

## ORIGINAL ARTICLE

# Covid-19 pandemic and care of transfusion-dependent patients of thalassaemia: Experience from a paediatric centre in North India

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**Aim:** Covid-19 has presented an unprecedented challenge to health services and has significantly affected the management of non-Covid illnesses, like thalassaemia. The present study documents the impact of Covid-associated restrictions and disruptions on working of the pediatric thalassaemia day care centre (TDCC), and measures taken by TDCC and blood transfusion services to adapt to and mitigate the negative impact of Covid pandemic and associated lockdown on patient care.

**Methods:** Pre-transfusion haemoglobin and packed cell transfusion requirement were compared across three time periods, namely pre-lockdown, lockdown and post-lockdown in paediatric transfusion-dependent thalassaemia (TDT) patients. Caregivers were interviewed to document any problems faced by them.

**Results:** The study involved 181 TDT patients. There was a significant reduction in mean pre-transfusion haemoglobin and red cells transfused during lockdown phase as compared to pre-lockdown phase. Regular care was interrupted in 45% of patients and 76% of patients getting blood from outside could not get leukoreduced red cells. Investigations, monitoring and continuity of iron chelation were also affected. Blood centre faced 30.5% reduction in blood supply during lockdown. TDCC and blood centre took several steps, including prolongation of service hours and staggering of transfusions to ensure maximum transfusions while ensuring social distancing.

**Conclusion:** The Covid-19 pandemic imposed many unprecedented challenges to the routine care of thalassaemic patients; however, some of them could be dealt with by a proactive approach and micro-planning at the institution level. Other similar resource-limited settings could learn from experiences for continued quality care for chronic medical conditions during pandemic like situations.

**Key words:** Covid-19 pandemic; management; thalassaemia; transfusion.

## What is already known on this topic

- Covid 19 pandemic and associated lockdowns had affected health care services tremendously.
- Very scanty literature is available on care and management of Transfusion dependent Thalassaemia in covid 19 pandemic.
- Few studies have shown the impact of covid 19 pandemic on the care of thalassaemic children in terms of deprivation of regular blood transfusion and access to healthcare services. Blood supply was badly hit and continuation of transfusion services became a challenge.

## What this paper adds

- To the best of our knowledge, this is the largest single-centre study of pediatric transfusion-dependent thalassaemia (TDT) patients during Covid 19 pandemic.
- The present study documents the impact of Covid-associated restrictions and disruptions on the working of the pediatric thalassaemia day care center (TDCC) and blood bank.
- This study demonstrates the impact of Covid 19 pandemic on the Pre-transfusion hemoglobin and packed red cell transfusion requirements during pre-lockdown, lockdown, and post-lockdown period in pediatric TDT patients. It also documents the extra financial burden, and logistic issues faced by parents as well as by the health care facility.
- It documents different mitigation strategies to resolve these challenges.

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The Covid-19 pandemic has been a major disruptor of health-care provisions for non-COVID chronic illnesses. This was due to sudden spurt of cases, totally overwhelming the already overcrowded health institutions, as well as, due to restriction on mobility and access due to lockdowns at local or national level.<sup>1–5</sup> While COVID-19 has not been reported to have a direct impact on thalassaemia, studies indicate that it did adversely affect its management.<sup>6,7</sup> The best practices for management of patients with transfusion-dependent thalassaemia (TDT) include transfusion of better matched (ABO, Rh, and Kell antigen matched, Coombs cross-matched and leuco-reduced) packed red cells and iron chelation. The present study documents the impact of Covid-associated restrictions and disruptions on working and utilisation of services at thalassaemia day care centre (TDCC) and blood transfusion services of a leading public sector hospital in North India. We employed different mitigation strategies to resolve these challenges.

## Materials and Methods

This prospective observational study included paediatric TDT patients under regular follow-up at our TDCC, run at no cost to the patient. In our centre, we give pre-storage leukoreduced, Rh-kell profile matched red cells to all thalassaemia patients. However, if profile matched unit is not available and has to be sourced from other hospital, then bedside leukodepletion filters are used. We compared pre-transfusion haemoglobin and packed cell transfusion requirement across three time periods, namely pre-lockdown (1st January to 23rd March 2020), lockdown (24th March to 31st May 2020) and post-lockdown (1st June to 31st July 2020) from the available records. The parents and caregivers were interviewed to document the problems and additional cost faced by them, after obtaining their consent to participate in the study. Institutional Ethics Committee approval was also obtained.

