Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Convalescent plasma bank facility location-allocation problem for COVID-19

Vijaya Kumar Manupati\textsuperscript{a}, Tobias Schoenherr\textsuperscript{b,}\textsuperscript{*}, Stephan M. Wagner\textsuperscript{c}, Bhanushree Soni\textsuperscript{d}, Suraj Panigrahi\textsuperscript{a}, M. Ramkumar\textsuperscript{e}

\textsuperscript{a} Department of Mechanical Engineering, National Institute of Technology Warangal, Warangal, Telangana 506004, India
\textsuperscript{b} Department of Supply Chain Management, Broad College of Business, Michigan State University, 632 Bogue St., East Lansing, MI, USA
\textsuperscript{c} Chair of Logistics Management, Department of Management, Technology, and Economics, Swiss Federal Institute of Technology Zurich, Weinbergstrasse 56/58, 8092 Zurich, Switzerland
\textsuperscript{d} Department of Preventive and Social Medicine, Jawaharlal Institute of Postgraduate Medical Education and Research, Gorimedu, Puducherry 605006, India
\textsuperscript{e} Operations and Quantitative Methods Group, Indian Institute of Management Raipur, Atal Nagar, Kurru (Abhanpur), Raipur 493 661, India

ARTICLE INFO

Keywords:
Convalescent plasma
Location-allocation problem
COVID-19
Plasma supply chain
Mixed integer linear programming
CPLEX optimization
NSGA-II
NSGA-III

ABSTRACT

With convalescent plasma being recognized as an eminent treatment option for COVID-19, this paper addresses the location-allocation problem for convalescent plasma bank facilities. This is a critical topic, since limited supply and overtly increasing cases demand a well-established supply chain. We present a novel plasma supply chain model considering stochastic parameters affecting plasma demand and the unique features of the plasma supply chain. The primary objective is to first determine the optimal location of the plasma banks and to then allocate the plasma collection facilities so as to maintain proper plasma flow within the network. In addition, recognizing the perishable nature of plasma, we integrate a deteriorating rate with the objective that as little plasma as possible is lost. We formulate a robust mixed-integer linear programming (MILP) model by considering two conflicting objective functions, namely the minimization of overall plasma transportation time and total plasma supply chain network cost, with the latter also capturing inventory costs to reduce wastage. We then propose a CPLEX-based optimization approach for solving the MILP functions. The feasibility of our results is validated by a comparison study using the Non-Dominated Sorting Genetic Algorithm-II (NSGA-II) and a proposed modified NSGA-III. The application of the proposed model is evaluated by implementing it in a real-world case study within the context of India. The optimized numerical results, together with their sensitivity analysis, provide valuable decision support for policymakers.

1. Introduction

The coronavirus disease 2019 (COVID-19) has created a public health emergency of international magnitude spreading across more than 200 countries and territories around the globe. As of September 24, 2021, the pandemic outbreak counted more than 230 million confirmed cases, and more than 4.7 million reported deaths worldwide (WHO 2021). India reported the second-highest number of
Specifically, the shelf life of plasma is 40 days, or up to 12 months if stored below 18 degrees Celsius. This necessitates an interconnected supply chain to enable the most effective and efficient distribution of plasma so as to prevent wastage. The plasma that is extracted from individuals after having overcome the infection is referred to as convalescent (i.e., “immune”) plasma, since it contains antibodies. The treatment with antibodies is currently one of the few short-term treatment strategies to have shown an immediate effect on the immune system (Zhang et al., 2020). The therapy improves clinical symptoms via neutralizing viremia, is well-tolerated, and has only limited side effects. In most acute viral diseases, viremia usually peaks during the first week and a patient’s primary immune response is initiated by day 10–14, which is followed by viral clearance. Considering the infectious process, CP therapy is most effective when given early in the course of the disease, during the viremia or seronegative stage, i.e., before day 14 (Zeng et al. 2020).

CP therapy has been appraised as a treatment of prime importance for COVID-19 patients (Rojas et al. 2020). However, due to the surge in COVID-19 cases, the demand for plasma has been outpacing supply, also due to the absence of plasma banks (Gehrie et al. 2020). It is in these plasma banks where the blood’s plasma component from recovered COVID-19 patients is stored (Im et al. 2020). The question however now arises where these plasma banks should be established so as to be most effective in providing relief. The design of a connected network to cover the demand and supply across the country is thus critical. Such a design can serve as the foundation for providing CP therapy whenever and wherever it is required most, while at the same time considering the plasma’s shelf life. In this vein, the plasma itself has properties that make it different from blood, with plasma being more perishable in nature. Specifically, the shelf life of plasma is 40 days, or up to 12 months if stored below –18 degrees Celsius. This necessitates an interconnected supply chain to enable the most effective and efficient distribution of plasma so as to prevent wastage. Within this challenging context, this study develops a novel plasma supply chain network that facilitates both the location of plasma banks and the allocation of facilities to deliver to these plasma banks. The overarching objective is to determine the optimal distribution of the plasma supply to save lives. Additionally, as per the WHO (2021), plasma collection facilities should be setup as close to the plasma collection point as possible. To achieve this, we develop a multi-objective mixed-integer linear program (MILP) model with the objective to minimize both the overall plasma transportation time and the overall plasma supply chain network cost. Unlike most inventory models in extant research that consider stock items able to being kept in inventory indefinitely, we consider the perishability of plasma and incorporate a deteriorating rate to reduce wastage. Since plasma has only recently been required in such significant quantities, and due to the inhomogeneous escalation in the number of patients, we consider the actual demand as unknown but following a predictable prior distribution. In addition, transportation cost is considered as stochastic, since the demand by hospitals is also variable depending on pandemic situation. Within this setting, we propose a CPLEX-based optimization methodology to facilitate the location of plasma banks. As such, we model a supply chain that includes regional and local hospitals, rather than building new plasma banks, which conserves both time and monetary resources. The objective of the model is to minimize both time and cost, which are dual considerations especially relevant within the context of developing countries. While timely plasma distribution and the associated matching of supply and demand is paramount, developing countries generally do not have the luxury to optimize this objective at all costs, providing the rationale for our dual considerations. Finally, using a real-world case study with the context of India, a developing country, we validate the feasibility of the proposed method by comparing the results with the NSGA-II algorithm. This is followed up with a modified version of NSGA-III specifically designed for the proposed problem. Through these efforts, we aim to contribute to society by proposing a plasma supply chain network model that increases the efficiency and effectiveness of plasma delivery to hospitals in order to save lives.

The remainder of this paper is organized as follows. After a review of the literature in Section 2, Section 3 describes the problem and formulates the mathematical model, including notations and assumptions. Section 4 presents the solution methodologies employed, followed by the application of the proposed model within a real-world context (India) in Section 5. Section 6 presents the results and their discussion, with Section 7 concluding and offering avenues for future research.

2. Literature review

COVID-19 has triggered the increased need for CP therapy, with the literature specific to plasma supply chain distribution being scant. This is especially the case within the unprecedented pandemic context. Guidance can however be provided by multi-echelon location allocation models applied in emergencies and the general application of CP therapy. These literatures, which form the basis for our investigation, are reviewed in this section. We commence with a traditional supply chain model and modify it to accommodate the unique features of our current pandemic situation, specifically in terms of supply, demand and distribution considerations given by the unique features of plasma (cf. Stanworth et al. 2020).

2.1. CP therapy and its applications

Our review of the CP therapy literature illustrates its application in prior epidemics, including the severe acute respiratory syndrome (SARS) epidemic in 2002 (Cheng et al. 2005) and the Middle East respiratory syndrome coronavirus (MERS-CoV) outbreak (Arabi et al. 2016). These studies found that CP therapy was responsible for a faster patient recovery rate in comparison to regular
drugs. These findings were extended by Beigel et al. (2017), who examined the efficacy of CP in influenza infection. Within the context of COVID-19, Lu (2020) and Bloch et al. (2020) demonstrated the positive effects of CP therapy in COVID-19 patients, validating its use and importance as a treatment regimen. Similar results were obtained by Duan et al. (2020), who determined CP as a promising rescue option for severe COVID-19 cases. Not only in line with these encouraging results, Thorpe et al. (2020) noted that the demand for plasma-derived products has increased exponentially over the last ten years, fueling the attention that CP supply chains have been receiving. This emphasis is warranted, since there are multiple organizational challenges associated with the development and implementation of a CP program, including policies for testing and approving plasma donations (Stanworth et al. 2020). Parallels can be seen in Dhiman et al. (2020), who focused on the cost-effective collection and supply of blood and its components, and Hamdan and Biabat (2020), who modelled a blood supply chain under disruption risks. Most recent evidence by Chen et al. (2020), showing a reduction of 21% in mortality rate for COVID-19 patients with the use of CP therapy, is encouraging. With these promising results and the surge in plasma demand, further guidance is needed for the effective collection and distribution of plasma. We provide such guidance in this paper.

