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Vaccination for the novel coronavirus disease in hematological disorders

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ABSTRACT

The coronavirus disease-19 (COVID-19) caused by the SARS-CoV-2 virus, is now an ongoing pandemic. First detected in December 2019 at Wuhan, China, this disease has now spread to all parts of the world. COVID-19 may affect anyone, without regard for age, sex, or underlying disease condition. Patients with benign or malignant diseases when affected, usually have a more severe outcome than people without comorbidities. Increasing one's immunity by vaccination against COVID-19 will help to improve the disease outcomes of COVID-19 in patients who already have some underlying disease. The live-attenuated or killed and recombinant viral protein vaccines currently available can elicit both humoral and cellular immunities. However, in immunocompromised patients (either due to the disease pathology or treatment-related immunosuppression), immune response may not be as effective as expected. Depending on the underlying disease pathogenesis, the patient may not be able to mount an adequate immune response post-vaccination. However, in view of the severe risks posed by COVID-19 disease, vaccination is of utmost importance. This review aims at understanding the importance of SARS-CoV-2 vaccination in patients with hematological disorders, and also aims to understand the side effects which arise post-SARS-CoV-2 vaccination. We have tried to ascertain the best way to vaccinate patients with hematological disorders.

Keywords: COVID-19, SARS-CoV-2 vaccination, Hematological disorders, Benign, malignant

INTRODUCTION

The novel coronavirus disease-19 (COVID-19), the pandemic which has swept the globe, is now a familiar disease condition. It was first detected in December 2019 at Wuhan, China, and since then, it has travelled to all corners of the world, wreaking havoc on the lives of many.[1] This disease has affected everyone disregarding age, gender, or underlying disease conditions.[2,3] It is little wonder that patients having hematological diseases have also been affected by COVID-19.[4]

Although, there is no definitive therapy for COVID-19, the advent of vaccination has given hope to control this disease.[5] Vaccination acts by modulating the body's own immunity against a specific antigen.[6] Depending on the type of vaccine used – live attenuated or killed, there are differences in pathogenesis of mounting an immune response and the side effects experienced.[6,7] Most patients with hematological diseases are more susceptible to serious COVID-19-related adverse effects due to immunosuppression.[4] Patients with hematological malignancies who have an increased risk of infections and a higher risk of mortality should be vaccinated.[8] It has been seen from a meta-analysis that patients with hematological malignancies who were hospitalized for COVID-19 had a mortality rate of 34%, further emphasizing the need for vaccination.[9]

Thus, increasing one's own immunity by means of vaccination will help to improve the disease outcomes of COVID-19 in patients who already have some underlying disease. However, hematological disorders comprise a vast spectrum of diseases, both benign and malignant. Depending on the underlying disease pathogenesis, the patient may not be able to mount an adequate immune response post-vaccination.[10] In patients with underlying immunocompromised conditions, avoiding a live vaccine will be a better option.[10,11] A live vaccine can lead to uncontrolled replication in a patient who is already immunocompromised.[6] On the other hand, a killed vaccine may sometimes mount an inadequate response in patients with immunodeficiency disorders.[6] An inactivated vaccine is to be administered at least 2 weeks before starting immunosuppressive therapy, while live vaccines are to be administered at least 4 weeks before starting immunosuppression.[11]

This review will aim to understand the importance of SARS-CoV-2 vaccination in patients with hematological disorders.

MATERIALS AND METHODS

The type of vaccine to be administered and the timing of administration of the same will be analyzed. The adverse effects, if any, post-vaccination will also be studied. All available published literature regarding COVID-19 vaccination in various hematological conditions have been reviewed by a PubMed search. In addition to the following keywords – COVID-19, SARS-CoV-2, and vaccination; names of specific disease entities have been used for our literature search. The recommendations and treatment guidance published by various recognized societies have also been considered while writing this review. This being a new disease, there is a lack of clear consensus between different committees, and the data is constantly being updated as new information pours in. This review is not aimed at analyzing individual vaccines.

