COVID-associated Immune thrombocytopenia (COVID-ITP) in pandemic

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Citation: Khan MA. COVID-Associated Immune Thrombocytopenia (COVID-ITP) in Pandemic. Haematol J Bangladesh. 2021;5(2):44-46

DOI: http://doi.org/10.37545/haematoljbd202178

Received: 21 November 2021
Accepted: 21 November 2021
Published: 30 November 2021

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Key words: Thrombocytopenia, COVID-ITP, VITT, COVID-19 vaccine.

Transient immune thrombocytopenia has emerged as an important sequela of complication in COVID-19 infection and post vaccination in the pandemic era. Usually, pattern of this thrombocytopenia is mild or moderate in nature but may be severe in a few cases. In my daily haematological consultation, I have observed that many asymptomatic patients are worried of marginally low platelet count at post COVID-19 infection or post vaccination status. Majority of the thrombocytopenic patients had very mild or no bleeding episodes. Life threatening bleeding is uncommon unless it is very severe thrombocytopenia. In this write up I will focus the cause, effect, clinical problems and treatment of post COVID-19 vaccine induced thrombocytopenia without thrombotic episodes. In this text I also will share my clinical experience of dealing with such thrombocytopenia associated with post-COVID-19 vaccination. Here thrombocytopenia (without thrombosis) were associated with COVID-19 infection or and COVID-19 vaccination; therefore I mentioned the condition as COVID-immune thrombocytopenia (COVID-ITP).

ITP is an autoimmune disease characterized by a platelet count <100 x 10^9/L, usually diagnosed by method of exclusion of other causes of low platelet count.1 Environmental (infection, medicine, autoimmune etc.) or genetic predisposition are known risk factors for ITP. There is no single test that can identify ITP, but it is essential to correlate with clinical presentation of patient and relevant investigations to reach diagnosis of ITP. Over the last three months, I have observed about sixty patients of 4th to 6th decade age groups of male predominance who came with mild to moderate thrombocytopenia. Most of them were found to have low platelet count on routine checkup for other conditions and rarely did they have any bleeding manifestation. Majority of them had mild weakness and fatigue but were afebrile. On clinical history, some of them were suffered from COVID-19 infection within the last 6 months, but all had the history of double doses of COVID-19 vaccination. There were no association of headache, blurring of vision, chest pain, abdominal pain and leg pain which are common clinical findings of vaccine induced thrombotic thrombocytopenia (VITT).2 On
careful clinical examination there were no signs of surface or internal bleeding, sign of thrombosis, leg edema, cellulitis or tenderness in the limbs.

A systematic approach was followed for every patient to identify the common causes of thrombocytopenia such as Helicobacter pylori, HBV, HCV, Dengue infection, DIC, Sepsis, Heparin prophylaxis, use of multiple antibiotics and SLE or other immunological diseases. Coagulopathy as well as VITT is a very rare adverse effect of COVID-19 vaccination that can be diagnosed with important criteria, such as: onset of symptoms 5-30 days after vaccination against SARS-CoV-2, presence of thrombosis, thrombocytopenia, high D-dimer & low fibrinogen level and presence of antibodies to PF4 detected by enzyme-linked immunosorbent assay(ELISA).2

In my clinical practice I advised those patients for laboratory investigations such as CBC, PBF, PT, APTT, D-dimer and fibrinogen level but not anti-PF4 antibody as it is not yet available in Bangladesh. Hb, TC & DC of WBC were within normal limit, but platelet count was in a range between 50x10^9/L to 135x10^9/L with often morphologically large platelets. They were also investigated for anti-COVID-19 antibody by ELISA method and were found to have high titer of COVID-19 IgG antibodies in their blood.

In Bangladesh ~27% of population received single dose and ~19% of population received double doses of COVID-19 vaccine of different types (ChAdOx1nCoV-19 by Oxford-AstraZeneca; Sinovac by China’s Sinopharm; BNT162b2 by Pfizer-BioNTech; mRNA-1273 by Moderna). So far, no single case of confirmed or suspected VITT was reported in Bangladesh, but Covid-19 vaccine associated thrombocytopenia (COVID-ITP) was commonly observed. Complement activation, immune dysregulation, and coagulation cascade perturbations have been described as the most potential mechanisms for COVID-19 disease.

SARS-CoV-2 infection or COVID-19 vaccine induced immune response produces antibodies to spike protein which may cross react with platelet and causes immune mediated platelet destruction similar to that of immune mediated thrombocytopenia (ITP) without thrombosis.3 However, in VITT, components of the vaccine (including virus proteins and free DNA) bind to PF4 and generate a neoantigen. Anti-PF4 antibodies causes pancellular (monocytes, neutrophils & endothelial cells) activation along with platelets & coagulation cascade resulting devastating thrombotic complication.4,5 About 100 cases of severe thrombocytopenia and bleeding without thrombosis that were induced or revealed after exposure to the messenger RNA-based vaccines produced by Moderna (mRNA-1273) and Pfizer-BioNTech (BNT162b2) have been reported.6

There are several options of treatment approaches for immune thrombocytopenia such as glucocorticoids, IVIG, Anti-D, and several second line drugs. But the management of COVID-ITP without bleeding is only counselling and careful follow-up without any platelet agonist or steroid unless the platelet count is less than 50x10^9/L. Medication as well as supportive care should be considered only when there is severe thrombocytopenia with bleeding manifestation. Cardiac patients who are on anti-platelet drug should continue under supervision if platelet count is 50x10^9/L or more. In VITT intravenous immune globulin (IVIG), systemic glucocorticoid (methyl prednisolone) & non-heparin-based anticoagulation are the primary treatment.

New onset of immune thrombocytopenia with mild to moderate platelet count without bleeding manifestation have been observed in this pandemic associated high COVID-19 IgG antibody titer. These phenomena have been noted following AZ, Sinopharm, Moderna and Pfizer vaccines in our OPD patients. Patients with isolated thrombocytopenia and continued absence of thrombosis may have post-Covid-19 vaccine associated ITP and not VITT.7
They are managed conservatively on follow up only. Patients with pre-existing ITP or other causes of thrombocytopenia may have transient further lowering of platelet count following COVID-19 vaccination.

It is very essential to be aware of low platelet count associated with COVID-19 infection or COVID-19 vaccination and more important is to follow up those patients. Only a very few of them may need systemic treatment. Considering the pandemic disease and risk of thrombo-embolism thrombopoietin (TPO) agonist should not be used frequently.

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