Overall, this stream of research suggests that the collection of plasma and the associated distribution network design within the current pandemic context is a critical undertaking. Since the pandemic is so unprecedented in its magnitude and impact, further insight is needed to respond to this dynamic and novel situation. While prior work can serve as a formidable starting point, it may not be perfectly applicable to our current situation (Stanworth et al. 2020). Therefore, building on the works reviewed above, we aim to provide such insight for the unique pandemic environment we are currently in. In developing our model, we also consider guidance provided by the WHO (2021) and Stanworth et al. (2020), as well as the unique dynamics created by the pandemic, such as demand uncertainty for plasma due to new discoveries made at lightning speed. As such, we for instance perform rationality and sensitivity analysis to capture this potential demand uncertainty.

2.2. Healthcare location-allocation models

The application of location-allocation models within the context of healthcare and emergency supply chains is well established, with researchers utilizing the location allocation model to design networks for blood banks and hospitals (e.g., Jabbarzadeh et al. 2014; Sharma et al. 2019). These models provide valuable guidance for decision makers to conduct effective resource planning, assign donors to blood banks and hospital patients, and determine the locations for blood banks or emergency hospitals (e.g., Ramezanian and Behboodi 2017). The design of networks for effective blood distribution, especially in emergencies, has become a national importance in many countries (Beliën and Forcé 2012).

Allocation modelling within the context of healthcare has been utilizing multi-objective optimization techniques. Examples include Sahin et al. (2007), who formulated various mathematical models for the regionalization of blood services in Turkey, and Waldman (2014), who looked at stockpile location and equipment distribution strategies of essential supplies during the influenza pandemic. This context was also chosen by Mogale et al. (2018), who applied Pareto-based multi-objective algorithms with measured parameters to optimize network cost and total lead time simultaneously. Along similar lines, Sha and Huang (2012) proposed an emergency blood supply scheduling model to assist in times of crisis, taking into account the minimization of transportation cost, moving cost and inventory cost. Mitropoulos et al. (2006) solved a multi-objective optimization problem for locating primary healthcare centers and hospitals using the constraint method. The objectives were to minimize travel distance between assigned facilities and patients, while at the same time ensuring an equitable distribution of the facilities.

Literature leveraging allocation models to offer decision support in emergencies, such as floods, earthquakes or the influenza pandemic, provide a further foundation for our work. For example, Sharma et al. (2019), within a post-disaster context, designed a model for locating temporary blood banks to serve the demand of hospitals and reduce minimum response time. Yi and Ozdamar (2007) proposed an integrated location-distribution model for selecting temporary centers that result in a maximum coverage of medical need. For safer blood transfusion services, Hosseini-Motlagh et al. (2020b) determined the optimum location-allocation and inventory management decisions, and Fiedrich et al. (2000) used a dynamic combinatorial optimization model for assigning available resources to minimize the total number of fatalities after an earthquake. Within the context of the current pandemic, Singh et al. (2021) considered the disruptions of food and healthcare logistics and proposed multiple supply chain models based on various mitigation strategies.

Overall, the review of the literature suggests the adaptation of standard supply chain models to the specific needs and requirement of the context considered. The design of blood supply chains in particular has received great interest, providing a sound knowledge base for networks with multiple depots. These designs however cannot be readily applied to the plasma supply network problem needed in our current pandemic. Challenges exist in the form of the limited availability of plasma, its perishable nature, and the absence of fixed plasma depots that meet its special storage needs. For example, Islam et al. (2020) caution that plasma must be collected, stored and defrosted under optimal conditions within 24 h and then administered within 40 days. Lengthy distribution delays thus cannot be afforded, necessitating the supply chain network design to enable an efficient and effective distribution of plasma. We capture this in our model by integrating a deterioration rate (Dolgui et al., 2018).

In addition, applying our model within the context of India, we develop recommendations for depot locations using ArcGIS software. These depot locations are determined by minimizing overall plasma transportation time and total plasma supply chain network cost. Limited resources in our developing country context substantiate the cost focus, constraining the number of depots to be set up. At the same time, the dire need and distribution speed required substantiate the focus on time. Our mathematical model thus balances demand and supply, while keeping the urgency caused by the worsening pandemic situation in mind.
2.3. Summary of the literature

We build on and extend these works in the present paper by devising a location-allocation model for the stochastic plasma supply chain. To the best of our knowledge, no research has looked at this important and timely location-allocation model within the context of a pandemic. In addition, the proposed model provides a new line of thinking for plasma supply chain design in that it improves efficiency and timely access to high-quality services (cf. Hosseini-Motlagh et al., 2020a). Due to the current crisis, there is a significant need for a stochastic plasma supply chain model.

3. Problem description

We formulate an optimal supply chain model for the collection and distribution of plasma consisting of four echelons: donor groups, plasma collection facilities set up at regional hospitals, plasma banks, and COVID-19 treating hospitals at the local level (Fig. 1). Considering the rise in COVID-19 cases and soaring demands for plasma, our model incorporates four primary considerations: (i) satisfying the demand of COVID-19 treating hospitals; (ii) providing adequate transportation means enabling speedy delivery and a minimization of transportation time; (iii) integrating the deterioration rate to prevent wastage of plasma; and (iv) aiming to minimize overall plasma supply chain network cost. The second consideration is given utmost priority considering the life and death situation imposed by the severity of the virus, while however also being cognizant of limited financial resources especially in a developing country context, such as India, and the perishability of plasma. With these considerations, our model has the promise to significantly increase the efficiency of the plasma supply chain and thus reduce mortality.

The plasma supply chain model is formulated via a multi-objective MILP model. The process is initiated by assigning donor groups to the plasma collection facility in the designated hospitals. The plasma is then transported to local hospitals that are in need of such for the treatment of COVID-19 patients, based on the hospitals’ estimated demand. Any surplus in plasma is transported via road and/or air transport to plasma banks where it is stored and distributed further to other districts in need, or it is stored for future needs considering the propagated trend of the COVID-19 disease. As such, the plasma from the nearest plasma bank is transported via roadways and/or airways to the regional hospital of the district, and from there to the local hospitals to fulfil their plasma demands. The model however also interconnects the local hospitals and plasma collection facilities for immediate fulfilment of plasma requirements to and from any level/city/district. Since plasma is a perishable product, we have chosen such a complex integrated approach to avoid wastage. Transportation requirements are strategically planned and will be determined via mathematical modelling with cost considerations. As such, we formulate a multi-objective MILP mathematical model considering overall plasma transportation time, overall plasma supply chain network costs, and constraints. The main aim of our model is to determine and specify the location

![Fig. 1. Diagram of the plasma supply chain network.](image-url)
and number of plasma banks, as well as the allocation of the collection facilities to these banks, to minimize transportation time for the entire supply chain network while minimizing cost and wastage. A key challenge is to ensure that the proposed model is both time- and cost-efficient in addressing demand fluctuation.

