

IMPACT OF COVID-19 PANDEMIC ON BLOOD TRANSFUSION SERVICES IN A TERTIARY CARE TEACHING HOSPITAL FROM KOLKATA, INDIA WITH SPECIAL REFERENCE TO THALASSEMIA PATIENTS OF THE THALASSEMIA CARE UNIT: A REAL LIFE SCENARIO¹*Prakas K. Mandal, ²Avriti Baveja, ³Kanjaksha Ghosh and ⁴Tuphan K. Dolai¹Associate Professor, ²Senior Resident, ⁴Professor and Head, Department of Hematology, NRS Medical College; Kolkata-700014; India.³Ex-Professor and Director, National Institute of Immunohaematology (NIIH), Mumbai-400 012; India.***Corresponding Author: Prakas K. Mandal**

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ABSTRACT

Background: A subset of patients with Haemoglobinopathies require regular blood transfusions along with adequate iron chelation therapy (ICT) throughout their life. Access to regular and safe blood transfusions has always been an issue of concern for thalassemia patients. Corona virus disease (COVID-19) pandemic fueled the crisis in blood transfusion service across the world endangering these patients particularly in developing world where the condition is common and transfusion service is not up to the mark. With the lockdown in our country with travel restrictions, demand and supply has become precarious for the life of thalassaemic patients. Materials and Methods: This study is a retrospective analysis of the transfusion records of thalassemia patients attending the thalassemia day care centre in one of the largest medical colleges from West Bengal, India. Status of transfusion in thalassaemics during the COVID-19 pandemic was recorded from 25st March 2020 to 24th July 2020 (=4 months) and this was compared with the status of transfusions for the same period in the preceding two years. Results: This study identified that average number of transfusions for thalassemia patients from study duration in 2020 is 6.91/day. The average number of transfusions for this duration of COVID 19 pandemic have significantly reduced from the transfusion in previous years occurring at the same stipulated time (p- value<0.05) in the thalassemia patients. Conclusion: The COVID-19 pandemic has overtly hampered the transfusion services and care in thalassaemic patients.

KEYWORDS: COVID 19 pandemic, Thalassemia patients, blood transfusion services.**INTRODUCTION**

World Health Organization (WHO) defines “pandemic” as a spread of a new disease over a wide area, crossing borders and impacting a large population globally.^[1] In the past, many viral outbreaks have been witnessed and SARS-CoV-2 outbreak named as COVID-19 was declared as a pandemic by WHO on 11 March 2020.^[2] On 30 January 2020, WHO declared COVID 19 as a Public Health Emergency of International Concern (PHEIC).^[3]

In India, 30th January 2020 is marked as the day for identification of the first positive case of COVID 19 in Kerala soon to be followed by reports from other states.^[4,5] This urged the government of India, to devise containment steps for preventing the community spread of COVID-19 across the country. Breaking the chain of the community spread was felt as the need of the hour departments of health services. Thus, Prime Minister of

India declared an essential nationwide lockdown from 25 March 2020. Accordingly, all the hospitals in India have closed their regular outpatient services (OPD) and cancelled routine surgeries; only emergency services remained functional. Pandemics generate many lateral and collateral damages to mankind and takes heavy toll on health care services. Similarly, this pandemic posed challenges for the blood transfusion services across the country.^[6] The major challenges to blood transfusion services are recruitment of healthy blood donors, follow-up of donors and patients, staff safety, adequacy for emergency work as well as management of inventory and consumables.^[7]

Thalassaemias are inherited disorders characterized by defective hemoglobin (Hb) production, leading to the hemolysis of RBC and destruction of its precursors within the bone marrow (i.e. ineffective erythropoiesis; the patients develop chronic anemia of varying severity.^[8,9] If not treated adequately, Thalassemia

patients may develop multitude of problems- both acute and chronic ranging from growth retardation, hepatosplenomegaly, bony deformities, endocrinopathies, heart failure and infections.^[10-12] Patients with transfusion-dependent thalassemia (TDT) depend on lifelong regular blood transfusions for survival, usually starting before the age of 2 years, and die in the first or second decade of life if untreated.^[13] Blood transfusions provide fresh normal RBCs in thalassemic patients not only compensate for chronic anemia but also prevent bone deformities by limiting bone marrow expansion, corrects ineffective erythropoiesis, facilitate normal growth and activity levels, and allow patients to have a good quality of life (QoL).^[10,12] TIF and other thalassemia organizations in UK and US have set guidelines with different thresholds for initiating and maintaining transfusion in patients with NTDT and TDT.^[13-15]