TYPES OF VACCINES CURRENTLY AVAILABLE

There are many different vaccines currently available against COVID-19.[5] As of June 3, 2021, according to the WHO, the following vaccines are safe and efficacious – AstraZeneca/Oxford, Johnson and Johnson (both live attenuated); Moderna, Pfizer/BioNTech (both mRNA vaccines), Sinopharm, and Sinovac.[12] Three vaccines are authorized for use in the USA - Pfizer/BioNTech, Moderna, and Johnson and Johnson/Janssen and four vaccines are currently in use in Europe – Pfizer/BioNTech, Moderna, AstraZeneca/Oxford, and Johnson and Johnson/Janssen.[13,14] At present, in India, there are two vaccines approved for use – CoviShield (AstraZeneca) and Covaxin, both manufactured indigenously.[15-17] A Russian vaccine Sputnik V has also been approved for use in India.[15]

CoviShield (ChAdOx1-S recombinant genetically modified virus) and Covaxin (a whole-virion inactivated SARSCoV-2 antigen)[16,17] are recommended for immunization in individuals >18 years of age. The vaccines act as a signal for the immune system, stimulating it to produce antibodies, without causing the disease. Many newer vaccines are under development.

SARS-COV-2 VACCINATION AND SPECIFIC DISEASE CONDITIONS

In a Cochrane analysis (2011), it had been clearly highlighted that the possibility of protection afforded by vaccines far exceeds the risks or side effects in patients with hematological malignancies.[9] The live-attenuated or killed and recombinant viral protein vaccines currently available can elicit both humoral and cellular immunities. However, in immunocompromised patients (either due to the disease pathology or treatment-related immunosuppression), the immune response may not be as effective as expected.[6,18] There are no trial results till date to support or refute this statement accurately, and results are still awaited.[18] In absence of conclusive evidence of an increase in immune response to COVID-19, it will be advisable to practice other measures post-vaccination, such as, masking and maintaining distance or washing hands.

MALIGNANT DISEASES

Acute leukemias

Patients with acute leukemias, acute lymphoblastic leukemia, or acute myeloid leukemia are more susceptible to poorer outcomes with COVID-19 due to impaired immune responses to SARS-CoV-2 virus.[18] Although response to vaccination may not be as expected, patients should be vaccinated with preferably an attenuated or a killed vaccine. An inactivated or recombinant viral protein vaccine should preferably be administered at least 2 weeks before starting immunosuppressive therapy.[11]

Chronic lymphocytic leukemia (CLL)

Patients with CLL have been known to show suboptimal response to vaccination.[19] In the study by Roeker *et al*., it has been shown that nearly half of all patients with CLL and most patients who received BTK inhibitors, such as ibrutinib, failed to mount a satisfactory immune response.[20] In a prospective study by Herishanu *et al*., the antibody response to BNT162b2 mRNA COVID-19 vaccine was severely reduced and factors such as a younger age, female sex, immunoglobulin levels, or lack of ongoing therapy with CD20 inhibitors predicted this response to vaccination.[21] Although few prospective trials are available regarding SARS-CoV-2 vaccines in CLL patients, similar to the recommendations of administering influenza or pneumococcal vaccines to patients with CLL, SARS-CoV-2 vaccines are also

advisable for all CLL patients, and it should be administered preferably before starting immunosuppressive therapy.

Chronic myeloid leukemia (CML)

CML patients are considered appropriate for receipt of SARS-CoV-2 vaccine. All patients, whether newly diagnosed, on therapy, in deep molecular response or off therapy should be vaccinated when possible.[22] Chelysheva *et al*. have described how the incidence and disease course of COVID-19 among CML patients appear to be similar to that of the general population, and the patients tolerated vaccination well.[23] To know the exact immunological outcomes with SARS-CoV-2 vaccines, prospective studies are to be undertaken.