3.1. Assumptions

1. Plasma collection facilities and regional plasma banks have limited capacities
2. The vehicles transporting plasma have a fixed capacity
3. The number of transporting vehicles at each facility and bank is limited
4. There are two types of uncertainty: (a) the uncertainty of plasma demand in each period; and, (b) due to unforeseen conditions, the uncertainty in costs for transporting plasma from the facilities to the plasma banks, and from the plasma banks to the hospitals
5. The location of donor groups and hospitals is fixed
6. The length of each decision period is one day (Milenković et al., 2015)
7. There are three types of vehicles with different capacities (Sinha et al. 2021)
8. The collection costs for plasma include maintenance, testing, and component costs

3.2. Indices

| M          | Set of Donors group indexed by m |
|------------|---------------------------------|
| N          | Set of potential locations for a plasma collection facility indexed by n |
| B          | Set of potential locations for a regional plasma bank b |
| i          | Mode of transportation |
| k          | Time period for plasma production |
| t          | Time period |

3.3. Parameters

| Parameter | Description |
|-----------|-------------|
| \( c_n \) | Cost for opening a plasma collection facility at location n |
| \( c_{nm} \) | Cost for collecting plasma from donor group m at location n |
| \( c_b \) | Cost for opening a regional plasma bank at location b |
| \( c_{nb} \) | Cost of transporting plasma from plasma collection facility n to regional plasma bank b through transportation mode i |
| \( I_b \) | Holding cost for plasma at regional plasma bank b |
| \( c_{nh} \) | Cost of transporting plasma from plasma collection facility n to hospital h via transportation mode i |
| \( P_b \) | Penalty cost at regional plasma bank b; this is considered to be a large number to prevent plasma shortage; this penalty cost is included to avoid bottleneck situations in the interconnected supply chain network |
| \( \text{trans}_{nbhi} \) | Travel time between plasma collection facility n and regional plasma bank b via transportation mode i |
| \( \text{dist}_{nb} \) | Distance between plasma collection facility n and regional plasma bank b |
| \( \sigma \) | Number of stochastic coefficients varying from their nominal values and including plasma demand in each period |
| \( \sigma^* \) | Number of stochastic coefficients varying from their nominal values and including transportation cost from the plasma collection facility to the regional plasma bank in each period |
| \( \sigma^{**} \) | Number of stochastic coefficients varying from their nominal values and including transportation cost from the regional plasma bank to the hospital in each period |
| \( R_{mn} \) | Travelling distance between donor group m and plasma collection facility n |
| \( r \) | Distance range for opening a plasma collection facility from a donor group |
| \( d \) | Distance range for opening a regional plasma bank from a plasma collection facility |
| \( \lambda \) | A large constant value |
| \( C_{nt} \) | Capacity of plasma collection facility n in time period t |
| \( V_{bn} \) | Limit for plasma supply of donor group m |
| \( CV_{nb} \) | Capacity of regional plasma bank b |
| \( D_{bn} \) | Plasma demand at regional plasma bank b in period t |
| \( D_{bh} \) | Plasma demand at hospital h in period t |
| \( CV_{nbh} \) | Capacity of vehicle i for the transportation of plasma from plasma collection facility n to regional plasma bank b |
| \( CV_{nbhi} \) | Capacity of vehicle i for plasma transportation from plasma collection facility n to hospital h |
| \( CV_{bni} \) | Capacity of vehicle i for the transportation of plasma from plasma bank b to regional hospital n |
| \( V_{hi} \) | Availability of vehicles i for the transportation of plasma at regional plasma bank b in period t |
| \( V_{ni} \) | Availability of vehicles i for the transportation of plasma at plasma collection facility n in period t |
| \( \rho_{kt} \) | Fraction of plasma units produced at period k that deteriorates in period t |
| \( l \) | Lost cost per plasma unit |
### 3.4. Decision variables

| Variable | Description |
|----------|-------------|
| $A_{mnt}$ | Quantity of plasma collected from donor group $m$ from plasma collection facility $n$ in period $t$ |
| $A_{nbti}$ | Quantity of plasma transported from plasma collection facility $n$ to regional plasma bank $b$ in period $t$ via transportation mode $i$ |
| $A_{nbthi}$ | Quantity of plasma transported from regional plasma bank $b$ to regional hospital $h$ in period $t$ via transportation mode $i$ |
| $W_{bh}$ | Plasma inventory level at regional plasma bank $b$ in period $t$ |
| $F_i$ | Equals to 1 if the collection facility is open at location $n$, otherwise 0 |
| $L_m$ | Equals to 1 if the donor group $m$ is allocated to the collection facility $n$ in period $t$. Otherwise 0 |
| $L_{nb}$ | Equals to 1 if the regional plasma bank $b$ is allocated to the collection facility $n$ in period $t$. Otherwise 0 |
| $V_{nb}$ | Number of vehicles $i$ required at plasma collection facility $n$ in period $t$ to transport plasma to regional plasma bank $b$ |
| $V_{nbh}$ | Number of vehicles $i$ required at plasma collection facility $n$ in period $t$ to transport plasma to hospital $h$ |
| $V_{bht}$ | Number of vehicles $i$ required at plasma bank $b$ in period $t$ to transport plasma to regional hospital $n$ |
| $D(t)$ | Deterioration rate |
| $e_{nb}$ | Dual auxiliary variable of location $n$ with respect to plasma bank $b$ |
| $e_{nh}$ | Dual auxiliary variable of location $n$ with respect to hospital $h$ |
| $\delta_{bnt}$ | Dual auxiliary variable of incremental increase in transportation cost from plasma collection facility $n$ to plasma bank $b$ |
| $\beta_{bh}$ | Dual auxiliary variable of incremental increase in transportation cost from plasma bank $b$ to hospital $h$ |
| $\gamma_{nb}$ | Unfulfilled amount of demand at plasma bank $b$ in period $t$ |

### 3.5. Objective functions

The objective is to determine the optimal allocation of plasma collection facilities and the setup of plasma banks so that both the transportation time of plasma between the various echelons and the overall cost of the plasma supply chain network is minimized. As such, the first objective is the minimization of transportation time. It includes the distance and the travel time, which depends on the transportation mode between plasma collection facilities and regional plasma banks, captured in equation (6) and depicted as a function in equation (7). The second objective is to minimize total plasma supply chain network cost, which consists of opening cost, collection cost, transportation cost, inventory and shortage costs. The opening cost includes the establishment of the plasma collection facilities and the plasma banks presented in equation (8). Equation (9) captures the plasma collection cost from donor groups. Equation (10) addresses the overall transportation cost incurred by plasma transportation from plasma collection facilities to plasma banks, and from plasma collection facilities to local hospitals, considering also the associated uncertainty. The uncertain parameters in the objective function, i.e., $c_{nb}$, $c_{nbh}$, and $D_{bh}$, were inspired by Bertsimas and Sim (2004) and are restricted by their boundary conditions reflected in the nominal values of $c_{nb}$, $c_{nbh}$, and $D_{bh}$, and the maximum values of $c_{nb}$, $c_{nbh}$, and $D_{bh}$, respectively. For example, $c_{nb}$ lies in the interval $[c_{nb} - \sigma_{nb} \tau_{nbh} + c_{nb}]$. We assume only positive deviations in the parameters.

Next, we introduce $\sigma^t$, $\alpha^t$, and $\sigma^s$ as the parameters to adjust the robustness level of the proposed model against the solution conservatism. In particular, $\sigma^t$ adjusts the uncertainty in plasma demand at the plasma banks for each $\tau$ changing in $[0, B]$; $\alpha^t$ and $\sigma^s$ adjust the uncertainty in transportation costs from the plasma collection facility to the plasma bank and to local hospitals for each $\alpha$ changing in $[0, A]$ and for each $\mu$ changing in $[0, H]$. It is unlikely that all facilities and hospitals will show uncertainty at the same time, however, our goal is to protect against all cases where the coefficients can change between $[\sigma^t]$, $[\alpha^t]$, and $[\sigma^s]$, respectively, i.e., $c_{nb}$ can change in $[(\sigma^t - |\sigma^t|) \tau_{nbh}]$. When $\alpha^t$, $\alpha^s$, and $\alpha^s$ are equal to zero, the objective functions become deterministic reflecting nominal conditions with no uncertainty at any plasma bank, plasma collection facility and local hospital; when the parameters are variable, the model acts conservatively. We also consider $\beta_{bh}$, $\kappa_{nbh}$, $\beta_{bh}$, and $\kappa_{nb}$ as dual auxiliary variables that help in improving the estimation efficiency for the uncertain parameters. Equation (11) captures the inventory cost at a regional plasma bank and the lost cost associated with the deterioration of plasma. Since plasma is a perishable product, we introduce a variable lifetime of inventory to reduce the deterioration rate. After a thorough study on growth rates of microorganisms responsible for deterioration (Juneja and Marks 2006, Mochizuki and Hattori 1987), we consider the deterioration rate as an exponential function with constants $A$ and $B$ as follows:

$$D(t) = Ae^{t/B}$$

(1)

where both $A$ and $B$ vary with product type and depend on environmental conditions such as required storing temperature, season, etc. In our model, $A$ represents the initial deterioration rate of plasma as soon as plasma taken from a donor. The dimensional unit of $A$ is the fraction of plasma deteriorating per unit of time. The parameter $B$ captures the time at which the deterioration rate of plasma becomes $e$ times of its initial value. It represents the Remaining Useful Life (RUL) for plasma, after which the plasma should be considered as defective or unfit for consumption. The fraction of plasma units produced at period $k$ that deteriorate in period $t$ is given by

$$
p_{kt} = \int_{j=1-k}^{t-1-k+1} D(t)dt$$

(2)

As the deterioration rate increases with time

$$p_{kt} > p_{k+1,t} (k < t)$$

(3)
Produced units either deteriorate or get consumed over time and hence items exceeding a certain time limit cannot be considered, i.e.,
\[ W_{bt} > W_{bt}^* \quad (t' > t) \] (4)

Hence, the holding cost and the lost cost for units produced in period \( k \) and stored as inventory at period \( t \) is,
\[ I(p_{bt}, W_{bt}) = I_b(1 - \rho_{bt})W_{bt} + I_{\rho_{bt}W_{bt}} \] (5)

As introduced later in the paper, we further consider shortage cost, disincentivizing not fulfilling the demand depicted in equation (12). Equation (13) thus represents the second objective function.

