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LETTERS



Investigating immunological interaction between lymphatic filariasis and COVID-19 infection: a preliminary evidence

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ABSTRACT

The foremost concerns of COVID-19 vaccines are safety and efficacy, which becomes grave in countries with a high burden of Neglected Tropical Diseases. Studies proposed helminthic infections might alleviate the efficacy of COVID-19 vaccines. We share preliminary evidence on the association between filariasis and COVID-19 infection. We collated 2 ml of blood from 174 participants residing in filariasis endemic area. To determine filarial antigen, the Og4C3 test and for COVID-19 antibodies, tests through ELISA was performed. COVID-19 antibodies were present among 74/174 (42.5%), whereas filarial antigens were detected in 24/174 (13.8%) participants. An insignificant association [OR = 0.855 (0.36–2.034)] between two was observed. Hence, people in filarial endemic regions can continue taking vaccines without worrying about their efficacy due to the helminthic load in community.

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Lymphatic filariasis;
COVID-19; vaccine;
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Dear Editor,

We would like to address the concerns related to the safety and efficacy of COVID-19 vaccines, especially in the low- and middle-income countries, such as India, with a high burden of Neglected Tropical Diseases. Lymphatic filariasis is a major public health concern in India, affecting more than 23 million people.¹ Lymphatic filariasis is a debilitating disease affecting the poorest of the poor and hence, exhibits complex social, economic, and healthcare challenges similar to COVID-19. With the emergence of COVID-19, it is imperative to take precautions for both these diseases where COVID-19 vaccines might play an important role. But, the safety and efficacy of these vaccines remain a major concern that becomes grave in filarial endemic areas. This needs greater attention as several studies have proposed that helminthic infections might alleviate the efficacy of COVID-19 vaccines through immunomodulation which further compounds in filariasis.^{2,3}

Filarial parasites induce Thelper 1 (Th) response during the microfilariae stage, whereas in the adults Th2 responses are activated predominantly. These parasites exhibit three main characteristics: muted Th 1 response, expansion of Th 2, and a rise in cytokine synthesis inhibitor i.e. interleukin-10 (IL-10), to survive for longer durations in the human body.⁴ They thus, get away from the immune surveillance via antigen-specific T cell hypoactivity. The inflammatory responses are down-regulated due to helminthic infection, which can potentially degrade the development of immunity.⁵

Developing an effective and safe vaccine has been the primary strategy to combat COVID-19, but the concerns regarding their efficacy in helminthic endemic areas rose from potential challenges. These theories were also supported by previous studies which show poor immunogenicity of other

vaccines such as BCG in helminth infected population of Ethiopia.⁶ Also, a meta-analysis on parasitic infections and immunization revealed, the chronic helminthic infection can lead to worse outcomes on immunization.⁷ Helminthiasis has also been associated with impairment of the efficacy of anti-influenza vaccines.⁸

Although, these theories and concerns have been proposed but, there is a paucity of primary evidence on the same. Here, we share a preliminary evidence on the association between filariasis and COVID-19 infection through an exploratory community-based observational study conducted in Jatni block of Khurda district, a lymphatic filariasis endemic region of coastal Odisha, India, from January to February 2021. We randomly selected two villages: Bhimpur and Padanpur, from Jatni block, and randomly included one adult (18 years and above), willing to give informed consent from every alternate household. The observed non-response rate was 16%, thus making our sample of 174 participants. Data on clinical and socio-demographic characteristics such as age, gender were collated along with 2 ml intravenous blood from each participant by a trained laboratory technician following aseptic conditions and transported under the cold chain to the testing facility. To determine lymphatic filarial antigen, the Og4C3 test was performed using TropBio, a quantitative Enzyme-Linked Immunosorbent Assay (ELISA) kit manufactured by Cellabs Pty Ltd., Australia, with a sensitivity and specificity of 95%. COVID-19 IgG antibodies were determined through an ELISA kit manufactured by Dia. Pro Diagnostic Bioprobes S.r.l., Italy with a sensitivity and specificity of 98%. Data were analyzed using STATA v.16 (STATA Corp, Texas). Descriptive measures were provided as frequency and percentage. Furthermore, the Chi-square test and Odds ratio were calculated with *p* values less than 0.05 considered to be significant. This study was approved by the Institutional Human

Table 1. Relationship between COVID-19 antibody and filariasis antigen status

Investigation results	Filariasis antigen positive	Filariasis antigen negative	Statistical analysis	Odds ratio
COVID-19 antibody positive	11 (6.3%)	63 (36.2%)	$\chi^2 = 0.124$	0.855 (0.36–2.034)
COVID-19 antibody negative	13 (7.5%)	87 (50%)	* $P = .724$	

*Not significant at $p < .05$.