Detailed proforma was designed to capture the information of patients including demographic profile (residing in/outside Delhi NCR), number of transfusions, transfusion interval and mean pre-transfusion Hb of patients during the three phases. Patients were also asked about the cause of delay in visiting TDCC. Though, no objective psychosocial scale was used, they were interviewed regarding the fear or anxiety related to the Covid-19 pandemic (Table 1). For patients who could not come to TDCC, details were noted regarding the alternate health-care facility (public/private sector) and type of care (type of transfusion and chelation, monitoring, etc.). The mean pre-transfusion Hb was compared between regular attendees (Group 1) versus patients who missed some or all of their visits (Group 2), across all the study phases and within same group across different phases and within same group across different phases.

We also documented the challenges faced and adjustments made by transfusion services and TDCC during these times.

## Statistical analysis

Descriptive data are presented as mean, standard deviation and range. Paired and unpaired *t*-tests were used to compare pre-transfusion Hb and amount of packed red cell received in three different phases within same group and two different groups, respectively.

## Results

The data were collected for 181 TDT patients (mean age  $8.75 \pm 4.21$  years, M:F ratio of 1.97:1) (Fig. 1) of which (59%) resided outside the region and thus were vulnerable to cross-border travel restrictions. About 55% of these continued uninterrupted care (Gp1) while others (Gp2) missed all (2%) or one or more scheduled visits (43%).

Problems due to lack of public transport were faced by 76% of patients during lockdown and 55% reported additional expenses for commuting. Only a few patients could access and use free emergency ambulances (6%).

Nearly 3/4th of the Gp2 cases (59 cases) got one or more blood transfusions from an alternative accessible health facility during lockdown. Among these, 45 (75%) used fully or partially free government health centres while rest used paid private health services. All the patients coming to TDCC received leukoreduced red cells. Among those who received transfusion from outside, 76% of the patients could not get leukoreduced red cell transfusions and rest had to purchase the filters. Table 3 details the additional expenses incurred on various accounts by the families.

The mean pre-transfusion Hb of patients during lockdown as well as post-lockdown was significantly lower than the pre-lockdown phase, for both the groups ( $P < 0.001$ ) (Table 2). During lockdown, there was a delay in care visits as only 8% of the patients had pre-transfusion Hb  $\geq 9$  g/dL, as compared to 68% in the pre-lockdown phase. Interestingly, the pre-transfusion Hb was significantly and similarly lowered in both the groups during lockdown and post-lockdown when compared with their pre-lockdown values ( $P < 0.001$ ).

The mean volume of packed red cells transfused during lockdown (adjusted for 30 days) was significantly less as compared to pre-lockdown phase ( $P < 0.001$ ). However, this increased significantly during post-lockdown phase as we tried to compensate for the lower Hb values ( $P < 0.001$ ) (Table 2).

Families had also spent out-of-pocket money to buy oral chelators and supplemental therapy like Calcium and Folic acid (Table 3). The supply of oral chelators was interrupted, due to lockdown and 19% of the patients received lower doses and 3% of the patients missed most of the doses, during lockdown period.

Some of the thalassaemia patients who received blood transfusion outside during lockdown could not get adequate monitoring due to lack of availability. Nearly 10% of patients could not get their CBC. Hepatic, renal functions and iron overload estimation could not be done in 21%, 19% and 25% of patients, respectively. Some families made out-of-pocket expenditure to get these done at nearby private labs.

## Psychosocial Aspects

Although we could not formally study the psychological impact using standard scoring system, however with general questionnaire, majority of our patients reported anxiety and fear due to COVID-19. Many patients were wary of coming to hospital and delayed/postponed their scheduled visits.