First Objective Function \( O_1 \):
Minimization of overall plasma transportation time = Transportation period from plasma collection facilities to regional plasma banks

The components of the objective function \( O_1 \) are as follows:

\[
\text{Transportation period from plasma collection facilities to regional plasma banks} = \sum_n \sum_b \sum_i \sum_t \text{trans}_{abi} \text{dist}_{aab} F_b
\] (6)

\[ \text{Minimize} O_1 = \sum_n \sum_b \sum_i \sum_t \text{trans}_{abi} \text{dist}_{aab} F_b \] (7)

Second Objective Function \( O_2 \):
Minimization of overall plasma supply chain network costs = Opening cost + Collection cost + Transportation cost + Inventory and lost cost + Shortage cost

The components of the objective function \( O_2 \) are as follows:

Opening cost = \[ \sum_n c_a F_n + \sum_b c_b F_b \] (8)

Collection cost = \[ \sum_n \sum_b \sum_i \text{c}_{ab} A_{abi} \] (9)

Transportation cost = \[ \sum_n \sum_b \sum_i \sum_t c_{abi} A_{abi} + \sum_n \sum_b \sum_i \sum_t c_{abi} A_{abi} + \beta \sigma^2 + \sum_{(b,h)\in N} \kappa_{nh}^2 + \beta \sigma^2 + \sum_{(b,h)\in N'} \kappa_{nh}^2 \] (10)

Inventory cost and lost cost = \[ \sum_l \left\{ \sum_b \sum_i (lp_{bt} + I_b(1 - \rho_{bt}))W_{bt} \right\} \] (11)

Shortage cost = \[ \sum_b \sum_t P_b \gamma_{bt} \] (12)

\[ \text{Minimize} O_2 = \sum_n c_a F_n + \sum_b c_b F_b + \sum_n \sum_b \sum_i \sum_t c_{abi} A_{abi} + \sum_n \sum_b \sum_i \sum_t c_{abi} A_{abi} + \beta \sigma^2 + \sum_{(b,h)\in N} \kappa_{nh}^2 + \beta \sigma^2 + \sum_{(b,h)\in N'} \kappa_{nh}^2 \]

\[ + \sum_l \left\{ \sum_b \sum_i (lp_{bt} + I_b(1 - \rho_{bt}))W_{bt} \right\} + \sum_b \sum_t P_b \gamma_{bt} \] (13)

Subjected to:
\[ F_n \leq 1 \forall n, t \] (14)
\[ L_{mnt} \leq F_n \forall m, n, t \] (15)
\[ R_{mnt} \leq r \forall m, n, t \] (16)
\[ A_{mnt} \leq A_{mnt} \forall m, n, t \] (17)
\[ \sum_n A_{mnt} \leq C_n F_n \forall m, t \] (18)
\[ \sum_n \sum_{m} A_{mnt} \leq V_m \forall m \] (19)

Constraint (14) limits the opening to only one plasma collection facility at one site. Constraint (15) ensures that only one facility is assigned to one donor group. The radius of the curvature under which a plasma collection facility should be opened for a donor group is presented in constraint (16). That a facility’s plasma donation is assigned to a particular donor group is ensured by constraint (17).
Constraint (18) indicates that the capacity of a plasma collection facility is limited. Constraint (19) ensures that a particular donor group does not donate more than its maximum amount of plasma.

\[
W_{bh(t-1)} + \sum_n \sum_i A_{nbti} - W_{bt} \geq \sum_h D_{ht} + \sum_h \sigma D_{ht} \forall b, t
\]  

(20)

\[F_b \leq 1 \forall b, t\]  

(21)

\[L_{bn} \leq L_{bn} \forall n, b, t\]  

(22)

\[\text{dist}_{nb} L_{bn} \leq d \forall n, b, t\]  

(23)

\[W_{bt} \leq inv_b \forall b, t\]  

(24)

\[(1 - \rho_{bt}) W_{bt} - A_{nbti} = W_{bt} \forall b, h, t, 1 \leq k < t \leq T\]  

(25)

Constraint (20) articulates the inventory level of plasma at regional plasma bank \(b\). That one plasma bank can only be opened at one site is ensured by Constraint (21). Constraint (22) ensures that only one regional plasma bank is assigned to one collection facility. Constraint (23) limits the radius of the curvature under which a regional plasma bank should be opened. That a regional bank has limited capacity is captured in constraint (24). The balancing of inventory across consecutive periods considering the deterioration in each period is captured in constraint (25).

\[
\sum_b V_{nhit} \leq \sum_b V_{nti} \forall n, t, i
\]  

(26)

\[
\sum_n V_{nhit} \leq \sum_n V_{nti} \forall n, t, i
\]  

(27)

\[
\sum_n \text{Veh}_{bh} \leq \sum_n \text{Veh}_{bt} \forall n, t, i
\]  

(28)

\[
V_{nhit} \geq \frac{A_{nhit}}{C_{nhit}} \forall n, h, t, i
\]  

(29)

\[
V_{nhit} \geq \frac{A_{nhit}}{C_{nhit}} \forall b, h, t, i
\]  

(30)

\[
\text{Veh}_{bh} \geq \frac{A_{bh}}{C_{Veh}} \forall n, b, t, i
\]  

(31)

\[
\sum_b \sum_i A_{nbti} \leq \sum_i A_{nhit} \forall n, \forall t
\]  

(32)

\[
\sum_b \sum_i A_{nbti} \leq \sum_i A_{nhit} \forall n, \forall t
\]  

(33)

Constraints (26) and (27) determine the maximum number of available transporting vehicles at plasma collection facilities for the transport of plasma to regional plasma banks and local hospitals, respectively. The maximum number of vehicles available at a plasma bank for the transport of plasma to regional hospitals is determined by constraint (28). The number of vehicles required in each case is captured by constraints (29), (30) and (31), respectively. Constraints (32) and (33) limit the load on each vehicle to transport plasma from plasma collection facilities to plasma banks and hospitals, respectively.

\[
\sum_b \sum_i A_{nbti} \geq D_{ht} \forall h, t
\]  

(34)

\[
\sum_b \sum_i A_{nbti} - \sum_h D_{ht} \geq \sum_i \sum_b A_{nbti} \forall t
\]  

(35)

\[
k^p + k^q \geq c_{nb} A_{nbti} (n, b) \in N^p, m, t
\]  

(36)

\[
k^p + k^q \geq c_{nb} A_{nbti} (b, h) \in B^p, m, t
\]  

(37)

\[A_{mn}, A_{nhit}, W_{bt}, D_{ht} \geq 0\]  

(38)

\[F_x, F_y \in \{0, 1\}\]  

(39)
4.3. Encoding mechanism

Now proceed with an explanation of the key components of NSGA-III. We propose a problem-specific NSGA-III to generate optimal results through the improvement of the convergence rate. We rely on these recent advances, we propose a problem-specific NSGA-III to generate optimal results through the improvement of the convergence rate. We introduce a clustering operator that replaces the crowding distance operator in NSGA-II. Relying on these recent advances, we propose a problem-specific NSGA-III to generate optimal results through the improvement of the convergence rate.

Mixed Integer Linear Programming formulations are computationally complex. We therefore propose a heuristic with two iterative phases that are performed until an optimal solution set is obtained. While the location phase determines the location coordinates for plasma banks, the allocation phase allocates the plasma collection facilities located in each district to those plasma banks. These two phases are iteratively performed until an optimal solution set is obtained.

