistosoma mansoni, and Trichuris trichiura implied lower probability of developing severe COVID-19. **Aim of work:** Does infection with intestinal parasites reduce the severity and virulence of COVID-19 disease and the relationship between re-infection with intestinal parasites and resistance to COVID-19 disease. **Conclusions:** The researchers found a negative relationship between co-parasitic infection and the severity of the coronavirus, and the presence of any parasitic infection besides a coronavirus infection led to a 60% reduction in the odds of severe COVID-19 infection.

KEYWORDS: COVID 19, intestinal parasites, severity infection, cardiovascular, chronic lung disease, diabetes and obesity.

Main text

Introduction

The Corona virus has a wide range of clinical manifestations and severity, including some factors that contribute to an increased risk of developing severe corona, such as cardiovascular disease, obesity, chronic lung disease and diabetes. (WHO, 2022).

The COVID-19 pandemic has led to a significant increase in the immunosuppressed population worldwide due to the disease pathology and extensive use of corticosteroids. This has subsequently increased the risk of opportunistic parasitic infections such as Toxoplasma gondii, Strongyloides stercoralis and other parasites in these patients. The reactivation of such parasites may remain unnoticed due to overlapping symptoms, the difficulty of diagnosis and lack of guidelines for opportunistic parasitic infections in COVID-19 management. Therefore, recommendations for systematic screening of high-risk patients in endemic regions and active research and surveillance to estimate the impact of these infections are required in COVID-19 policy guidelines (Elsaftawy et al., 2021).

Our study is aimed to Does infection with intestinal parasites reduce the severity and virulence of COVID-19 disease and the relationship between re-infection with intestinal parasites and resistance to COVID-19 disease.

Intestinal parasite infections can cause complications, if left untreated, you have symptoms such as severe abdominal pain, diarrhea, or nausea and vomiting (healthline.com) (Jill Seldi-Schulman, 2021).

Adults of any age with certain underlying medical conditions are at increased risk of developing serious illness from the virus that causes MERS-CoV. (WHO, 2022)

The immune system protects the body from infection, so a person with a weakened immune system may be more likely to develop frequent, potentially life-threatening infections. The causes of a weak immune system vary, so they usually require treatments that are tailored to the cause. (Luis F. García, 2020).

Egypt's health ministry announced the first case in the country at Cairo International Airport involving a Chinese national on 14 February. Egyptian authorities had notified the World Health Organization (WHO) and the patient had been placed in quarantined isolation in hospital.

A recent study Trusted Source has found that intestinal parasites may lower the severity of coronavirus disease 19 (COVID-19). However, other studies have found that parasitic infections may prevent the immune system from responding effectively to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes COVID-19. For scientists, this topic of debate is complex and difficult to study. Much more research is needed to determine how intestinal parasites may affect a person's immune reaction to a SARS-CoV-2 infection. In severe COVID-19, high levels of inflammation can be present in the body. This is referred to as a "cytokine storm" and can cause serious complications such as acute respiratory distress syndrome (ARDS).

Could the dampening effects of intestinal parasites on the immune system help to protect against these high levels of inflammation?

While there's some evidence that intestinal parasites may be associated with reduced COVID-19 severity, there's also evidence that intestinal parasites can hinder the immune system's ability to ward off a SARS-CoV-2 infection.

Intestinal parasites can dampen down certain aspects of the immune response in order to prevent being attacked by the immune system. This effect may protect against some diseases but may also worsen others.

Causes of weak immune system

1. Genetic causes

One of the reasons for the weakness of the immune system is the inherited primary immunodeficiency disorders that are transmitted by parents as a result of a defect in the genetic code (DNA (Milton et al., 2019)

- B-cell deficiency.
- T-cell deficiency.
- Combined deficiency of B and T cells (Terry, et al., 2019)
- Defective phagocytes (Nima Rezaei et al., 2016)

- Unknown reason.

2. Autoimmune diseases

There are more than a hundred diseases classified as causes of weak immune system, and most of them are long-term diseases, and their severity varies over time.