Non-CML myeloproliferative neoplasms (MPN), myelodysplastic syndromes (MDS), and MDS/MPN

Although, there are no known data to show that patients with MPN, MDS, or MPN/MDS are more susceptible to COVID-19, it is known that patients with malignancies including hematological malignancies usually have poorer outcomes with COVID-19.[4] Although the results of response to vaccination in this patient population are still awaited, vaccination with an attenuated or killed vaccine should be encouraged.

Lymphoma and myeloma

As evident in a study conducted for Herpes zoster vaccination, it was observed that B-cell malignancies or B-cell depleting therapy led to reduced humoral vaccine response.[19,24] Rituximab and other anti-CD20 therapy led to reduced humoral response post-vaccination.[25] Thus, as in case of vaccination for other diseases, a gap of at least 3–6 months would be prudent.[25] Prospective trials concerning patients who receive the SARS-CoV-2 vaccine are currently underway.

In patients with myeloma, the impaired immunity is due to the disease itself and the immunomodulatory drugs used. Male gender, advanced age, and associated kidney dysfunction are further factors leading to increased mortality in myeloma patients.[26] SARS-CoV-2 vaccination is advocated for patients with plasma cell neoplasms. In a study in the Royal Marsden Hospital, there was a 70% response to vaccination in myeloma patients.[27] In 30% patients who did not show a good antibody response to vaccination, supportive protective measures, such as masking or hand washing, should be continued.

BENIGN DISEASES

Inherited and acquired aplastic anemia (AA); paroxysmal nocturnal hemoglobinuria (PNH)

AA is a disease characterized by pancytopenia and reduced immunity. Patients who have clinical improvement, and are on cyclosporine therapy for 6–12 months, post-anti-thymocyte globulin (ATG) therapy, may mount a good immune response and are to be vaccinated after 6 months.[28] Those within 6 months of cyclosporine therapy or allogeneic transplantation will fail to mount an adequate immune response. There are also reports of few patients developing COVID-19 post first dose of vaccination or relapsing post-recovery.[29]

For patients with inherited AA, the same principles as acquired AA are followed. Inherited AA syndromes, such as Fanconi's disease or Diamond-Blackfan syndrome, are commonly seen in children and young adults. In many countries, children >12 years of age are eligible for COVID-19 vaccination, unlike in India, where the age of SARS-CoV-2 vaccination starts at 18 years.[15,30] Children with inherited bone marrow failure syndromes (IBMFs) such as, Diamond-Blackfan anemia, congenital dyserythropoietic anemia, or enzyme deficiency anemia, who have undergone allogeneic hematopoietic stem cell transplantation (HSCT) as treatment within a year, should be considered at high risk.

PNH patients should also be vaccinated against COVID-19. In case of a high PNH clone, sometimes, there may be a risk of thrombosis post-vaccination. However, there is no conclusive evidence for the same.[31] In another report by Gerber *et al*., four patients have been reported to have hemolysis post-vaccination, while two patients had no adverse effects.[32] Further prospective studies need to be carried out to conclusively assess the merits or demerits of vaccination in PNH patients. Thus, patients with PNH should be vaccinated with a strict observation for side effects.

Hemophilia and bleeding disorders

Patients with hemophilia or other bleeding disorders are not at an increased risk of COVID-19 infection, when compared to the general population.[33] Patients with such disorders should be vaccinated with SARS-CoV-2 vaccine, similar to the current guidelines for the general population. Till date, all types of SARS-CoV-2 vaccines available are to be administered through the intramuscular route.[5] In case of these bleeding disorders, patients should get an intramuscular vaccine shot through the smallest available needle gauge (25–27 gauge). Following the injection, pressure should be applied for at least 10 min at the site of injection.[33] As per Srivastava *et al*., an ice pack may be applied at the site 5 min before injection, to reduce chances of a hematoma.[34] In case of severe hemophilia or Type III von Willebrand disease, the vaccine shot should be administered after a prophylactic dose of FVIII or FIX and if factor level >10%, often hemostatic precautions were unnecessary.[33] Patients on the newer drug emicizumab may be vaccinated at any time, irrespective of the ongoing drug.[35]