4.1. Location phase

The location choices for the plasma banks can have a considerable impact on the entire supply chain in terms of both time and cost. As such, the location of a plasma bank is selected based on (1) the distance of the plasma bank’s location to each plasma collection facility, and (2) the cost of setting up a plasma bank at that location, the transportation time, and the means of transportation available at the output of this phase will serve as the input for the allocation phase.

4.2. Allocation phase

A distance matrix captures the distance between the plasma facilities and the plasma banks. The resultant problem is NP-hard in nature as it is an integration of multiple decision factors including location, inventory, and demand. These factors vary in each decision epoch for each plasma bank and local hospital, rendering the proposed problem stochastic in nature.

Generally, for such a stochastic multi-objective linear programming model, the existing literature primarily adopts heuristic algorithms. Although these algorithms have high computational efficiency, they cannot assure an optimal solution. We therefore utilize IBM ILOG CPLEX optimization studio version 12.9 for solving the mathematical model. The decision variables, i.e., the amount of plasma collected and the amount of plasma transported, are considered as integer values, while the dual auxiliary variables representing the demand and transportation are considered as float values, making the constraints non-linear. CPLEX optimization uses the branch and bound method, and as a result, we linearized the constraints before obtaining the solution from CPLEX.

Evolutionary algorithms can solve multi-objective optimization problems by generating non-dominated solutions i.e., Pareto frontiers, which are considered as optimal solutions. A wide range of such multi-objective evolutionary algorithms exists, which can be classified into two groups: NSGA and NSGA-II. While the NSGA group does not provide solution (elitism) conservatism (Srinivas and Deb 1994), the NSGA-II provides such a elitism mechanism, representing a more realistic capture of associated dynamics. Recent developments in evolutionary algorithms have therefore focused on obtaining Pareto solutions. This is also driven by NSGA-II, a modified version of NSGA, utilizing a non-dominated sorting genetic algorithm (Deb et al., 2000), which is computationally efficient and less dependent on a sharing parameter for diversity preservation. This was further extended with the introduction of the multi-objective algorithm NSGA-III (Deb and Jain, 2013), which is considered to be even more efficient for solving multi-objective problems. NSGA-III introduces a clustering operator that replaces the crowding distance operator in NSGA-II. Relying on these recent advances, we propose a problem-specific NSGA-III to generate optimal results through the improvement of the convergence rate. We now proceed with an explanation of the key components of NSGA-III.

4.4. Uniformly distributed reference points

The systematic approach proposed by Das and Dennis (2000) is used for generating reference points in the original NSGA-III. We propose to utilize a uniform design, which aims to determine a set of points that are uniformly distributed over the design space generating uniformly distributed reference points in a sphere \( O = \{ (o_1, o_2, \ldots, o_m) \mid \sum_{i=1}^{m} o_i^2, o_i \geq 0, i = 1, 2, \ldots, m \} \). For this, we...
generate a $D$ set of uniformly distributed points on $A = \{(a_1, a_2, \ldots, a_m) \mid 0 \leq a_1, a_2, \ldots, a_m \leq 1\}$, where $O$ is the number of uniformly distributed points in $A$, $m$ is the dimension of the problem. Let $\theta$ be a numerical value that yields the smallest discrepancy of a generated point set such that the integer matrix, i.e., the uniform array $[X_{ij}]_{O \times m}$, can be calculated as $X_{ij} = i\theta^{j-1} \mod O + 1$, where $i = 1, 2, \ldots, D$ and $j = 1, 2, \ldots, m$; the $i^{th}$ row can define a point $A_i = (a_{i1}, a_{i2}, \ldots, a_{im})$ with $a_{ij} = \frac{2x - 1}{2D} i = 1, 2, \ldots, D$. Next, $D$ represents a set of reference points uniformly distributed on $O$, and is represented by $N(D, m) = N_i = (n_{i1}, n_{i2}, \ldots, n_{im})$. This can be calculated by:

$$n_{ij} = \begin{cases} 
\prod_{o=1}^{m-1} \cos(0.5c_{i,o}\pi)j = 1 \\
\sin(0.5c_{i,m-j+1}\pi) \prod_{o=1}^{m-j} \cos(0.5c_{i,o}\pi) 1 < j < m \\
\sin(0.5c_{i,1}\pi)j = m 
\end{cases}$$  \hspace{1cm} (44)

The above equation (44) is a hyper-sphere formula that becomes circular for $m = 2$ and spherical when $m = 3$.

4.5. $\theta$-dominance

For given reference points $N(D, m)$ represented as $\{N_1, N_2, \ldots, N_D\}$, a reference line is defined by joining the origin with the reference point. Next, each individual is associated to a reference point by calculating the perpendicular distance of it from each of the reference lines. The reference line, which is at the shortest distance from the solution, is thus associated with the solution. This way, the population is split into $D$ clusters $A = \{(a_1, a_2, \ldots, a_m) \mid A_i$ is presented by the reference point $N_j, j = 1, 2, \ldots, D$. For an objective function $f(x)$ with a solution $x$, represented by $[f_1(x), f_2(x), \ldots, f_m(x)]$ and a reference line $P_j$ that passes through the origin $K$ and $N_j$, a penalty function can be articulated as $Q_j(x) = ||(f(x) - K)\alpha|| + \theta q_j, \text{perpendicular}^{(x)}, j = 1, 2, \ldots, D$, where $q_j, \text{perpendicular}^{(x)}$ calculates the perpendicular distance between $f(x)$ and $P_j$.

![Fig. 2. Iterative framework to obtain the optimal solution.](image-url)
We considered $\theta > 0$ as a predefined penalty parameter, set to be 2 for achieving the best mean quality of alignment. The $\theta$-dominance value is utilized to incorporate a fast non-dominating sorting on the population to divide it into various $\theta$-non-dominant levels. Fig. 2 summarizes the steps to obtain an optimal solution.

5. Case study

India was chosen as the illustrative context since this developing country’s minute 1.3% contribution to the healthcare sector out of its total GDP is coupled with its second rank in terms of population (1.3 billion) and first in terms of population density (382 persons per square kilometer). We felt that this context would be particularly receptive to any guidance provided in developing plasma supply chain networks in adverse conditions. In addition, the community spread of COVID-19 has been accelerating. As such, as of September 2021, India has a global 15% share of COVID-19 cases with a solid recovery rate of 98%. Convalescent plasma derived from treated patients has been successfully used as a treatment option for COVID-19 patients in India and has shown significant positive results. For example, in the state of Assam, as per the data available under the National Health Mission, 155 people donated 273 units of plasma, which was administered to 128 patients that showed signs of recovery. In addition, in the city of Hyderabad, Telangana, doctors from the Super Specialty Hospital’s Association declared a 75% recovery rate with the use of CP in critical cases.
The sudden emergence of the novel coronavirus took a toll on the Indian health management system. Along with that, a proportion of recovered patients refused to donate plasma due to fear of exposing themselves to the infection again, falling ill, becoming weak, or due to the anxiety of donating. Based on the data provided by Maharashtra Food and Drug Administration (FDA), until August 5, 290,343 patients have successfully recovered in its seven divisions, accounting for 70% cases in Maharashtra. However, only 1,236 units of plasma have been donated, which represents a mere 0.42%. The demand for blood components subsequently increased with soaring cases, but the collection, storage, and management of blood and its products remains a significant challenge (Arcot et al. 2020). We thus apply our model to the case of India, which especially recently has been suffering from a significant spike in cases.

5.1. Data collection

The number of COVID-19 cases in states and districts as of September 1, 2020, was obtained from covidindia.org, a government-run website. The list of medical institutions that could be used as a location for plasma banks is published by the Indian Council of Medical Research (ICMR). The latitude and longitude of districts and the hospitals were measured using ArcGIS software and then plotted on the map.