- Celiac disease: The immune system reacts to gluten in wheat and damages the small intestine. Lupus: This disease may affect many parts of the body, including the skin, muscles, joints, lungs, heart, and kidneys (Melinda Ratini, 2020).
- Rheumatoid arthritis: Rheumatoid arthritis damages the bones and cartilage, causing joints to become swollen and stiff. (Howard R Smith, et al., 2022)
- Graves' disease: which causes hyperthyroidism, which causes anxiety, heart palpitations, weight loss, and irritated or swollen eyes. (Mosin et al., 2021)
- Type 1 diabetes: the pancreas does not produce the required amount of insulin to regulate blood sugar levels, which leads to feelings of thirst, hunger, and frequent urination. (James and Vidya, 2021)

3. Acquired immunodeficiency

The immune system can be weakened by certain medications, chemotherapy or transplants, and infections such as influenza and measles can weaken the immune system for a short time (Peter J Delves, 2021). Also, the causes of a weak acquired immune system can be smoking, drinking alcohol and poor diet.

The life-threatening HIV virus that causes AIDS is an acquired viral infection that destroys white blood cells and weakens the immune system. (Edward R. Cachay, 2021; Usama Sadiq et al., 2022)

4. Allergic reaction

- While the immune system is doing its job, which is to defend the body from invaders, such as: (harmful bacteria and viruses), the immune system releases antibodies, which in turn send a message to the cells to stop the allergen and then the cells release histamine that causes the blood vessels to dilate (Nayana Ambardekar, 2022).
- When you suffer from food allergies, irritants, or asthma, your immune system will continue to fight back, causing the immune system to become overactive, so allergies are one of the causes of a weak immune system. (Nayana Ambardekar, 2020)

- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection results in a spectrum of clinical presentations. Evidence from Africa indicates that significantly less COVID-19 patients suffer from serious symptoms than in the industrialized world. On previously postulated a partial explanation for this phenomenon, being a different, more activated immune system due to parasite infections. In Africa, the investigation a potential correlation of co-infection with parasites with COVID-19 severity in an endemic area. (Atul Sharma, et al., 2020).

The immunomodulatory role of parasitic infections in COVID-19 severity is not clear. In general, Helminths secrete immunomodulatory proteins that skew the production of IL-10 in addition to the extension of the regulatory T (Treg) cell and the regulatory B cells, and thus more inhibition occurs to type-1 responses. prior studies demonstrated the possible therapeutic effects of helminthic infections in some autoimmune and allergic reactions (Johnston et al., 2008; Wilson et al., 2005), and recently scientists questioned the possibility of helminthic co-infection to modulate the severity of COVID-19 (Bradbury et al., 2020). Trichinella spiralis and Nematospiroides dubius (N. dubius) were able to lessen the immune-pathological changes caused by influenza A virus. Pulmonary viral titres were less in N. dubius co-infection, and Heligmosomoides polygyrus infections attenuated pulmonary diseases after respiratory syncytial virus infection (Chowaniec et al., 1972). Similarly, previous studies on animal models demonstrated the role of parasites against viral infections ‘parasites against virus phenomenon (Shen et al., 2019). Protozoal infections were also observed to modulate the severity of viral infections.

Concurrent infection with G. lamblia reduces the severity of diarrheal episodes in rotaviruses (Bilenko et al., 2004), in addition to the protective effect speculated between Plasmodium spp. and Chikungunya virus (Teo et al., 2018 a,b). In this context, may passive immunization of COVID-19 patients with serum from subjects with prior parasitic infections improve their clinical outcomes?

Patients co-infected with parasites had lower odds of developing severe COVID-19, with an adjusted odds ratio (aOR) of 0.23 (95% CI 0.17–0.30; $p<0.0001$) for all parasites, (Teklay Gebrecherkos et al., 2021) an adjusted odds ratio (aOR) 0.37 ([95% CI 0.26–0.51]; $p<0.0001$) for protozoa, and an adjusted odds ratio (aOR) 0.26 ([95% CI 0.19–0.35]; $p<0.0001$) for helminths.

