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COVID-19 vaccinations in patients with inflammatory bowel disease

Advances in the treatment of patients with inflammatory bowel disease (IBD) have substantially improved disease activity and quality of life, and reduced hospitalisation rates and the need for surgery. However, prolonged immunosuppression in these patients can result in increased susceptibility to opportunistic infections. Many of these infections are preventable through vaccination and immunisation strategies that should be undertaken as early as possible after diagnosis, because the risk of opportunistic infections increases following the first year of immunosuppressive therapy.[1]

The COVID-19 pandemic has led to substantial concerns for patients with IBD who are on immunosuppressive medications, many of whom are using additional protective measures. Although early COVID-19 studies have suggested that immunosuppressive medications are safe, robust and reproducible data are not available to adequately risk stratify patients with IBD, and current measures are mostly based on observational studies and theoretical risk.[2] Large scale, prospective, population-based registry studies and meta-analyses have identified key risk factors associated with a higher probability of mortality from COVID-19, including age, socioeconomic deprivation, diabetes, respiratory disease, obesity, and being from a Black, Asian, or other minority ethnic group.[3]

One of the best ways to mitigate against the risk of COVID-19 is the rapid development of safe and effective vaccines. Although initial phase 1/2 studies are promising,[4] patients on immunosuppressant medications have largely been excluded from these studies, creating potential future concerns regarding safety and generalisability of outcomes for individuals with IBD.

To achieve a sufficient degree of herd immunity, vaccination programmes are primarily successful only when there are high rates of coverage and acceptance. The importance of patients with IBD being included in vaccine trials is compounded by the concern that these patients have a lower response to vaccinations and that vaccinations are generally underused in this population. Melmed and colleagues[5] showed that in patients with IBD there was an uptake of only 22–46% for the influenza vaccination, and a mere 9% were vaccinated for pneumococcal pneumonia, despite both vaccines being recommended in the British and European IBD guidelines for vaccinating patients.[6] A patient survey showed a perceived lack of benefit from vaccination as the most frequent reason for low vaccine uptake, as well as concerns regarding side-effects, risk of disease flares, needle aversion, and inconvenience.[7] However, in the present pandemic, both perception of risk and health awareness might be very different, with implications for vaccine acceptance.

In patients with IBD who were vaccinated against influenza, an immune response was induced, but use of concomitant infliximab and immunomodulatory therapy were associated with inadequate rates of seroconversion.[8] In adult populations vaccinated with the pneumococcal vaccine PSV-23, an impaired immune response was shown in patients with Crohn's disease taking combination immunosuppressive therapy.[1] Other vaccines such as those against hepatitis A and B virus, tetanus, and herpes zoster have also been shown to be potentially less effective in patients with IBD than in control groups.[9]

The extent to which medications might affect vaccine response, independent of underlying disease activity, is unclear. Of note, concurrent anaemia, which is a common finding in patients with active IBD, might impair response to vaccinations.[9] There is therefore an urgent need for better understanding of both the effectiveness of potential vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in patients with underlying health conditions, as well as the potential impact of effective disease control on rates of vaccine response.

Currently, the candidate vaccines in phase 3 trials include inactivated, mRNA, or vector-based approaches. The classic inactivated or live-attenuated vaccines raise safety concerns due to possible induction of the disease. However, the ChAdOx1 nCoV-19 trial vaccine uses a replication-deficient chimpanzee adenovirus to deliver a SARS-CoV-2 protein to induce a protective immune response. This vaccine seems to be promising for patients with IBD because adenovirus vectors do not integrate the viral genomic DNA into the host's genome, are highly immunogenic, and can induce robust innate and adaptive immune responses. The same adenovirus vaccine platform is also being assessed for use against malaria, HIV, influenza, and Ebola virus.[10] Nevertheless, the phase 1/2 trials of the ChAdOx1 nCoV-19 vaccine were done on young, healthy volunteers and as such do not address the potential immunity concerns in patients with chronic diseases or those on immunosuppressants.[4] Moreover, we cannot assume that data on one vaccine type in a specific group of people can be extrapolated to other vaccine types.

There needs to be a stronger emphasis on vaccinating patients with IBD within the broader health-care preventative scheme. It is important that these factors are considered when policy makers and national health services start to design and develop future COVID-19 vaccination programmes. Equitable access to COVID-19 vaccination programmes

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See Online for appendix

should be endorsed. If this is not feasible, then we propose that future community vaccination programmes support and promote vaccines that can be used by the high-risk cohort of patients with IBD.

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Effect of the COVID-19 pandemic on viral hepatitis services in sub-Saharan Africa

The global response to limit the spread of COVID-19 has diverted attention and resources from existing local health priorities, particularly in countries of low and middle income (LMICs).[1] As highlighted in a Comment in *The Lancet Gastroenterology & Hepatology* by Neil Gupta and colleagues,[2] the collateral damage on efforts to address the viral hepatitis epidemic in sub-Saharan Africa is of high concern. However, the potential effect of COVID-19 on viral hepatitis services has been poorly documented.[2]

We have recorded a striking decrease in use of outpatient services by patients with chronic hepatitis in three countries in sub-Saharan Africa. We retrospectively counted the number of new and known cases of chronic hepatitis B virus (HBV) or hepatitis C virus (HCV) infection seen at the main referral hospitals in Burkina Faso (Yalgado-Ouédraogo Hospital and Bodogodo Hospital, Ouagadoudou; and Souro-Sanou Hospital, Bobo-Dioulasso), Tanzania (Muhimbili National Hospital, Dar es-Salam), and The Gambia (Medical Research Council Clinical Services, Fajara) from Jan 1 to April 30, 2020, a period covering the time before and during the COVID-19 pandemic. We also asked a doctor in charge of hepatitis services at each centre about the type of clinical and laboratory services that were disrupted, and plausible reasons for such disruption, using a standardised questionnaire (appendix pp 1–3).

The number of patients reviewed monthly at the hepatitis clinics fell substantially from January to April, 2020, by 71% in Burkina Faso, 95% in Tanzania, and 83% in The Gambia for new cases, and by 73% in Burkina Faso, 77% in Tanzania, and 89% in The Gambia for patients in follow-up (appendix p 4). To exclude any annual seasonal effects, we compared the number of viral hepatitis cases (new patients and patients in follow-up) in 2020 against those seen during the same period last year (Jan 1 to April 30, 2019) in The Gambia and found no significant fluctuation in cases (data not shown).

Across these countries, doctors consistently cited the patient's fear of contracting severe acute respiratory syndrome coronavirus 2 at clinics as a primary reason for the drop in patient numbers. The decrease in number of outpatient visits seems to have started in February, 2020, preceding confirmation of the first COVID-19 cases in these countries (from the second to third week of March, 2020) and implementation of public health measures limiting social contacts by the respective governments (in March and April, 2020). In Burkina Faso, the number of patients regularly monitored for chronic viral hepatitis steadily fell over this period, even though clinics were maintained and treating doctors encouraged patients to be retained in care. By contrast, in Tanzania and The Gambia, hepatitis clinics were temporarily closed at the end of March, 2020, to prepare for the COVID-19 epidemic, and staff at hepatitis services were relocated to support COVID-19 preparedness, to receive patients who were febrile with a suspicion of COVID-19, and to mitigate COVID-19 outbreaks. Of the essential diagnostic tests to manage chronic hepatitis, rapid tests for HBsAg, alanine aminotransferase, and haematology were available without any disruption throughout