According to the Ministry of Home Affairs, the districts are divided into red, orange, and green zones depending upon the number of active cases. Red zones are the areas or hotspots with the highest caseload. Orange zones are areas with a limited number of cases. Green zones are areas with no confirmed cases within at least the last 21 days. Maharashtra, Tamil Nadu, and Delhi are areas with the most active cases of coronavirus, whereas Ladakh, Himachal Pradesh, Chandigarh, Nagaland, Mizoram, Sikkim, Manipur, Tripura, Meghalaya, Andaman and Nicobar Islands, Dadra and Nagar Haveli, and Daman and Diu show very few or an insignificant number of

| Donors | District                | Latitude  | Longitude |
|--------|-------------------------|-----------|-----------|
| L1     | East Godavari           | 16.95982  | 82.21727  |
| L2     | Kurnool                 | 15.82664  | 78.0243   |
| L3     | Guntur                  | 16.29923  | 80.43246  |
| L4     | Kamrup Metropolitan     | 26.12328  | 91.9375   |
| L5     | Patna                   | 25.60287  | 85.14129  |
| L6     | Delhi                   | 28.63329  | 77.21972  |
| L7     | South Goa               | 15.19791  | 74.10074  |
| L8     | Ahmedabad               | 23.01077  | 72.57898  |
| L9     | Surat                   | 21.18583  | 72.83816  |
| L10    | Gurugram                | 28.47649  | 77.07021  |
| L11    | Faridabad               | 28.38586  | 77.31379  |
| L12    | Srinagar                | 34.08478  | 74.80902  |
| L13    | Bengaluru Urban         | 12.96455  | 77.6108   |
| L14    | Dakshina Kannada        | 12.86533  | 75.24601  |
| L15    | Kalaburgi               | 17.31373  | 76.83692  |
| L16    | Thiruvananthapuram      | 8.498422  | 76.95826  |
| L17    | Mumbai                  | 18.95322  | 72.83483  |
| L18    | Thane                   | 19.18776  | 72.96461  |
| L19    | Pune                    | 18.50296  | 73.85474  |
| L20    | Indore                  | 22.71691  | 75.85791  |
| L21    | Bhopal                  | 23.26357  | 77.40106  |
| L22    | Ganjam                  | 19.3883   | 85.06231  |
| L23    | Khordha                 | 20.17398  | 85.61397  |
| L24    | Jodhpur                 | 26.26543  | 73.02915  |
| L25    | Jaipur                  | 26.90134  | 75.78324  |
| L26    | Alwar                   | 27.55488  | 76.61236  |
| L27    | Telengana               | 17.38758  | 78.46214  |
| L28    | Lucknow                 | 26.84009  | 80.91723  |
| L29    | Gautam Buddha Nagar     | 28.36101  | 77.51249  |
| L30    | Ghaziabad               | 28.66747  | 77.4388   |
| L31    | Kolkata                 | 22.55791  | 88.36506  |
| L32    | North 24 Parganas       | 22.73645  | 88.73689  |
| L33    | Howrah                  | 22.59602  | 88.25668  |
| L34    | Puducherry              | 11.92843  | 79.82401  |
| L35    | Papum Pare              | 27.292809 | 93.46904  |
| L36    | Raipur                  | 21.24438  | 81.63649  |
| L37    | Ranchi                  | 23.34717  | 85.31206  |
| L38    | East Singhbhum          | 22.94827  | 86.05279  |
| L39    | Ludhiana                | 30.91762  | 75.85159  |
| L40    | Jalandhar               | 31.33115  | 75.58253  |
| L41    | Haridwar                | 29.946881 | 78.15768  |
| L42    | Chennai                 | 13.08233  | 80.27634  |
| L43    | Chengalpattu            | 12.68273  | 79.98383  |
| L44    | Thiruvallur             | 13.12195  | 79.91111  |
cases. Fig. 3 indicates the red zones of all 25 Indian states/Union Territories in which we propose to develop the plasma supply chain network. Table 1 provides a complete list of red-zoned districts and Table 2 summarizes the available medical institutions that can serve as the location for a plasma bank. The distance parameters $\text{trans}_{ab}$ and $\text{dist}_{ab}$ and the data in Tables 1 and 2 are obtained using the ArcGIS Network Analyst Tool. The demand parameters $D_a$ and $D_b$ were collected from the National Blood Transfusion Council (NBTC), capturing information on shipments of plasma units at the aggregate level. This data was collected with respect to each blood group for specific dates across a three-month period. The data also contained information regarding the distribution sites (hospitals), and whether plasma units are distributed to patients or stored in inventory. Further, the available number of doses for each blood group was recorded. Table 3 provides further detail on these datasets obtained. In addition, Table 4 denotes whether the respective parameters were generated or are obtained from external sources. Table 5 defines the parameters settings for the NSGA-II and NSGA-III algorithms.

### Table 2

| Plasma Bank | Names of Medical Institutions | Latitude | Longitude |
|-------------|--------------------------------|----------|-----------|
| P1 | Smt. NHL Municipal Medical College, Ahmedabad | 23.01851 | 72.571226 |
| P2 | B.J. Medical College and Civil Hospital, Ahmedabad | 23.05297 | 72.60286 |
| P3 | Government Medical College, Bhavnagar | 21.76862 | 72.136835 |
| P4 | Government Medical College, Surat | 21.18961 | 72.812403 |
| P5 | Gujarat Medical Education & Research Society Medical College, Vadodara | 23.2193 | 72.6394 |
| P6 | Sumandeep Vidyapeeth and Institution, deemed to be University & Dhiraj Hospital, Vadodara | 22.29297 | 73.321743 |
| P7 | PDU government college, Rajkot | 22.30845 | 70.794819 |
| P8 | Sawai Man Singh Medical College, Jaipur | 26.6877 | 75.81365 |
| P9 | Mahatma Gandhi Medical College and Hospital, Jaipur | 26.77068 | 75.854856 |
| P10 | Dr. S.N. Medical College, Jodhpur | 26.26945 | 73.007499 |
| P11 | All India Institute of Medical Sciences, Jodhpur | 26.23609 | 73.006289 |
| P12 | SatguruPratap Singh Hospital, Ludhiana | 30.88421 | 75.887976 |
| P13 | B.J. Government Medical College, Pune | 18.52522 | 73.871877 |
| P14 | Sir H. N. Reliance Foundation Hospital and Research Centre, Mumbai | 18.95788 | 72.820353 |
| P15 | Rajasthan Chhatrapati Shahi Maharaj Government Medical College and CPR Hospital, Kolhapur | 16.70134 | 74.226155 |
| P16 | TMC & BYL Nair Hospital, & Kasturba Hospital, Mumbai | 18.98413 | 72.829906 |
| P17 | Government Medical College, Nagpur | 21.12728 | 79.091913 |
| P18 | Aditya Birla Memorial Hospital, Pune | 18.62516 | 73.775516 |
| P19 | Poona Hospital and Research Center, Pune | 18.51102 | 73.842296 |
| P20 | Seth Gordhandas Sunderdas Medical College (GSMC) and the King Edward Memorial Hospital, Mumbai | 19.0029 | 72.842512 |
| P21 | Smt. Kashibai Navale Medical College, Pune | 18.45656 | 73.820709 |
| P22 | Lokmanyta Tilak Municipal General Hospital, Mumbai | 19.03562 | 72.859969 |
| P23 | Madurai Medical College, Madurai | 9.928701 | 78.137182 |
| P24 | Madras Medical College, Chennai | 13.08061 | 80.272332 |
| P25 | Tirunelveli Medical College Hospital, Tirunelveli | 8.711452 | 77.751173 |
| P26 | Christian Medical College, Vellore | 12.879 | 79.130316 |
| P27 | PSG Institute of Medical Sciences & Research, Coimbatore | 11.02104 | 77.007747 |
| P28 | Jawaharlal Institute of Postgraduate Medical Education & Research, Puducherry | 11.95437 | 79.797105 |
| P29 | Gandhi Medical College, Bhopal | 23.26017 | 73.391157 |
| P30 | Mahatma Gandhi Memorial Medical College, Indore | 22.71359 | 75.883756 |
| P31 | Chirayu Medical College and Hospital, Bhopal | 23.26733 | 77.30882 |
| P32 | Sri Aurobindo Institute of Medical Sciences, Indore | 22.79653 | 75.846737 |
| P33 | R D Gardi Medical College, Ujjain | 23.23406 | 75.806013 |
| P34 | Government Institute of Medical Sciences, Noida | 28.43335 | 77.532536 |
| P35 | Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow | 26.74689 | 80.95063 |
| P36 | Super Specialty Pediatric Hospital and Post Graduate Teaching Institute, Noida | 28.57716 | 77.337741 |
| P37 | King George Medical University, Lucknow | 26.86821 | 80.91733 |
| P38 | Karnataka Institute of Medical Sciences, Hubli | 15.36096 | 75.12714 |
| P39 | Mysores Medical College, Mysuru | 12.31464 | 77.645496 |
| P40 | Hassan Institute of Medical Sciences, Hassan | 13.0055 | 76.102324 |
| P41 | Mandy Institute of Medical Sciences, Mandya | 12.52709 | 76.901664 |
| P42 | Bangalore Medical College and Research Institute, Bengaluru | 12.95872 | 77.574472 |
| P43 | Gandhi Medical College, Secunderabad | 17.42393 | 78.503839 |
| P44 | ESIC Medical College, Hyderabad | 17.44736 | 78.438848 |
| P45 | Postgraduate Institute of Medical Sciences, Chandigarh | 30.76193 | 77.775036 |
| P46 | Lady Hardinge Medical College and associated hospitals, New Delhi | 28.61831 | 77.104997 |
| P47 | VardhamanMahavir Medical college &Safdarjung Hospital, New Delhi | 28.56869 | 77.202849 |
| P48 | Ram Manohar Lohia Hospital, New Delhi | 28.62416 | 77.199006 |
| P49 | All India Institute of Medical Sciences, Patna | 25.56022 | 85.043147 |
| P50 | ESIC Medical College, Faridabad | 28.39353 | 77.294155 |
| P51 | All India Institute of Medical Sciences, Patna | 21.2583 | 81.581201 |
| P52 | Kurnool Medical College | 15.82175 | 78.039898 |
| P53 | Sri Venkateshwara Institute of Medical Sciences | 13.63666 | 79.40355 |