Immune thrombocytopenia (ITP)

ITP does not increase chances of getting the COVID-19 infection, however, like any other viral infection, COVID-19 often leads to a rapid fall in the platelet count.[36] Furthermore, there have been occasional reports of ITP developing post-receipt of SARS-CoV-2 vaccination.[37] Vaccine-induced thrombotic thrombocytopenia (VITT) or thrombosis with thrombocytopenia syndrome (TTS) is another entity noted post-vaccination.[38,39] The mechanism of the development of VITT/TTS is similar to heparin-induced thrombocytopenia (HIT). Thus, testing for PF4-polyanion antibodies should be considered in patients suspected to have TTS.[38] These patients respond well to immunoglobulin and non-heparin anticoagulation.[40] As the risks of COVID-19 infection are more serious than the rare side effects experienced post-vaccination, all ITP patients should also be considered for SARS-CoV-2 vaccination. Although there is no consensus on a safe platelet count for vaccination, most recommendations advice the safe limit to be >30,000/dl. The platelet cut-off may vary depending on individual institutional policies, being as low as 20,000/dl.[41] Most patients will respond well to standard ITP therapy.[38]

Patients on anticoagulation

In patients who are on anticoagulants, the vaccine can be injected if the INR is within (2–3) normal range (in case of Warfarin), or if there are no active bleeding complaints.[16,17] Aspirin may be withheld for 3 days before vaccination.[17] The North American Thrombosis Forum also states that adults on anticoagulants, for example, clopidogrel, should be vaccinated.[42]

Patients with inherited thrombophilia or other thrombotic disorders

Patients with inherited or acquired thrombophilia such as, Factor V Leiden; prothrombin 20210A mutation; antiphospholipid syndrome (APS); protein C, protein S or antithrombin deficiency), or a prior history of any thromboses, are not associated with thrombocytopenia and are unlikely to increase the risk of TTS post-vaccination.[43] Other pro-thrombotic states such as use of oral contraceptives also do not increase the chance of TTS. Thus, CDC approves use of any vaccine including the Johnson and Johnson/Janssen vaccine in patients with thrombophilia.[43]

In rare instances, there have been reports of TTS occurrences after use of Johnson and Johnson/Janssen vaccine. TTS has been reported in 7.0 cases/million and 0.9 cases/million, among Janssen COVID-19 vaccine doses given to women aged 18–49 years and ≥50 years, respectively.[43] In case of patients with heparin-induced thrombocytopenia (HIT type 2), the AstraZeneca vaccine is contraindicated.[44]

In a review by Talotta and Robertson, anti-phospholipid antibodies (aPLs) are considered a risk factor of thrombosis post-vaccination and require further studies.[45] The adenoviral vector-based vaccines may lead to platelet destruction, while mRNA-based vaccines may lead to activation of coagulation factors. In addition, a type I interferon response may be initiated in APS patients, leading to further generation of aPLs. All these may lead to a pro-thrombotic condition.[43] In some other preclinical and clinical studies, aPLs ± APS may appear post-tetanus toxoid, seasonal influenza, and human papillomavirus vaccines.[46-48] Further, studies will explain this association leading to thrombosis. According to the NHS recommendations, APS is not a contraindication for COVID-19 vaccination.[44]

Thalassemia and other hemoglobinopathies

According to the Thalassemia International Federation recommendations, all patients with hemoglobin disorders should be considered as high-risk patients and should be considered for SARS-CoV-2 vaccination.[49] According to the UK Haemoglobinopathy Panel, there are some specific groups of patients who require urgent vaccination for COVID-19.[49] The following patients should be considered for immediate vaccination – Sickle cell disease (SCD) patients, Thalassemia patients with iron overload, patients who underwent splenectomy, and patients with any underlying comorbidity.[49]

Patients with Thalassemia major often have underlying complications, such as heart disease, or endocrine disorders, making them a population vulnerable to the adverse effects of COVID-19.[50]