Parasite-driven immunomodulatory responses may mute hyper-inflammation associated with severe COVID-19. When stratified by species, co-infectio with Entamoeba spp., Hymenolepis nana, Schistosoma mansoni, and Trichuris trichiura implied lower probability of developing severe COVID-19 (Dawit Wolday 2021).

Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) results in a spectrum of clinical presentations. Whereas most people with COVID-19 develop asymptomatic or mild illness, at-risk patients can develop severe pneumonia and hypoxemia disease requiring hospitalization. In severe cases, COVID-19 can be complicated by acute respiratory distress syndrome (ARDS), sepsis, multi-organ failure, including acute kidney injury, and cardiac injury. (Dawit Wolday, 2021).

Low and medium-income countries (LMICs) differ significantly in disease prevalence and conditions from high-income countries (HICs). Infectious diseases have a markedly higher prevalence in LMICs, including so-called neglected infectious diseases (NIDs) (David and Daniel, 2019). Amongst NIDs, parasitic infections affect more than 2 billion people throughout the world, with dispro-portionately high prevalence rates in resource-poor settings. (Wiersinga W. Joost, 2020).

Multicellular and highly complex parasites such as Ascaris, hook worm, Trichuris, and Enterobius, (David & Daniel, 2019), as well as unicellular organisms including Entamoeba, Giardia, Cyclospora and Cryptosporidia (Dawit Wolday, et al. 2021) are among the major organisms that contribute to the global intestinal parasitic disease burden. Chronic and/or persistent parasitic infections are common in LMICs, and such chronic infections, possibly in part through direct modulation of the host's immune responses, were shown to alter clinical outcomes to other infections. Pre-existing parasitic infections may also modify the host's immune response to infection with SARS-CoV-2, with postulated beneficial and detrimental effects. (Teklay et al., 2021).

Several parasites are responsible for life threatening infections in immunocompromised patients. They occur in patients with a profound immunodeficiency affecting the T-cell mediated immunity. In AIDS patients, opportunistic infections are highly prevalent in those with CD4 lymphocyte counts < 200/mm3. Most of these parasites are intracellular protozoa (Jorge Botero-Garces et al., 2021).

Severe parasitic infections in immunocompromised hosts either results from the reactivation of a previously acquired infection, or from a primary acquired infection which manifests more severely because of the immune defect:

This is the case for intestinal protozoa, such as Cryptosporidium, Microsporidia, Cyclospora and Isospora belli which can be the cause of severe chronic diarrhea (Wang et al. 2018). Strongyloides stercoralis is the only helminth responsible for disseminated infection in immunocompromised patients. (Andres and Marcelle, 2022). Thus, the complex role of parasitic coinfections on the outcomes of COVID-19 is still elusive and must be focused upon in future studies. Considering that a large number of patients with COVID-19 will have some degree of immunosuppression, it is expected that they may be at risk of reactivation of dormant/latent parasitic infections, especially in endemic areas (Johnston et al., 2008). For instance, the protozoan T. gondii infects about 25–30% of the world's population, with a seroprevalence of 10–80% across countries. It is also noteworthy that some of the neurological and psychological clinical features of long-COVID are also known to exist in toxoplasmosis, and such patients who require additional post-COVID care may benefit from evaluation and management of Toxoplasma (Wilson et al., 2005). Another usually dormant opportunistic parasite, S. stercoralis, has been reported to infect 10–40% of the population in tropical and subtropical countries. A potential strategy to reduce the risk of Strongyloides hyperinfection/dissemination in COVID-19 patients has been suggested, which includes screening and treating patients in outpatient and presumptive treatment in inpatient settings (Bradbury et al., 2020). Many other parasites such as Cryptosporidium, Cyclospora, Cystoisospora, Leishmania spp., Trypanosoma cruzi and Microsporidia may also complicate COVID-19 illness, especially in patients with depleted lymphocytes and on corticosteroids. In a series of 375 patients with a diagnosis of COVID-19 from Egypt, evidence of parasitic infections including T. gondii, Cryptosporidium, Blastocystis and Giardia was reported in 72% of mild and 20% of severe cases (Shen et al., 2019). A serological screening approach for T. gondii, S. stercoralis, Leishmania spp. and T. cruzi may be considered for patients selected for corticosteroid therapy and/or with progressive lymphopenia for prophylaxis or treatment of these infections. Nevertheless, there are many challenges in diagnosing superinfections during the course of a COVID-19 illness (Chowaniec et al., 1972).