The Government of India enforced complete nationwide lockdown from 25th March 2020 (phase 1) that passed through phase 4 (18–31 May) in view of containing the further spread of COVID-19 infections with ban on people from stepping out of their homes and many other issues.^[16,17] Passing through the different phases of stepwise unlock process India is now in the phase of unlock 3.0 (1–31 August).^[18] The measures taken to contain the COVID-19 pandemic during the lockdown and unlock phases reduced the access to treatment centers challenging the management and regular follow up of patients with chronic diseases including thalassemia. Since the transfusion services at large are being hampered across the country and are facing numerous challenges, thalassemics also appear to be impacted by this badly.^[7] The present study aims to study the effects of COVID-19 pandemic on overall blood transfusion services in a tertiary care teaching hospital with special reference to thalassemia patients.

MATERIALS AND METHODS

It was a retrospective study where all the diagnosed patients of thalassemia attending the day care center of thalassemia care unit (TCU) in the department of hematology of a tertiary care teaching hospital from eastern India between the duration from March 25 to July 24 (=4 months) for three consecutive years 2018, 2019 and 2020 were included in the study. Ours is a

thalassemia care & control unit from the eastern region of the country; serves as a nodal center and center of excellence. After an appropriate diagnosis, guidelines are optimized for the needs of the patients which include the pre-transfusion hemoglobin levels, iron chelators and chelation doses.^[12] The thalassemia patients who are staying in the specified catchment area and many others from remote areas with rare blood groups or challenged by alloimmunization who have difficulty in arranging blood in the TCUs in the district and sub-divisional level are planned for regular transfusion in our center. We, retrospectively reviewed our records for the dates given for transfusion for three consecutive years i.e. 2018, 2019 and 2020 for the given study period of 4 months (March 25 to July 24).

We also collected the data related to attendance and the number of transfusion which were provided to the patients during these study periods. The parameters studied included- type of thalassemia and blood group of all the patients. Apart from these, records of blood bank reviewed relating to transfusions for non-thalassemia causes at our hospital. The overall blood donations/collections and blood units transfused were also documented.

Statistical analysis was performed using SPSS software version 25 (SPSS Inc., Chicago, USA). The collected data were evaluated and statistically analyzed using Chi-Square Test for the difference in transfusion dates and transfusion provided to the patients. These were analyzed for the transfusion status over 4 months in the lockdown/unlock phase (year 2020) with the previous years (2018 and 2019). The study had a power >90% at a 5% level of significance by the log-rank test. Two-sided $P < 0.05$ was considered significant.

RESULTS

Retrospective analysis of the records during the similar study period of four months from March 25 to July 24 for three consecutive years 2018, 2019 and 2020 showed that 836, 823 and 629 patients respectively attended the thalassemia day care center for red cell transfusion. Detailed analysis of total number of blood transfusions in the same time period in the years 2018, 2019 and 2020 are summarized in table 1.

Table 1: An account of total number of blood transfusions in thalassemia patients across different blood groups during the same time period (=4 months) in the years 2018, 2019 and 2020.

	A+	A-	B+	B-	AB+	AB-	O+	O-	Total
Total no. of transfusions from 25/3/20 to 24/7/20 (working days = 91 days)									
Thalassemia major	61	0	71	2	17	0	56	0	207
E beta thalassemia	103	1	184	7	29	0	89	0	413
SCA/S beta thal	1	0	1	0	2	0	2	0	6
other hemoglobinopathies	1	0	1	0	0	0	1	0	3
Total =	166	1	257	9	48	0	148	0	629
Total no. of transfusions from 25/3/19 to 24/7/19 (working days = 96 days)									
Thalassemia major	54	2	92	2	24	0	69	1	244

