Experts' views on COVID-19 vaccination and the impact of the pandemic on patients with Gaucher disease

The current outbreak of the novel severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), causing coronavirus disease 2019 (COVID-19), has become a worldwide pandemic with high morbidity and mortality in individuals with chronic disorders.[1] The pandemic introduced many unanticipated challenges for patients with chronic and rare diseases, such as Gaucher disease (GD).[2] GD is the most common inborn error of metabolism, caused by biallelic glucosylceramidase beta (*GBA*) variants and affecting the recycling of cellular glycolipids; GD manifests as hepatosplenomegaly, thrombocytopenia, anaemia and bone disease.[3]

We performed a cross-sectional study using an online survey regarding attitudes of GD experts towards COVID-19 vaccination for patients with GD, and the impact of the pandemic on their patients. The full methods and results are available in the Supplementary Data.

A total of 19 GD experts from 10 countries, collectively treating 1417 patients with GD, responded to the survey, revealing overall support of COVID-19 vaccination for patients with GD. This support is mainly explained by the concern that the pathophysiology of GD may put the patients at higher risk of severe COVID-19, coupled with the absence of contraindications for vaccination in this population, which is consistent with professional guidelines.[4–7] Specifically, mRNA-based vaccines were favoured by GD experts compared to adeno-associated virus (AAV)-vectored DNA-based vaccines due to their overall efficacy, tolerance and safety profiles, as appears from clinical trials and worldwide experience.[8,9] Concerns regarding the AAV-vectored vaccines may be underestimated amongst our cohort, as the questionnaire was distributed when data on only one such vaccine was available (AZD1222, Oxford-AstraZeneca), and some responses were prior to the regulatory authorisation, thus lacking knowledge on its side-effects.

Our present study revealed that of the 82 patients with GD who contracted COVID-19 (5·8% of the entire cohort), 93·9% were either asymptomatic or mildly affected, while two had severe/critical infection. It is also possible that these numbers are an underestimation, as asymptomatic or mildly symptomatic patients may have not been tested for COVID-19 or may have not reported on contracting COVID-19 to their GD clinic. To date, four reports have been published on COVID-19 infection in patients with GD, all reporting of asymptomatic/mild infections, and only one of severe disease in a patient with multiple comorbidities.[10–13] This makes ours the largest cohort reporting on patients with GD contracting COVID-19 and the second to report on patients with GD developing critical disease. Thus, it can be concluded that GD does not confer excess risk of severe COVID-19 compared with the general population. Additionally, it is not likely that GD offers protection from SARS-CoV-2 infection and/or its complications as previously speculated.[14] Currently, when assessing the risk factors for patients with GD to develop severe COVID-19 infection, clinicians should follow the same guidelines as for the general population. When a patient with GD develops COVID-19, it is important they communicate with their GD clinic, specifically for those on oral therapy due to potential risk of drug–drug interactions,[2] but also regarding enzyme-replacement therapy (ERT) treatment during confinement lockdown and general disease management.

The full impact of the pandemic on the management of patients with chronic diseases remains to be determined. Preliminary data showed disruption of therapy in 24–49% of patients with GD receiving hospital-based intravenous ERT during certain periods of the pandemic.[12,13,15] As home therapy is available in all countries in our present cohort, we could not infer whether unavailability of home ERT led to an increased treatment switch to orally administered substrate-reduction therapy (SRT). However, even in countries where home treatment is available, at least some of the patients with GD are treated by ERT in a hospital setting. This could be attributed to many factors, such as local unavailability of home treatment, physician or clinic policy, patient's preferences or others. The proportion of patients switching ERT location to a home setting in this cohort was 2%, which may be an over-estimation, as this number represents information only from experts who provided full data regarding ERT regimen changes and excludes clinics where no changes to ERT treatment were made. However, this finding is much lower than the 31% change reported in an Italian study at the beginning of the pandemic, possibly due to the severe impact of the pandemic at early stages in Italy[12] and the observation that 7% of the patients in our present cohort switched treatment type to orally administered SRT. Possibly, a higher proportion of the patients in our cohort were already on home ERT, not requiring a change of setting. Of the 1471 patients with GD, 803 (56·7%) are from Israel, where home therapy is widely utilized. Interestingly, of patients who made any changes to their ERT treatment

doi: 10.1111/bjh.17693

regimen, most switched to SRT (59%) rather than home treatment (14%), while 27% paused their treatment altogether. Although this result is based on a small cohort, it may nonetheless reflect patient management challenges during a pandemic.[2]

Of the 47 patients starting new treatment during the pandemic, 27 started ERT [57%, 95% confidence interval (CI) 43–72%] and 20 patients started SRT (43%, 95% CI 28–57%). The age of patients who began treatment during the pandemic in our present cohort was unavailable, as well as data on pre-pandemic treatment preferences of patients; therefore, this finding is difficult to interpret. However, based on the authors' personal experience, this is a relatively high ratio of patients beginning SRT as a first-line treatment, and might either reflect the pandemic effect and/or timely attitude change toward SRT.