There's some evidence that intestinal parasites may reduce COVID-19 severity. However, this data comes from just one study and more research into this topic needs to be done.

In Saudi Arabia The researchers were collected Fecal samples from 136 immunocompromised patients (52 females and 84 males), aged 22 to 69 years, they have COVID-19. Specimens were fixed with 10% formalin for 30 min (2-3 g fecal-1) and then concentrated by a formalin-ether sedimentation technique. Samples were examined as wet saline mounts and in iodine preparation for detection of protozoan oocysts, cysts, helminthic eggs and larvae. Permanent stained smears were performed for intestinal coccidian parasites by the modified Ziehl-Neelsen technique and the modified trichrome stain. Intestinal parasites were detected in 54 (39.7%) most of them (25.7%) were with diarrhea (Clarke, and McIntyre, 1996). More specifically the following parasites were detected Cryptosporidium parvum 11(8.1%), Giardia lamblia 9 (6.6%), Cyclospora cayetanensis 8 (5.9%), Entamoeba histolytica 7 (5.2%), Entamoeba coli 5 (3.7%), Strongyloides stercoralis 3 (2.2%), Ascaris lumbricoides 1 (0.7%), Hymenolepis nana 1(0.7%), and Hook worm 1 (0.7%).

The most common parasite associated with diarrhea in patients, was Cryptosporidium parvum ($p<0.001$), followed by Giardia lamblia, Cyclospora cayetanensis and Entamoeba histolytica. (Sharaf et al., 2021).

In Ethiopian COVID-19 patients were enrolled and screened for intestinal parasites, between July 2020 and March 2021. The primary outcome was the proportion of patients with severe COVID-19 (Saro Abdella et al., 2021). However, differences between different age groups were statistically non-significant. Similarly, no significant difference in the infection rate were found between male and female patients (McFarlane et al., 2017), co-infection with enteric parasites, both protozoa and helminths, is associated with lower odds of developing severe COVID-19 in African patients. Notably, this association was maintained even after adjusting for sex, age, residency, education level, and presence of comorbid conditions, factors that are commonly associated with COVID-19 severity (Teo et al., 2018,a,b).

A 2022 letter expresses skepticism about the findings above. In it, the writers express concerns about potential bias in the study, as participants were first tested for SARS-CoV-2 prior to being tested for intestinal parasites. (Abdelrahman et al., 2022).

Additionally, a 2020 review Trusted Source notes that parasitic infections, particularly with helminths, have been previously found to increase the severity of other infectious conditions, such as HIV, tuberculosis, and malaria. (Amir Abdoli 2020).

As such, the reviewer notes that it's possible that having a parasitic infection could potentially inhibit the immune system from responding effectively to COVID-19. This may actually increase disease severity in some cases.

Vaccination is the most effective way to protect against serious illness and death due to COVID-19. However, in order to be effective, vaccines need to initiate an immune response. Could the immune effects of intestinal parasites affect this?.

There's actually some evidence that parasitic infections can decrease the effectiveness of vaccines. However, no research has assessed the effect that parasites have on COVID-19 vaccines specifically.

Researches were found that having a parasitic infection at the time of getting a vaccine results in a poorer vaccine outcome. Chronic helminth infections are more likely to negatively affect vaccination effectiveness.

No research has been done on how parasites may impact the effectiveness of the COVID-19 vaccines. This is certainly something that researchers will investigate in the future.

CONCLUSIONS

The researchers found a negative relationship between co-parasitic infection and the severity of the corona virus, but the presence of any parasitic infection besides a coronavirus infection led to a 60% reduction in the odds of severe COVID-19 infection, and they recommended by more studies in this field.