E beta thalassemia	140	4	194	7	77	0	146	1	569
SCA/S beta thal	2	0	2	0	0	0	2	0	6
other hemoglobinopathies	1	0	1	0	0	0	2	0	4
Total =	197	6	289	9	101	0	219	2	823
Total no. of transfusions from 25/3/18 to 24/7/18 (working days = 98 days)									
Thalassemia major	50	2	70	4	43	0	89	1	259
E beta thalassemia	145	4	199	9	53	0	154	1	565
SCA/S beta thal	2	0	2	0	0	0	3	0	7
other hemoglobinopathies	1	0	1	0	1	0	2	0	5
Total =	198	6	272	13	97	0	248	2	836

In 2018, there were 98 working days in the study period; total numbers of 933 appointments were provided for transfusion from the day care. Meanwhile in the blood bank the total no of donations (collections) and transfusions were 10556 and 10312 respectively (table 2). Among these, 8.1% (n=836/10312) blood units were provided to the thalassemic patients attending the thalassemia day care center with an average of 8.53 patients being transfused per day; the rest 9476 units

were released for transfusion for other non-thalassemia causes. The transfusions for E-beta thalassemia, thalassemia major, sickle beta thalassemia and other haemoglobinopathy were 565 (67.5%), 259 (30.9%), 7(0.8%) and 5 (0.59 %) respectively. The common blood groups utilized for transfusions in thalassemia patients were 'B' positive, 'O' Positive and 'A' positive in 272 (32.5 %), 248(29.66%) and 198 (23.6%) cases respectively.

Table 2: Detailed account of blood transfusion services for thalassemias and other indications during the same time period (=4 months) in three consecutive years.

Study period (March 25 to July 24)	Demand of packed red cell units	Total no. donations (collections), blood units	Total transfusions, blood units	Units consumed for thalassemia patients	Units consumed for other patients (non-thalassemsics)
Year 2020	6640	5332	5156	629	4527
Year 2019	11456	10848	10480	823	9657
Year 2018	11076	10556	10312	836	9476

Similarly in 2019, from March 25 to July 24, there were 96 working days; total numbers of appointments provided for transfusion from the day care were 937. The blood bank received 10848 units of donations (collections) and 10480 units were released for transfusion in the hospital. Among these, 8.13 % (n=823/10480) blood units were provided to the thalassemic patients attending the thalassemia day care center with an average of 8.57 patients being transfused per day during the day; the rest blood units were dedicated for transfusion of non-thalassemic patients. The transfusions for E beta thalassemia, thalassemia major, sickle beta thalassemia and other haemoglobinopathy were 569 (69.1%), 244(29.6%), 6 (0.72%) and 4 (0.48 %) respectively. The common blood groups utilized for transfusions were 'B' positive, 'O' Positive and 'A' positive which were 289 (35.1%), 219 (26.66%) and 197 (23.9%) respectively.

And in 2020, in the same study period, there were 91 working days. Appointments provided to 899 transfusions and comparing this with that in the same time period in 2018 and 2019 and on application of Chi-Square test it shows that there was a significant difference in the two groups (p=0.005). Meanwhile in the blood bank the total no of donations (collections) and transfusions were 5332 and 5156 respectively. A significant (p<0.01) reduction of 50.52 % and 50 % was

seen for the total collections and total released units from blood bank in 2020 when compared to the data of 2018 (summarized in table 2). Thalassemic patients attending the day care center during this duration were provided with 12.9% (n=629/5156) blood units and on an average 6.91 patients were being transfused per day with a significant reduction in transfusion given as compared to the preceding years 2018 and 2019 (p-value<0.05). The absenteeism rate in 2020 was 30.03 % (n=270/899) which was 10.39% (n=97/933) and 12.16% (n=114/937) for same the same period in 2018 and 2019 respectively. The transfusions for E-beta thalassemia, thalassemia major, sickle beta thalassemia and other haemoglobinopathy were 413 (65.56%), 207 (32.9%), 6(0.95%) and 3(0.47%) respectively. Figure-1 summarizes the change in trends in transfusions rates across all blood groups over the same time period in three consecutive years.