Overall, our present findings can assist in reassuring patients with GD worldwide of the expected mild nature of COVID-19, in supporting of COVID-19 vaccination and informing of their conduct during the pandemic. It would be of value to conduct future research on the views of patients with GD themselves on vaccination, whether they have consulted any GD experts on their decision to get vaccinated, and to compare vaccination rates of patients with GD to those in the general population. Time and more studies are needed to assess whether home ERT and increased use of SRT, as well as other measures implanted during the pandemic, such as digital health and networking, had a positive effect on the management and well-being of patients, and how it might affect the future of healthcare in this population of patients.

Ethics approval and consent to participate

The study was approved by the Tel Aviv Sourasky Medical Center Institutional Review Board. Committee reference number: 0018-21-TLV.

Consent for publication

Not applicable.

Availability of the data and materials

Data sharing is not applicable for this study.

Competing interests

Ian J. Cohen has received honoraria for scientific talks, grants and advice from: Sanofi-Genzyme, Protalix, Pfizer and Takeda-Shire. Noa Ruhrman-Shahar has received honoraria for scientific talks, grants and advice from: Sanofi-Genzyme, Pfizer and Takeda-Shire. Tova Hershkovitz has received honoraria for scientific talks, grants and advice from: Sanofi-Genzyme, Pfizer and Takeda-Shire. Claus Niederau has received honoraria for scientific talks, grants and advice from: Abbvie, Alexion, Biogen, Falk, Sanofi-Genzyme, Gilead, MSD and Takeda-Shire. The SZMC Gaucher Unit receives support from Sanofi/Genzyme for participation in the ICGG Registry, from Takeda for the GOS Registry and Pfizer for TALIAS. The Unit also receives research grants from Takeda, Pfizer, Sanofi-Genzyme and Centogene. Ari Zimran receives honoraria from Takeda, Pfizer, Sanofi and BioEvents and consultancy fees from Takeda, AVOBIO, Insightec, Todos Medical and Prevail therapeutics. Shoshana Revel-Vilk receives grant/research support, honoraria and advisory fee from Takeda, Pfizer and Sanofi-Genzyme. Maria Domenica Cappellini is a member of the advisory board for: BMS/Celgene, Sanofi-Genzyme, Novonordisk, Vertex/CRISPR and Vifor. Hagit Baris Feldman has received honoraria for scientific talks, grants and advice from: Sanofi-Genzyme, Protalix, Pfizer and Takeda-Shire. The remaining authors declare that they have no competing interests.

Author contributions

Uri Hamiel and Hagit Baris Feldman conceived and designed the study, analysed and interpreted the data, wrote the first draft and revised the paper incorporating contributions from co-authors. They had access to all the data and decided on submission. Alina Kurolap conducted database management quality assurance, analysed and interpreted the data and critically revised the manuscript. Ian J. Cohen, Noa Ruhrman-Shahar, Tova Hershkovitz, Claus Niederau, Ari Zimran, Shoshana Revel-Vilk and Maria Domenica Cappellini interpreted the data, contributed to the discussion and critically revised the manuscript.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Fig S1. Gaucher disease (GD) expert views on COVID-19 vaccination for patients with GD. Opinion of GD experts regarding the recommendation of any type (A), mRNA-based (B), and AAV-vectored DNA-based COVID-19 vaccine (**C**) for patients with GD.

Fig S2. Patients with Gaucher disease (GD) and their management during the pandemic. (A) In clinics where full data regarding regimen changes for patients with enzyme-replacement therapy (ERT) is available, most patients on ERT did not change their treatment setting (88%), (B) Most of the patients that made a change to their ERT treatment during the pandemic switched to orally administered substrate-reduction therapy (SRT; 59%) or paused treatment entirely (27%), (C) Most of the patients with GD who contracted COVID-19 had an asymptomatic or mild disease.

Table SI. Characteristics of GD experts that responded to the survey.

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