Patients with SCD are at serious risk due to COVID-19 infection, as the dreaded acute chest syndrome in SCD is common after respiratory tract infections.[51] According to the National Haemoglobinopathy Panel, splenectomized patients are not at an added risk for serious COVID-19 effects.[52] Children who have undergone allogeneic transplant for SCD within the past 1 year and/or are on immunosuppression should also be considered as high-risk group patients.[52] It should be kept in mind that due to various iron overload-related adverse effects compromising the patient's immunity and also because many patients may be splenectomized, patients with thalassemia may not be able to mount an adequate immune response to SARS-CoV-2 vaccines.[53]

According to the British Columbia Center for Disease Control, the AstraZeneca vaccine is currently not being offered to patients of thalassemia, due to the rare adverse effect of TTS.[53]

Primary immunodeficiency syndromes (PIDs) and other immune disorders

People with immune diseases, such as PIDs or autoimmune lymphoproliferative syndrome, are more prone to infections,

including COVID-19. Patients with T-cell deficiency alone may have milder COVID-19 infection, while the disease is more severe and prolonged in patients with B-cell deficiency disorders.[54] It has been seen in a study conducted that lack of a proper immune response in PIDs may lead to a less severe COVID-19 infection.[55] These patients with PID should receive a killed SARS-CoV-2 vaccine, as a live vaccine may lead to T-cell responses and reactions.[54] It is recommended that all patients with PID, including their close contacts, should be vaccinated. Patients with hypogammaglobulinemia should also be vaccinated.[10,56] Patients on intravenous immunoglobulin (IVIg) should be vaccinated 2 weeks after an IVIg infusion.[57]

Until now, the vaccines have not been approved for children below the age of 12 years.[30] Patients with immune disorders should be closely monitored as COVID-19 may lead to altered immune responses in occasional patients with underlying immune disorders. Wahlster *et al*. have highlighted a case of autoimmune hemolytic anemia in a patient with chronic ITP.[58]

Other reasons for a weakened immunity in patients, such as human immunodeficiency virus (HIV) infections, should also necessitate vaccination for COVID-19. In all patients with immunodeficiency disorders, those on immunosuppressive therapy or with HIV infections, no data are available regarding the safety of SARS-CoV-2 vaccines, and the immune response may be attenuated.[10,59]

HSCT AND CHIMERIC ANTIGEN RECEPTOR-T (CAR-T) CELL THERAPY

Post-HSCT patients or patients who have received CAR-T therapy are at an increased risk for severe COVID-19 infection because they are immunosuppressed due to conditioning regimens, radiation or CAR-T cells.[60] There are already published studies regarding the time of administration of vaccines for other diseases, post-transplant, or CAR-T therapy.[61] In a study by Cordonnier *et al*., it has been shown that an earlier vaccination post-HSCT is not inferior to the immune response mounted when the patient receives vaccination at a later date.[62] Thus, SARS-CoV-2 vaccination may also be considered at an earlier date to prevent COVID-19. However, trials are lacking regarding the exact time for vaccination post-transplant.

Patients may be administered any type of SARS-CoV-2 vaccine available. Both mRNA vaccines reduce COVID-19 infection and hospital admissions.[14] At present, mRNA SARS-CoV-2 vaccines may be administered as early as 3 months post-HSCT or CAR-T.[63] Of the available vaccines, the Johnson and Johnson/Janssen vaccine (Ad26.COV2.S) may not be as efficacious in this population as pre-existing antibodies to Adenovirus may neutralize the vaccine's effects.[63]

Immunosuppressants are often used as maintenance therapy post-HSCT or CAR-T therapy, and this reduces a proper immune response.[14,25] Lower rates of immune responses have also been noted in solid organ transplant recipients.[14] Thus, it is advised that vaccines be taken before initiation of B-cell suppressing therapies or in between receipt of B-cell suppressing therapy. A gap of 2 weeks should be allowed after the second dose to allow for T-cell immune response to develop.[63] Sometimes, patients with hypogammaglobulinemia are given IVIG to enhance their immune status. According to information issued by CDC, there is no minimum gap between the receipt of IVIG and SARS-CoV-2 vaccines.[43]