V.K. Manupati et al.
6. Results and discussion

Computations for an experimental study of our proposed mathematical model were carried out on a PC with Intel Core i5-4302Y (1.70 GHz, 512 KB L2 cache) having a Windows 10 Home operating system with 8 GB RAM. The Multi-Objective MILP was conducted on CPLEX 12.9 and the optimal cost and time were obtained as depicted in Table 6.

6.1. Locating the optimal number of plasma banks

The mathematical model from Section 3 was applied to obtain the optimal number of plasma banks and to allocate the collection facilities to them. The following input parameters were considered: (1) the location coordinates of district-based plasma collection facilities, (2) the available location coordinates for the plasma banks, (3) the distance between the plasma collection facilities, and (4) the distance between plasma collection facilities and plasma banks.

The optimization of the objective functions led to the location of seven plasma banks that ensure a proper flow of plasma in the supply chain network. Table 5 summarizes the results for the location coordinates of plasma banks and the assigned plasma collection facilities, which is also visualized in Fig. 4. The optimization yielded a total of seven plasma banks, ensuring the proper flow of plasma. As can be seen from Table 7, plasma bank #6 functions as a central plasma bank since most facilities are allocated to it.

6.2. Assessing solution quality

To assure that the obtained results represent the optimum solution, we conducted a comparison study by applying an evolutionary genetic algorithm, specifically Non-Dominated Sorting Genetic Algorithm-II (NSGA-II) and NSGA-III, which are the most used multi-objective evolutionary algorithm in the literature (Wang et al., 2019, Ma et al., 2019, Zhou and Zheng, 2020). The comparison presented in Table 8 suggests that the CPLEX optimization is very effective in obtaining the optimal solution, as the resultant total cost is less compared to the NSGA-II (i.e., 0.8% better) and the NSGA-III (i.e., 0.06% better). In addition, the average computational time for CPLEX was less compared to that of the NSGA-II and NSGA-III methods. In particular, CPLEX took 1.3 min while the computational time of NSGA-II was noted as 5.4 min and for NSGA-III it was noted as 2.8 min.

6.3. Rationality analysis

The parameters $\beta$ and $\mu$ represent the rationality index that considers the transportation of plasma from the collection facility to the plasma bank, and from the collection facility to the local hospitals, respectively. As the rationality index increases, the percentage of donors increases. Tables 9 and 10 articulate the effects of the rationality indices on the required number of vehicles for transporting plasma from the plasma collection facilities to the plasma banks, and from plasma collection facilities to local hospitals, respectively. As such, the rationality index captures the impact on transportation requirements based on an increase or decrease in donors. This provides guidance for decision makers to play through different scenarios based on the number of donors and the ensuing transportation needs.

6.4. Sensitivity analysis

The demand for plasma in this pandemic has become stochastic and the supply is irregular. Managing the supply to fulfil the required demand is thus not simple. A further complicating factor is that plasma is perishable. As a result, shortages may increase the mortality rate and the cost of plasma therapy. At the same time, plasma donors are a scarce resource. In this model, since historical data was not available, the Bertsimas and Sim (2004) method is utilized to accept a suboptimal solution for the nominal values of the generated data to ensure that the results remain feasible and near optimal when the data varies. This method offers full control over the degree of conservatism for each constraint of the model by protecting the violation of constraint $i$ deterministically when only a pre-specified number $\beta_i$ of the coefficient changes. As a result, guarantying the solution is feasible if less than $\beta_i$ uncertain coefficients change. This is captured in (46).

### Table 3

| Dataset | Attribute | Description | Format |
|---------|-----------|-------------|--------|
| $D_{be}$ | date      | Available units after shipment on a particular date | date |
|         | A         | Total number of blood group A units | integer |
|         | B         | Total number of blood group B units | integer |
|         | O         | Total number of blood group O units | integer |
|         | Total     | Total number of plasma units | integer |
|         | Hospital_ID | Unique ID for each hospital | string |
|         | Receive date | Date on which the number of units ordered at nearby plasma bank arrives | date |
|         | Bloodgroupunits | Blood group of a particular plasma unit that arrives | string |
|         | Product_quantity | Number of doses of the particular plasma unit (250 ml = 1 dose) | string |
Min $\sum_{i,j} c_{ij} x_j$

$s.t.: \sum_j a_{ij} x_j \geq b_i, \forall i$

$x_j \geq 0, \forall j$

where $a_{ij}$ are uncertain coefficients, and $\beta$ is the uncertain budget that adjusts the uncertainty level in each row changing in $[0, |\beta|]$. The role of $\beta$ is to adjust the robustness of the proposed model against the solution conservatism level that when $a_{ij} = |\beta|$, the objective function will exhibit its worst value.

We investigate the sensitivity of the objective function by conducting experiments using different degrees of conservatism for the uncertain parameters considering divergence rates of 5%, 10%, 15%, and 20% variability from their nominal value. As such, due to the uncertain and unprecedented context of the pandemic, the sensitivity analysis allows the variation of the uncertain parameters, so that the impact of potential changes can be investigated and taken into consideration when leveraging the model for decision making.

Specifically, the above solution suggests 44 plasma collection facilities and seven plasma banks, yielding a corresponding degree of conservatism for transportation costs $c_{nbi}$ to be an integer value in the range $[0, 44]$ and a degree of conservatism for demand at plasma banks $D_{bt}$ to be an integer value in the range $[0, 8]$. We also note that our goal was to form an interconnected plasma supply chain network that can address the plasma demand of each and every state in the country. We thus considered the regional and local hospitals as interconnected to address each other’s plasma demand. However, for better communication and faster transport, we implemented the seven plasma banks to prevent waste. The parameter $\sigma_1$ is defined as the stochastic coefficient of $|N|$ and can take values in the range $[0, |N|]$ for parameter $c_{nbi}$. Similarly, $\sigma_2$ is defined as the uncertain coefficient of $|B|$ and takes values in the range $[0, |B|]$ for parameter $D_{bt}$.

Figs. 5 and 6 depict the results for the sensitivity analysis of the proposed model. Fig. 5 illustrates the worst value occurring when
the degree of conservatism has the maximum value, i.e., when all plasma banks’ demand fluctuates from their expected demand. This is represented by $\sigma = |B|$. In the case of transportation cost, as illustrated in Fig. 6, the worst value is obtained before the degree of conservatism reaches the peak value, i.e., $\sigma = 20 < |N| = 44$. Here, when 20 out of 44 facilities show uncertainty due to the rationality

![Fig. 4. Location allocation of Plasma banks and plasma collection facilities.](image)

**Table 7**

| Sr. no. | Plasma Banks     | Coordinates         | Allocated facilities                  |
|---------|------------------|---------------------|---------------------------------------|
|         |                  | Latitude            | Longitude                            |                                      |
| 1       | Plasma bank 1    | 23.05297            | 72.60286                              | L8, L9, L20, L21, L24                |
| 2       | Plasma bank 2    | 18.95788            | 72.820353                             | L7, L17, L18, L19                    |
| 3       | Plasma bank 3    | 13.08018            | 80.272732                             | L11, L13, L42, L43, L44, L14, L16    |
| 4       | Plasma bank 4    | 17.44736            | 78.438848                             | L1, L2, L3, L15, L27, L35, L36       |
| 5       | Plasma bank 5    | 28.61831            | 77.104997                             | L6, L10, L12, L30, L39, L40, L41     |
| 6       | Plasma bank 6    | 25.56022            | 85.043147                             | L4, L15, L31, L32, L33, L37, L38, L22, L23 |
| 7       | Plasma bank 7    | 28.39353            | 77.294155                             | L25, L26, L28, L29                   |