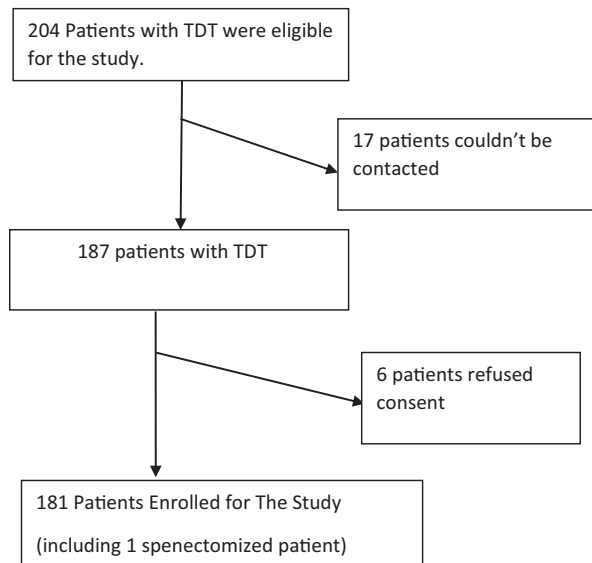
## Impact on our TDCC and blood bank functioning due to COVID-19

The actively changing pandemic, health-care re-organisation and restrictions required frequent assessment of the services to

**Table 1** Proforma used for study

Epidemiological details of patients: (especially including Res – Delhi/ NCR*/Outside NCR details);
Packed red cell transfusion reviewed:
Pre-lockdown (1st January to 23rd March 2020)
Lockdown (24th March to 31st May 2020)
Post-lockdown (1st June to 31st July 2020)
Mean pre-transfusion haemoglobin:
Pre-lockdown (1st January to 23rd March 2020)
Lockdown (24th March to 31st May 2020)
Post-lockdown (1st June to 31st July 2020)
Laboratory investigations:(Sent during lockdown if due):
LFT
KFT
Serum ferritin
During lockdown:
1 No of blood transfusions (BTs) due during lockdown period:
2 BTs received during lockdown over April–May:
3 Details of blood transfusion received outside KSCH:
a) Received packed cell/whole blood outside:
b) Usual matched blood transfused:
c) Filter used for outside BT:
1 Logistic issues:
a) Visit in lockdown period:
b) Visited regularly
c) Visit delayed:
d) Visited less frequently:
Reason for above:
• Fear of coming to hospital
• No transport facility
• No blood donor
• Any other
Any problem in T.D.C.C.D. during lockdown period:
• Staff availability-Faculty, SR, PG, nurses: yes/no
• Mask and protective material related: sanitizer: yes/no
• Social distancing-reduced per day transfusions: yes/no
• Transfusions given outside TDCC: yes/no
• Filter availability during transfusion at TDCC: yes/no
• filtered blood availability from blood bank: yes/no
• Chelator availability: yes/no
• Tele-communication during lockdown period: yes/no
Received blood outside during lockdown period: yes/no
Details of blood received outside:
Govt./private institute
Did you get filter outside
Whether PRBC/whole blood
Cross match – usual ABO Rh or extended
If splenectomised on penicillin prophylaxis: yes/no
Any specific complication:
Any psychological stress:
Related to Covid-19 infection
Related to logistic issues
Monitoring related referral (if required during lockdown period (done/ not done):

optimise its usage. Frequent assessment of the shortfall was done and fresh coping strategies were formed based on root cause analysis.



**Fig. 1** Study flow chart.

Unlike many hospitals in our state which were turned into a purely COVID-19 hospital, our centre continued services to both COVID and non-COVID cases. We pro-actively identified all those patients who were missing appointments for tele-consult and counselling, informing that we were continuing services at our TDCC and they were given fresh appointments. Some needed counselling on fear of getting COVID-19 at TDCC. Those who showed a complete inability to travel to our facility were suggested alternative care propositions near their place of stay.

Infection control measures were strengthened in the TDCC and Covid symptom screening of the thalassemia cases (and their caregivers) was done to identify and segregate anyone with COVID-like symptoms and were offered testing. Dedicated team of nursing staff were assigned the work of medical counselling regarding covid symptoms, hygiene practices and awareness about the disease. Face masks and sanitisers were provided to all patients and their caregivers.

In the pre-pandemic time, our 14-bed TDCC was working at overcapacity, servicing 20–25 patients per day in a single shift. However, with the onset of the Covid-19 pandemic, the number of patients per day had to be reduced as we strictly followed ‘one patient – one bed’ policy to avoid overcrowding and maintain social distancing. Timings of TDCC were extended and transfusions were done in staggered manner to ensure maximum number of transfusions, while maintaining social distancing. Any interrupter walking in unscheduled or with a poor Hb was adjusted by extending the services at TDCC or other sister units for blood transfusion. Better coordination was done with blood centre so as to get early blood for first half of the shift, so that few could be accommodated in the latter half as the beds got vacated.