List of abbreviation

1. COVID — Coronavirus disease
2. aOR — Adjusted odd ratio
3. WHO — World Health Organization
4. MERS-CoV — Middle East Respiratory Syndrome coronavirus
5. SARA-CoV-2 — A virus of species severe acute respiratory syndrome- related coronavirus (SARS-CoV)
6. ARDS — Acute respiratory distress syndrome
7. DNA — Deoxyribonucleic acid
8. HIV — Human Immunodeficiency virus
9. AIDS — Acquired Immunodeficiency Syndrome

10. LMICs	Low and Medium-income Countries
11. HICs	High-income Countries
12. NIDs	Neglected Infection Diseases

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Avail of Data and Materials

Not applicable

Competing interests

The author declare that she has no competing interest

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Author contributions

RI worked on conceptualization of manuscript and final approval.

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REFERENCES

1. Abdelrahman M Makram, Marcel Alied, Zeeshan Ali Khan and Nguyen Tien Huy Parasites Protect From Severe COVID-19. MYTH OR REALITY? International Society For Infectious Diseases, 2022; 119: P117-118. DOI:https://doi.org/10.1016/j.ijid.2022.03.027:

2. https://www.ijidoline.com/article/s1201-9712(22)00167-3/fulltext.
3. Andres L. Mora Carpio, and Marcelle Meseeha Strongyloides Stercoralis. Treasure Island (FL): StatPearls, 2022 May 10.
4. Amir Abdoli Helminths and COVID-19 Co-Infections: A Neglected Critical Challenge. ACS Pharmacol Transl Sci., 2020 Oct 9; 3(5): 1039–1041. Published online 2020 Sep 30. doi:10.1021/acsptsci.0c00141https://www.ncbi.nlm.nil.gov/pmc/articles/pmc7552170/
5. Atul Sharma, Swapnil Tiwari, Manas Kanti Deb, and Jean Louis Martyc Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2): a global pandemic and treatment strategies, 2020 Aug; 56(2): 106054. Int J Antimicrob Agents. doi: 10.1016/j.ijantimicag.2020.106054.
6. Bilenko N, Levy A, Dagan R, Deckelbaum RJ, El-On Y, Fraser D. Does co-infection with Giardia lamblia modulate the clinical characteristics of enteric infections in young children? Eur J Epidemiol, 2004; 19: 877–8813.
7. Bradbury RS, Piedrafita D, Greenhill A, Mahanty S. Will helminth co-infection modulate COVID-19 severity in endemic regions? Nat Rev Immunol, 2020; 20(6): 342.
8. Chowaniec W, Wescott RB, Congdon LL Interaction of Nematospiroides dubius and influenza virus in mice. Exp Parasitol, 1972; 32: 33-44.
9. Clarke, SC McIntyre, M Modified detergent Ziehl Neelsen technique for the staining of Cyclospora cayetanensis. J Clin Pathol, 1996; 49: 511-512. DOI: 10.21608/AEJI.2021.57107.1129.
10. David E. Bloom and Daniel Cadarette Infectious Disease Threats in the Twenty-First Century: Strengthening the Global Response. Front. Immunol., 28 March 2019 | https://doi.org/10.3389/fimmu.2019.00549.
11. Dawit Wolday, Teklay Gebrecherkos, Zekarias Gessesse Arefaine, Yazezew Kebede Kiros, Atsbeha Gebreegzabher, Geremew Tasew, Mahmud Abdulkader, Hiluf Ebuy Abraha, Abraham Aregay Desta, Ataklti Hailu, Getachew Tollera, Saro Abdella, Masresha Tesema, Ebba Abate, Kidist Lakew Endarge, Tsegaye Gebreyes Hundie, Frehiwot Kassahun Miteku, Britta C Urban, Henk H D F Schallig, Vanessa C Harris, Tobias F Rinke de Wit (2021): Effect of co-infection with intestinal parasites on COVID-19 severity: A prospective observational cohort study, 2021 Sep; 39: 101054. EClinicalMedicine. doi: 10.1016/j.eclinm.2021.101054. Epub, 2021 Jul 31.
12. Edward R. Cachay Human Immunodeficiency Virus (HIV) Infection, Apr 2021 MAS, University of California, San Diego School of Medicine, 2021.