According to the ASH recommendations, in case, the patient acquires a COVID-19 infection post 1st dose of vaccination, the 2nd dose should be delayed.[63] Furthermore, if the patient had received a SARS-CoV-2 vaccine before undergoing a HSCT or receiving CAR-T cell therapy, he will need to be revaccinated, as these therapies will destroy any memory cells.[14] Vaccination should be delayed by 90 days in patients who have gotten a COVID-19 infection or who have been treated with COVID-19 convalescent plasma or monoclonal antibodies for SARS-CoV-2.[63]

There are some situations where SARS-CoV-2 vaccines should be withheld, according to EBMT recommendations.[14] Those include – severe acute GVHD Grade III–IV patients; patients who received B-cell destroying or suppressing therapy within the past 6 months; patients who received CAR-T therapy within the past 6 months; and patients recently treated with ATG or alemtuzumab. Children <16 years age are also not under consideration for vaccination until it is approved in studies.[14] Children with SCD, thalassemia, or IBMFs who have received an allogeneic HSCT within the past 1 year should be considered as high-risk group patients.[52]

Regarding allogeneic HSCT, the donor's vaccination should not be delayed. According to the ECDC recommendations, there is no risk to vaccinate donors with mRNA or protein subunit vaccine, and there is no risk to receive stem cells from such donors either.[64] A gap of 3–7 days should be there before starting GCSF for collection of stem cells from the donor.[64] Although, the transplant donation should not be delayed, the ECDC also recommends that donors who have received vector-based or live-attenuated vaccines should be deferred for 4 weeks after vaccination.[14,64] ASH recommends a gap of at least 2 weeks post-vaccination, before the donor can donate stem cells.[63]

Post-HSCT, patients of MM are continued on maintenance therapy, such as lenalidomide. According to EBMT, there are no clear-cut recommendations regarding vaccination, and physicians can exercise their discretion.[14]

It is advisable for patient's caregivers and health-care personnel to be vaccinated.[14] There is no recommendation from any of the established societies, regarding serologic

testing post-vaccination, unless if required for a trial protocol.[63]

GENERAL CONSIDERATIONS FOR VACCINATION IN PATIENTS WITH HEMATOLOGICAL DISORDERS

When to administer vaccine?

Considering the seriousness of the current pandemic, vaccination against COVID-19 should take precedence over the regular immunization schedule. In case of all hematological disorders, even if a patient has been affected by COVID-19, he or she should be considered for SARS-CoV-2 vaccination. As reinfection is uncommon within 90 days of the initial disease, vaccination can be considered after 90 days.[15,56]

If the patient had received convalescent plasma (unclear recommendations of use) or was treated with monoclonal antibodies, before vaccination or after the 1st dose, the next dose should be deferred for 90 days.[43,65] However, SARS-CoV-2 vaccination if received within 90 days of receipt of antibody therapy, need not be repeated.[43] According to the information issued by the Government of India, SARS-CoV-2 vaccination should be deferred by 4–8 weeks in the following conditions: acutely unwell or hospitalized patients, patients who have received convalescent plasma or monoclonal antibodies.[66]

Coadministration with other vaccines

Earlier, it was recommended that SARS-CoV-2 vaccine should preferably be administered alone.[14] Vaccines for influenza and pneumococcal infections, and all other vaccines should be avoided, within 14 and 28 days, respectively, both before and after receipt of the COVID-19 vaccine.[14,56] This gap may be altered if there is a strong indication for administration of the other vaccines.[14] On an average, a gap of 6–8 weeks should be maintained between the vaccines.[14] However, recent recommendations from CDC emphasize that such a gap is not required, and COVID-19 vaccines may be simultaneously administered with other vaccines, albeit at different injection sites.[43]

Gap between two doses?