Under normal circumstances, we aim to maintain pre-transfusion Hb at 9.0–10.5 g/dL and transfuse around 16 mL/kg of packed red cells during during each visit. Usually, follow-up visit is scheduled 3–4 weeks later, depending on the adequacy of the haemoglobin levels. However, the staggering of

**Table 2** Mean packed red cells transfused (ml/kg) and mean pre-transfusion Hb (g/dL) in three phases of lockdown

Parameter	Pre-lockdown mean and SD	During lockdown mean and SD	Post-lockdown mean and SD
Mean packed red cells transfused (ml/kg)	12.21 ± 2.71	8.57 ± 3.32	14.04 ± 5.13
Mean pre-transfusion Hb (g/dL)	9.21 ± 0.73	7.35 ± 1.32	7.38 ± 1.42

**Table 3** Extra expenditure incurred by patients related to transfusion during lockdown phase

Type of extra expenses	Proportion of patients incurring extra expenses	Mean ± SD (Rs)	Range (Rs)	Median (Rs)
Total expenditure	126/181 (70%)	3474 ± 3705	30–16 900	1500
On travel	75/137 (55%)	3873 ± 3333	240–15 000	3000
Expenditure on BT	23/59 (39%)	3197 ± 2873	40–9000	2750
On leukodepletion filter	8/137 (6%)	2087 ± 2778	150–8500	800
On investigations (CBC/LFT/KFT/Ferritin)	15/181 (8%)	697 ± 467	100–1600	800
On chelator	7/181 (4%)	3901 ± 2423	700–8600	3710
On folic acid	61/181 (34%)	153 ± 23	12–650	90
On calcium	60/181 (33%)	411 ± 259	70–1200	300

Data expressed as mean (SD), range and median.

visits had to be done to maintain social distancing and as sharing of beds was stopped. Shortage of blood availability and staggered or interrupted visits resulted in significantly lower pre-transfusion Hb during lockdown phase and its impact continued even in post-lockdown phase among both the groups. There was 30.54% fall in blood donations in lockdown phase as compared to pre-lockdown phase. Blood units collected per month (inhouse and voluntary blood donation) during three phases of study were 870 (average 29 U/day), 604 (average 20 U /day) and 789 (average 26 U /day), respectively.

Due to mobilisation of resources and personnel for Covid care, TDCC and blood centre faced staff shortages. Health-care workers themselves getting the disease or going under quarantine added to the problem. Redistribution and rearrangement often necessitated additional work load for the available staff so that the services could continue uninterrupted.

Blood centre also faced decline in donations. The in-hospital donations declined more than the voluntary blood donations. Many donors, who gave history of recent close contact with COVID case or were from the COVID containment zones, had to be deferred. However, blood requirement also declined (apart from hemoglobinopathies, aplastic anaemias, leukaemias, etc.) due to cancellations/postponements of routine hospital surgeries. Covid care directly did not impose additional burden on blood transfusion services, as most of the Covid patients did not require blood transfusions. During all three phases, there was no compromise on pre-transfusion testing of patients. All the SOPs regarding issue of blood to thalassaemic patients were strictly adhered to. However, logistic problems were faced by blood centre (e.g. delay in supply of consumables, antisera, etc.), due to travel restrictions.

## Discussion

The COVID-19 pandemic presented an unprecedented challenge to health-care services as well as its users. As the health services reoriented to the uncharted territory of a pandemic of this proportion, it affected management of non-Covid illnesses like TB, cancer, and thalassaemia.<sup>2–16</sup> Thalassaemia patients, dependent on regular hospital visits due to blood transfusion therapy, bore the brunt of disruption. Although haemoglobin disorders are not generally associated with respiratory viruses, splenectomy and underlying co-morbidities, secondary to iron overload in thalassaemia, may increase the risk of complications due to Covid-19.<sup>11–13</sup> There is very limited evidence on direct impact of Covid on the disease pathology as well as of the pandemic related disruptions on thalassaemia care and management.<sup>6,7,11,14–16</sup> Hence the study was planned to assess the impact of Covid and associated lockdown on thalassaemia care and also to share the strategies evolved to meet the challenges faced.