13. Elsaftawy A Enas, Rita M Wassef, Noha M Amin Can endemic parasitic diseases and/or vectors play a role in the COVID-19 pandemic?. PARASITOLOGISTS UNITED JOURNAL, 2021; 14(1). DOI: 10.21608/puj.2021.52193.1098.
14. Howard R Smith, Adam Brown, Herbert S Diamond, Katherine K Temprano: Rheumatoid Arthritis (RA). Drugs & Diseases, Rheumatology, Jan 31, 2022.
15. James R Waymack and Vidya Ssndareshan Acquired Immune Deficiency Syndrome. September (NLH) National Library of Medicine, 2021.
16. Jill Seldi-Schulman Effect of Intestinal Parasites on COVID 19: Increased Risk or Added Protection? . Healthline, May 2022. (healthline.com)
17. https://www.healthline.com/healthy/covid-and-parasites#parasites-and-the-immune-system.
18. Johnston MJG, Macdonald JA, McKay DM. Parasitic helminths: a pharmacopoeia of anti-inflammatory molecules. Parasitology, 2008; 136(2): 125-147.
19. Jorge Botero-Garcés, Esteban Villegas-Arbeláez, Sofía Giraldo, Johanna UránVelásquez, Laura Arias-Agudelo, Juan Carlos Alzate-Ángel, Gisela María GarcíaMontoya, Ana Luz Galván-Díaz Prevalence of intestinal parasites in a cohort of HIV infected patients from Antioquia, Colombia. Biomédica, 2021; 41(Supl.2): 153-64 doi: https://doi.org/10.7705/biomedica.5992.
20. Luis F. Garcia Immune Response, Inflammation, and the Clinical Spectrum of COVID-19., Front. Immunol. June, 2020.
21. McFarlane AJ, McSorley HJ, Davidson DJ, Fitch PM, Errington C, Mackenzie KJ et al. (2017): Enteric helminthinduced type I interferon signalling protects against pulmonary virus infection through interaction with the microbiota. J Allergy Clin Immunol, 2017; 140: 1068– 1078.
22. Melinda Ratini Celiac Disease, July, 2020, WebMD.
23. Milton H. Saier, William Margolin, Edi Understanding the Genetic Code. 2019 Aug .J Bacteriol, 2019; 201(15): e00091-19. Published online. Prepublished online 2019 Apr 22. doi: 10.1128/JB.00091-19.
24. Mosin S. Khan, Suhail S. Lone, Sunia Faiz, Iqra Farooq and Ssbhiya Majid Graves's Disease: Pathophysiology, Genetics and Mangement. May 2021 book view Section 2, Chapter 4. Doi:http://dx-doi.org/10-5772/intechopen.98238, 2021.
25. Nayana Ambardekar What Is an Allergic Reaction?. on March 13, 2022. WebMD
26. Nima Rezaei, Francisco A. Bonilla, Mikko Seppänen, Esther de Vries, Ahmed Aziz Bousfiha, Jennifer Puck, and Jordan Orange (2016): Phagocytes Defects. Introduction on

Primary Immunodeficiency Diseases. Primary Immunodeficiency Diseases pp 245–294 Cite as, Uwe Wintergerst MD, Taco W. Kuijpers MD, PhD, Sergio D. Rosenzweig MD, PhD, Steven M. Holland, Mario Abinun MD, Harry L. Malech MD & Nima Rezaei MD, PhD Chapter, First Online, 02 December 2016. 1919 Accesses.1 Citations