Ethical Committee of ICMR-Regional Medical Research Center, Bhubaneswar. Informed written consent was obtained from all participants prior to the enrollment.

Out of 174 participants, 79/174 (45.4%) were males, while 95/174 (54.6%) were females with a mean age of 46.8 (18–92) years. None of the participants received COVID-19 vaccines, as the samples were collected before community vaccination started in the area. COVID-19 antibodies were positive among 74/174 (42.5%) participants, whereas filarial antigens were detected in 24 (13.8%). We observed, 11/174 (6.3%) participants were positive for both COVID-19 antibodies as well as Lymphatic Filarial antigen (Table 1). Further, it was observed that more number of participants 63/174 (36.2%), did not have filarial antigen but tested positive for COVID-19 antibody while filarial antigens were detected among 13/174 (7.5%) of the participants who did not have COVID-19 antibodies. 87/174 (50%) individuals neither tested positive for filarial antigen nor for COVID-19 antibodies. Further, we analyzed the relationship between filarial antigen and COVID-19 antibody status through the Chi-square test ($\chi^2 = 0.124$, $P = .724$), which was not significant at a 95% confidence interval. We observed an insignificant association [OR = 0.855 (0.36–2.034)] between COVID-19 antibody and filarial antigen status, which further did not represent any relationship between the two.

The broad understanding of the complex immunological interaction between SARS-CoV-2 and filariasis is yet to be fully explored, but to the best of our knowledge, this is the first preliminary evidence on the association between the two. We estimated COVID-19 IgG antibodies and antigen status of filariasis among people residing in an filariasis endemic area and further explored their associations. Filarial antigen were detected amongst 13.8% of the participants, which is lower than the findings of a previous study by Chhotray et al.⁹ reporting 16.8% and 17.8% filarial antigenemia in Puri and Ganjam districts of Odisha indicating the region has successfully reduced the burden of filariasis with mass drug administration. IgG antibodies against COVID-19 were observed amongst 42.5% of participants, which signifies a high rate of past SARS-CoV-2 infection which is comparable with the findings of a previous COVID-19 sero-survey reporting 31.1% antibodies in Berhampur, a coastal filariasis endemic district of Odisha.¹⁰

IgG antibodies reflect past infection, which also confirms that despite a high burden of filariasis in the region, a considerable proportion of population was infected with COVID-19. These infected individuals successfully produced antibodies against it. Further, it implies that COVID-19 vaccination too will produce antibodies similar to natural immunity, thus dismissing the concerns about the effectiveness of COVID-19 vaccines based on the immunogenic response of other vaccines. Pathogens exhibit varied immunological responses to helminth, which cannot be generalized to COVID-19.

Some hypothesis suggested helminth infection and subsequent COVID-19 disease interaction can lead to negative outcomes whereas others favored a mitigating effect.^{11,12} In the present study, there was no significant association observed between the two infections, which implies that filariasis was not protective for COVID-19 or vice-versa. This is of potential significance for countries with a high burden of filariasis both in terms of assurance regarding vaccine efficacy and further planning the programmatic rolling of COVID-19 vaccines in filarial endemic regions.

The major limitation of our study is that we reported antigen status for filariasis whereas antibody status for COVID-19 infection. Although, our sample is randomized yet, it is not representative to generalize the findings. Further, studies with a large sample size and uniform testing procedures are warranted for a better understanding of this complex interaction between helminth and COVID-19 infection.

To summarize, we did not find a significant association between filariasis and COVID-19 infection. Although information on COVID-19 is evolving yet, our study concludes people in filarial endemic regions can continue taking vaccines without worrying about their efficacy due to the helminthic infection load in the community. Further, there is no need for chemo-prophylactic measures before administration of COVID-19 vaccines in filariasis endemic areas.

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Authors' contribution

PS and AS conceptualized the study. AS, PS, and SP were involved in data collection, testing, and analysis. AS wrote the first draft, which was refined by PS and SP. SP supervised the study and provided overall guidance. All authors have approved the final version of the manuscript for publication.

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