The gap between two doses of the vaccine depends on the type of vaccine being used.[10,13,14,16,17,43,67] As the second dose of vaccination leads to an increase in the immune response, in hemato-oncologic disorders, a prolonged gap between two doses of vaccination is not advocated.[68]

Booster doses?

At present, there are no recommendations for booster doses.[43]

Antiviral therapy

Many hematology patients may be on anti-viral prophylaxis. According to CDC information, this does not interfere with COVID-19 vaccination.[43]

Which vaccine is better with respect to adverse effects?

Of the currently approved vaccines, there is no comparative study yet, to consider one better than the other. All are live-attenuated/replication incompatible/subunit/killed vaccines, and in most countries, the availability decides which vaccine is to be received by the patient.

Patients who develop anaphylaxis post the 1st dose of vaccination should avoid the next dose.[66]

The Johnson and Johnson/Janssen vaccine is approved only above the >18 years age, citing the rare TTS occurrences, more common among females aged 18–49 years.[43] Few cases of TTS, including cerebral venous thromboses and other unusual site thrombosis, have been detected post use of the AstraZeneca vaccine.[14,44] However, the benefits of the vaccine far outweigh the rare risks.[44]

Can a different SARS-COV-2 vaccine be used post the 1st dose of vaccination?

Although there are trials underway, until further data are available, it is better to not mix different vaccines, till further results are available.[10]

How to proceed if a vaccinated person develops COVID-19?

With the recently appearing variants of the SARS-CoV-2 virus, patients may develop the disease even if they are fully vaccinated. They should be treated according to protocols for COVID patients.[43]

How to proceed if a patient develops TTS after the 1st dose of vaccination?

Among the reported adverse events, it has been noted that there is a lesser incidence of TTS post the 2nd dose, compared to the 1st dose of vaccine.[44] Thrombosis alone as a side effect is considered an idiosyncratic event to the 1st dose of the AstraZeneca vaccine, and the second dose should be given to patients.[44] However, if there is TTS in the cerebral vein or other unusual sites, the second dose should be delayed till clotting stabilizes, and a different vaccine should be considered for the vaccination.[44] TTS responds well to Immunoglobulin and non-heparin anticoagulation.[40]

Management of other adverse reactions post-vaccination

The antipyretics or analgesics are usually sufficient to manage the local site pain, mild fever, or myalgia. Allergy or anaphylaxis should be managed according to established treatment strategies.[43] In case of other thrombotic side effects, treatment is as per established protocols for thrombosis or thromboembolism.

A rare side effect of acquired hemophilia has been detected post-vaccination and should be managed as per established guidelines for acquired hemophilia.[69]

Polyethylene glycol (PEG), often present in recombinant or plasma-derived factors used in hemophilia patients, is used to increase the shelf-life of the products. If a patient has a reaction to PEG, then he/she should discuss this before taking the SARS-CoV-2 vaccination.[70]

SPECIAL SITUATIONS: PREGNANCY AND LACTATION

Pregnancy and contraception, though mild prothrombotic states, they do not likely confer a higher risk of thrombosis.[44] According to CDC, pregnant or lactating women may receive any of the available COVID vaccines.[42] Based on current information, COVID-19 vaccines are unlikely to be a risk to the pregnant female or fetus.[43] According to the recent Indian government guidelines, pregnant females may receive the vaccine at any trimester.[67] Furthermore, vaccination can be given anytime during lactation.[67] Since killed vaccines are more safe in pregnancy, Covaxin may be considered as the 1st choice.[67]

CONCLUSION

The risks associated with COVID-19 far outweigh the rare post-vaccination risks. Patients with comorbidities, in both benign or malignant hematological disorders, are more susceptible to severe COVID-19. Therefore, it will be advisable to vaccinate patients with hematological disorders, even though some of them may not be able to mount an adequate immune response. This review does not advocate the supremacy of any one vaccine over the other, but from the extensive research carried out, we are of the opinion that all patients should be vaccinated, and close caution should be exercised in view of adverse reactions, if any. Various practices may be changed, as more information pours in regarding this novel disease.

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Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

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