27. Peter J. Delves Acquired Immunity. Sep, MSD MANUAL Consumer Version. University College London, London, UK, 2021.
28. Saro Abdella, Masresha Tessema, Geremew Tasew, Atkure Defar, Asefa Deressa, Feyisa Regasa, Frehiwot Teka, Eyasu Tigabu, Dereje Nigussie, Tefera Belachew, Million Molla, Amare Deribew,Workeabeba Abebe, Tegbar Yigzaw, Tsinuel Nigatu, Getnet Mitike, Tewodros Haile, Haftom Taame,Muhammed Ahmed, Frehiwot Nigatu, Tola Tolesa, Eskinder Wolka, Wondwossen Amogne,Arnaud Laillou, Misker Amare, Yaregal Fufa, Alemayehu Argaw, Woldesenbet Waganew, Akilili Azazh, Aschalew Worku, Berhane Redae, Menbeu Sultan, Miraf Walelegn, Muluwork Tefera, Sisay Yifru, Rahel Argaw, Natinael Brehau, Sisay Teklu, Getachew Demoz, Yakob Seman, Mihretab Salasibew, Eshetu Ejeta, Susan J. Whiting, Dawit Wolday, Getachew Tollera, Ebba Abate and Dereje Duguma Prognostic factors and outcomes of COVID-19 cases in Ethiopia: multi-centercohort study protocol. BMC Infect Dis., 2021; 21: 956. https://doi.org/10.1186/s12879-021-06652-0.
29. Sharaf A Mohammad; Ayman El-Ashkar; Ezzat I Omran; Ihab ZF Elhakimorcid Prevalence of Parasitic Infections and Related Morbidity in Pediatric Patients on Regular Hemodialysis in Ain Shams University Pediatric Hospital, Cairo, Egypt. Afro-Egypt J Infect Endem Dis., 2021; 11(2): 134-145.
30. Shen SS, Qu XY, Zhang WZ, Li J, Lv ZY. Infection against infection: parasite antagonism against parasites, viruses, and bacteria. Infect Dis Poverty, 2019; 8(1): 49.
31. Teklay Gebrecherkos, Zekarias Gessesse, Yazezew Kebede, Atsbeha Gebreegzabher, Geremew Tasew, Mahmud Abdulkader, Hiluf Ebuy, Abraham Desta, Atakilti Hailu, Vanessa Harris, Tobias Rinke de Wit5, Dawit Wolday Effect of co-infection with parasites on severity of COVID-19. February 3, 2021. doi: https://doi.org/10.1101/2021.02.02.21250995;
32. Teo TH, Lum FM, Ghaffar K, Chan YH, Amrun SN, Tan JJL, et al. Plasmodium co-infection protects against Chikungunya virus-induced pathologies. Nat Commun 2018a; 9: 3905.

33. Teo TH, Howland SW, Claser C, Gun SY, Poh CM, Lee WW, et al. Co-infection with Chikungunya virus alters trafficking of pathogenic CD8+ T cells into the brain and prevents Plasmodium-induced neuropathology. EMBO Mol Med, 2018b; 10: 121–138.
34. Terry W Chin, Noufa Alonazi, Mary L Windle, Harumi Jyonouchi B-Cell and T-Cell Combined Disorders. Aug 08, 2019.
35. Usama Sadiq; Utsav Shrestha; Nilmarie Guzman Prevention Of Opportunistic Infections In HIV/AIDS. May 23, 2022. National Library of Medicine (National Center for Biotechnology Information), 2022.
36. Wang, Quan Liu, Huan-Huan Liu, Shuang Li, Li Zhang, Yong-Kun Zhao and Xing-Quan Zhu Prevalence of Cryptosporidium, microsporidia and Isospora infection in HIV-infected people: a global systematic review and meta-analysis. Parasites & Vectors, 2018; 11: 28. DOI 10.1186/s13071-017-2558-x.
37. WHO Middle East Respiratory syndrome Corona virus (MERS-COV), tell February, 2022. WHO.
38. Wiersinga W Joost, Andrew Rhodes, Allen C Cheng , Sharon J Peacock , Hallie C Prescott Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19). JAMA, 2020 Aug 25; 324(8): 782-793. doi: 10.1001/jama.2020.12839.
39. Wilson MS, Taylor M, Balic A, Finney CAM, Lamb JR, Maizels RM Suppression of allergic airway inflammation by helminth-induced regulatory T cells. J Exp Med, 2005; 202: 1199-1212.