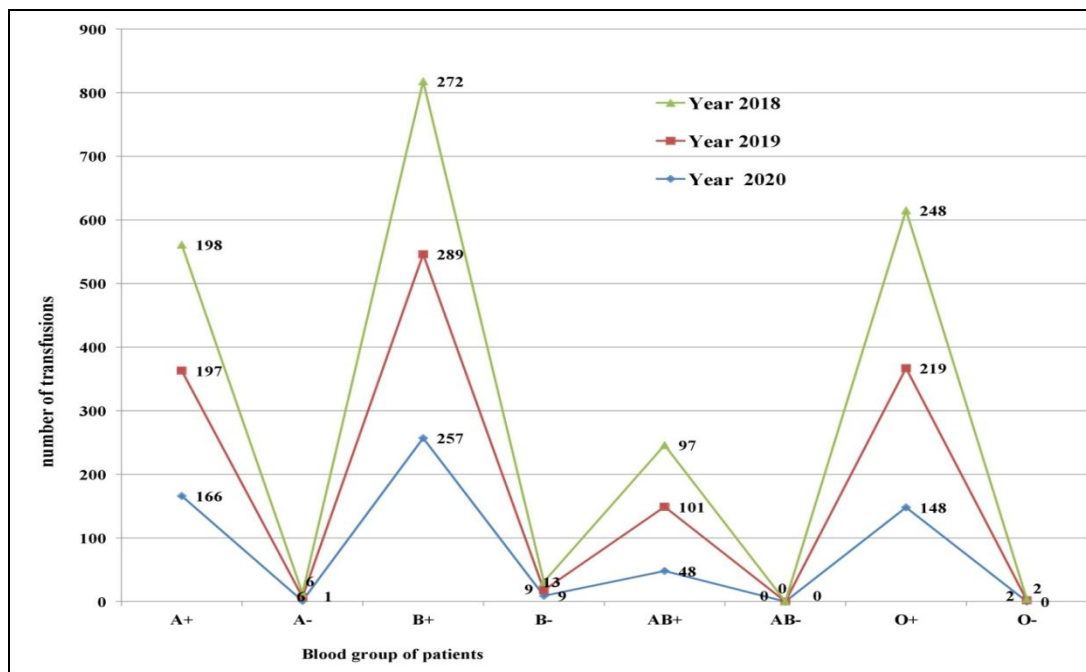


Figure 1: Trends on total number of transfusions in thalassemia patients across different blood groups over a period of 4 months (March 25 to July 24) in three consecutive years under study.

DISCUSSION

In India, blood transfusion services (BTS) are decentralised and lacks many vital resources like manpower, adequate infrastructure and financial base; the licensed blood banks are run by Government and also various organisations controlled by government of India under Ministry of Health and Family Welfare (MOFW).^[19] WHO estimated that blood donation by 1% of the population is the minimum needed to meet a nation's very basic requirements for blood; however, the average donation rate is 15 times lower in developing countries than in developed countries.^[20] The first records of the voluntary blood donation initiative in India can be traced back to 1942, during World War II when the first blood bank was established in Kolkata, West Bengal.^[21] The number of donations (both voluntary and replacement donations) vary from 1,000 units to 70,000 units in a year in these collection centers. Despite a huge population, the demand-supply gap for blood units persists in many healthcare facilities in the country. As per the reports of West Bengal state AIDS prevention and control society there are 79 Government blood banks in the West Bengal state.^[22] Most of the blood banks across the country including West Bengal and Kolkata face acute shortage in donations.^[23, 24] During summers, blood collection dips by nearly 40% but the situation has worsened due to the coronavirus outbreak.^[25] There has been a significant drop in blood donations (collection) in 2020 by 49.5% and 50.8% as compared to that in the years 2018 and 2019 respectively during the same time period (p value < 0.05). As evident in table 2, there is a reduction in requirements in units transfused for causes other than thalassemias also. As reported by Mascaretti L et al from Italy, with lockdown impositions taken by the Government like enforcing social distancing there was a

bothersome decrease in the number of blood donations.^[26]

Apart from demand and supply crisis because of logistic issues occurring due to the COVID-19 outbreak there are other concerns sprouting regarding viral shedding in plasma or serum because if transmission of SARS-CoV-2 (2019-nCoV) infection through blood products is a matter of concern. Though this risk appears more to be theoretical but still transmission of coronaviruses can occur through the transfusion of labile blood products; this concern strengthens with increase in asymptomatic COVID-19 cases.^[27] Moreover the medical, nursing and other ancillary staffs in blood banks face an added risk of getting infected from the asymptomatic donors; blood safety in this scenario needs to be addressed. There still needs to be careful assessment on any measures regarding deferral of donors, screening for SARS-CoV-2 RNA, testing for virus-related antibodies, or use of pathogen-inactivated blood products.^[27] The setting of standard guidelines for issuance of uninterrupted and safe blood supply is the also a need of the hour.^[28]