Enforcing lockdown was an essential step for pandemic control, but it created a major hurdle for almost all of our patients in reaching the transfusion centre due to: restriction on crossing state borders, closure of public transport, non-availability or non-affordability of overcharging alternative transport. Many health facilities in both public and private sectors had been converted to COVID hospitals and were not providing care for any other type of illness. As a consequence, nearly a half (45%) of the patients missed one or more visits as neither they could reach TDCC, nor would the local facility accept them. While nearly 3/4th of these patients did manage to get blood transfusion from alternative accessible and convenient centres, but these centres were not always equipped with best provisions or skills for comprehensive management. Hence, the transfusion was either given without a leukodepletion filter or the family had to buy it. The

provision of chelators as well as monitoring of its adverse effects as well as monitoring of iron toxicity was either suboptimal or non-existent. A similar experience has been reported from UK during lockdown period with a reported 24% fall in hemato-oncology patients seeking chemotherapy and also reported 71% fall in full blood counts done in primary care settings.<sup>17</sup> Families had to incur out-of-pocket expenses to access care or to make provisions for medicines or investigations. This may have impacted the family's finances more as the lockdown had affected the earnings of many self-employed, daily wagers or private-sector workers.

Challenges were faced in providing adequate care with social distancing norms, due to shortage of medical staff, shortage of blood supply, breaks in supply lines affecting procurements of chelators, reagents and other supplemental drugs, and reaching patients who were not able to come due to lockdown.

We feel that the continuation of services was possible due to active and empathetic role played by the hospital administration, TDCC team and blood transfusion services. Several challenges could be dealt using a proactive approach and microplanning at institutional level. Staggered transfusions at TDCC ensured maximal utilisation of thalassemia beds. The staggering of transfusion timings to create more slots for transfusion by utilising the bed twice in the same day was made possible by our blood centre testing and releasing the blood products for these patients in multiple small batches instead of usual practice of a late morning release in a single batch.

After the first lockdown, we have started keeping more than 45 days' supply of reagents and consumables as buffer stock.

Tele-communication and tele-medicine facilities were adopted to provide maximal support to engage the caregivers so that the child's problem was kept in the active yet doable sphere among many other challenges families were facing during the lockdown. This regular communication helped us to advise for continued transfusion at alternate places till they could reach us. We could also support the provision of free oral chelators and supportive therapy to some of those who were unable to come due to lockdown but had the possibility to collect these drugs from other patients who were visiting hospital.

In spite of all the efforts made by the team, we had certain difficulties which could not be completely surmounted. Blood is not a product we could have procured from anywhere so the non or low availability of appropriately matched blood and staggering of visits led to a situation where the mean pre-transfusion Hb could not be maintained at optimal levels even for those who attended as per their appointments. The impact lasted even in the immediate post-lockdown phase despite the mean 'packed red cells transfused' being higher. Similar observations were made in studies from Pakistan and Bangladesh.<sup>6,7,18</sup>

The major logistic issues faced by the blood centre were scarcity of healthy potential blood donors, due to closure of offices, colleges, transport restrictions, and other social distancing measures. Psychological stress (fear of getting infected) also tremendously reduced the voluntary donations. These were in part alleviated by arranging local camps and encouraging donations from among our health-care workers and doctors. Covid pandemic actually created world-wide shortage of blood supply.<sup>19–21</sup> Though virus itself is not transfusion transmissible, social and economic aspects of pandemic and disruption in everyday lives contributed to blood shortages.<sup>21</sup> American Red Cross reported the cancellation of more than 4600 blood drives in initial weeks of Covid outbreak,

diminishing the blood supply by 143 600 units.<sup>19,21</sup> Divya *et al.* reported drop in total units of blood collected in early months of lockdown period, in district hospital of rural India.<sup>22</sup>

In view of non-leukoreduced blood transfusions having been given to some of our patients in other organisations, we have started a stringent antibody screening on their return, to pick up any new cases of alloimmunization.

## Conclusion

There is a paucity of literature on how the Covid-19 pandemic has impacted health-care services, particularly for children with thalassaemia. Our study is one of its kind, highlighting the impact of pandemic on children with thalassaemia and the institutional coping strategies used to meet the challenges.

## Ethics Statement

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of our institute. Informed consent was obtained from all subjects involved in the study.

## Data Availability Statement

Data used for this study are available on request from the corresponding author.

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