Before the COVID-19 emergence our Thalassemia day care center in preceding years provided an average of 935 appointments for transfusion with an average of 8.53 and 8.57 per day being transfused in 2018 and 2019 respectively; this Average transfusion rate in the TDC reduced to 6.91/day. Considering 29.2 % patients attending our centre were coming from outskirts of the city, the reduction appears to be due to the lockdown impositions across the country and the logistics of reaching the transfusion centre is the major cause. The absenteeism rate in 2020 is 30.03 % which was about 3 times more than absenteeism for transfusion in preceding

years. In India, almost half of children with β -thalassemia major are under-transfused.^[29] With the lockdown in our country, patients and their parents find it difficult to visit TCU for blood transfusions.^[24]

In addition, patients on iron chelation therapy were having difficulty in getting the medicine from hospital supply free of cost and thus underlying co morbidities secondary to iron overload, notably endocrinopathies, cardiomyopathy and chronic liver disease, may increase the complications and mortality in this group of patients as the restrictions are going on for extended periods.^[30, 31]

As per the suggestions published in the 'frequency asked questions' section in the American Society of Haematology (ASH) disclaimer for COVID 19 pandemic, there are no set guidelines for maintenance of pre-transfusion haemoglobin levels; pattern of transfusion should be maintained as per the pre-COVID regimens.^[32] But, the most important point which transfusion centres should insist on is provision of safe environment for patients scheduled for transfusions. The patients attending these clinics should be screened for fever and respiratory symptoms and interventions should be directed accordingly. Personnel protective equipment should be donned by all health care personals; use of surgical mask, alcohol-based hand sanitizer and gloves to be considered in all.^[33] Contingency plans should be set according to the local and national scenarios for modulating the transfusion regimens and obtaining donor units depending upon the patient need even addressing the issue of alloimmunization such that significant shortage is not ensued.^[31]

What are the solutions to these challenges considering the uncertainty about where is the end of this pandemic? More decentralization of the transfusion centres and regular blood transfusions at healthcare facilities other than TCUs also should be encouraged. But this can only happen by increasing the testing facilities and donations at these peripheral blood banks. Yadav U and Pal R from India suggested mobile blood collection units at doorsteps of the donors and mobile transfusion services at the door steps of the patients may be an answer to this problem and can help in replenishment of blood banks.^[19] Committed blood donors list in blood bank should be encouraged for safe donations. Extended family members of thalassemia patients, their friends and relatives need to come ahead and donate blood for the cause. Organizing webinars on a regular basis for training of physicians and other healthcare workers at peripheral transfusion centres may help managing thalassaemic patients. Tele-consultations should be brought at gross route levels so that these group of patients can have an access to the specialist and they can address these problems may play a role in this regard. Media, social workers and NGOs should be sensitised to extend their support and help in fighting this crisis.

Though it is not wise to extrapolate the present study data to the whole state of West Bengal, yet considering the fact that the nature of transfusion service is similar across big institutions where 80% of the total TDT patients in the state get transfused every month, 30% reduction in transfusion clearly indicates that a huge number of thalasseemics could not get their monthly transfusion in time during this phase. The government at the central and state level was very much active in running the TCUs in its normal form; but due to various reasons (lack of transport facilities, fear of corona virus infection, joblessness among the parents etc), many of the patients could not manage to attend TCUs in need. India has one of the highest densities of transfusion dependent hemoglobinopathies in the world and covid-19 pandemic has not spared any state in this country of 1.35 billion. However there is very little data on transfusion crisis for this subset of patients from India and the present study is an attempt to fill this gap.

CONCLUSION

COVID-19 pandemic has overtly hampered the transfusion services and care in thalassaemic patients as well as non-thalassaemic patients also. The average number of transfusions at the same stipulated time period during COVID-19 pandemic has significantly reduced from that in the preceding years.

Authorship contributions

PKM, AB and KG designed the study, literature search and statistical analysis. PKM and AB were involved in acquisition, analysis and interpretation of data, statistical analysis and wrote the first draft of the manuscript. PKM, KG and TKD edited and revised the manuscript. All the authors approved the final version.

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