V.K. Manupati et al.
Table 8
Comparison results with NSGA-II and NSGA-III.

| Function          | CPLEX  | NSGA-II | Solution Gap (%) (NSGA-II) | NSGA-III | Solution Gap (%) (NSGA-III) |
|-------------------|--------|---------|---------------------------|----------|-----------------------------|
| Total Cost        | 441107113.00 | 444635969.90 | 0.8                       | 442906217.88 | 0.06                        |
| Travel time (hrs) | 63     | 63.7    | –                         | 63.1     | –                           |
| Time (minutes)    | 1.3    | 5.4     | –                         | 2.8      | –                           |

Table 9
Effect of $\beta^r$ on the required number of airplanes for transporting plasma.

| $\beta^r$  | 0.10 | 0.50 | 0.75 | 1     |
|------------|------|------|------|-------|
| Increase in transport from the plasma collection facility to the plasma bank | 6%   | 20%  | 36%  | 50%  |
| Number of airplanes | 1    | 1    | 2    | 2    |

Table 10
Effect of $\beta^r$ on required number of ambulances for transporting plasma.

| $\beta^r$  | 0.10 | 0.50 | 0.75 | 1     |
|------------|------|------|------|-------|
| Increase in transport from the plasma collection facility to the local hospital | 10%  | 50%  | 75%  | 100% |
| Number of ambulances | 4    | 7    | 8    | 10   |

in donor groups, the function exhibits its worst output.

Table 11 summaries the effects of the main parameters on the objective functions. As can be seen, as the number of donors increases, a drastic growth is seen in total cost, i.e., a 20% and 30% increase in demand will result in a 33% and 41% growth, respectively. The increase and decrease in demand illustrate the impact on the objective function, but the percentage change is less in comparison to the donors. This can be explained by the fact that as the number of donors increases, the collection and transportation costs increase as well, resulting in an overall increase in total cost. In contrast, with an increase in demand, shortages may arise in certain plasma facilities, necessitating the transport of plasma from plasma banks, increasing both transportation time and cost.

7. Theoretical and managerial insights

We now proceed with theoretical and managerial implications of our proposed model. The model aids in the smooth transport of plasma across India in time of crisis, focusing on addressing the need for especially every red zone. Considering the perishability of plasma and the current COVID-19 situation characterized by demand surpassing the supply of plasma, locating plasma banks and allocating cities to these banks is a critical decision. This can have fundamental implications for the time needed to provide plasma to patients. Another critical aspect that makes the plasma supply chain network so unique and challenging to design is the perishability of plasma. We therefore captured the deterioration rate of plasma to minimize wastage, which represents one of our theoretical contributions within the context of COVID-19. This interconnected model can thus help healthcare policymakers to plan and organize the timely transport of plasma. While being of immense practical value, the theoretical advances our paper provides are in the form of our

Fig. 5. Sensitivity in the proposed model with respect to fluctuation in demand.
model development, which can serve as a starting for other scholars to design supply chain networks with similar characteristics, such as those for organs and other blood components. Our model highlights that if proper care is not taken, the distribution may be sub-optimal leading to plasma spoilage in certain areas and unfulfilled plasma need in others. Therefore, small storage facilities should be set up in each regional and local hospital so that, in case of emergency, there is sufficient availability. In addition, to quickly and efficiently transport the plasma from one place to another in the right amount, the capacity of the available transportation vehicles needs to be accurately considered and defined.

Insights derived from our analysis can be invaluable for decision makers for the design of their supply chains in times of crises. As such, the optimal locations for plasma banks can be determined, and guidance for an optimal allocation is provided. By also considering the cost of storage and transportation renders the model practically applicable. In addition, we captured the challenging contexts of the pandemic situation, which can reflect in demand uncertainty and transportation unavailability. The results obtained from the rationality analysis and the sensitivity analysis can help in tackling such uncertainties by planning for the proper flow of plasma at each echelon. Specifically, the study’s rationality analysis can assist decision makers in predicting the number of vehicles required for transportation, with the sensitivity analysis providing insights about the resources required in uncertain situations.

From a theoretical angle, our findings also contribute to the general transportation literature addressing transportation implications of supply chain designs. As such, our results have implications for the design of transportation routes, which is determined based on the results of the location-allocation problem. With the insights generated we for instance extend the work of Hamdan and Diabat (2020) and Liu et al. (2020). In addition, with our results we offer guidance on the impact that the supply chain design has on transportation costs, as part of the overall plasma supply chain network cost, which we aimed to minimize after minimizing overall plasma transportation time. As such, we extend the large body of work that has considered transportation cost as a critical element (e.g., Kamyabniya et al., 2021; Ramezanian and Behboodi, 2017). Furthermore, we offer insight into the effect of decisions on the required number of ambulances and airplanes, providing guidance for transportation and logistics professionals on the resources needed for the transportation network. We believe these decision aspects to be particularly critical in developing countries such as India (cf. Tu et al. 2018), due to the frequently limited resources devoted to healthcare (in India, it is a merely 1.3% of GDP). Considering such constraints makes the focus on cost minimization paramount. We thus add to the body of literature that has highlighted the unique nature of developing nations (e.g., Fang et al. 2020), and offer valuable decision support for policymakers in these

![Fig. 6. Sensitivity in the proposed model with respect to fluctuation in transportation cost.](image-url)
contexts. We believe that the implications of the proposed model can help policymakers within the Government of India to tackle some of the challenges associated with the disease. In addition, positive advertisements using hoardings, media exposure, and excerpts in newspapers can spread the word about the benefits of plasma therapy into the treatment regimen of COVID-19 and the crucial need for plasma donations by patients that recovered from COVID-19. A tracking system could be established to contact recovered COVID-19 patients to appeal for the donation of plasma. Providing a token amount or some sort of recognition as an incentive by the Government of India could further mobilize the donation drive. Apart from this, transportation options to and from the residence to the collection facility will ease the process of donation.

8. Conclusion

The Indian government has taken a step towards setting up plasma collection facilities in every district to provide an adequate amount of plasma to patients suffering from COVID-19. While the projected demand is high, there has been a significant shortage of donors, also having implications for the lead time and cost of plasma units. This research conceptualized a novel plasma supply chain network considering donor groups, plasma collection facilities (set up at regional hospitals), local hospitals, and plasma banks. To support the Government of India in its decision-making process, a Mixed Integer Linear Programming model was developed with two objective functions, i.e., the minimization of overall plasma transportation time and overall plasma supply chain network cost. The proposed model determined the optimal location for setting up plasma banks, allocating the plasma facilities to these plasma banks under demand uncertainty, considering transportation time, transporting modes, transportation cost, and holding and lost costs to avoid a plasma shortage. The problem was optimized via CPLEX, with the results then being compared to the results obtained with the NSGA-II and NSGA-III algorithms. In addition, rationality and sensitivity analyses were conducted to examine the impact of the stochastic parameters on solution quality.

While our study was able to provide invaluable guidance for decision makers on how to design the plasma collection and distribution, our research is not void of limitations. First, the conditions and assumptions made in building the model, while reasonable and substantiated, might not capture the true dynamism and complexity of the current unprecedented pandemic environment, especially when it comes to the multitude of uncertainties still pertaining to treatment and immunizations. A lot is still being learned as approaches are implemented. Second, we did not consider a collection facility or a plasma bank being closed due to lockdown measures or other disruptions, which certainly represents a limitation. While this situation is unlikely, since every effort is expected to be expended to keep these life-saving facilities open, we note not considering the closure of facilities as a limitation. And third, while we addressed the important problem of plasma collection and distribution considering time and cost objectives to treat COVID-19 patients, we did not consider how the spread of COVID-19 can be controlled or prevented. As we unfortunately have had to observe, this is a challenging undertaking, and even now more than a year since the start of the spread, we are still seeing surges in different parts of the world, especially India. This thus brings our research into focus, in which we aim to offer effective means for the collection and distribution of plasma to people in need.

We foresee multiple extensions of this model. For instance, goal programming can be performed to increase the utility of the model, in addition to considering factors from the donor’s viewpoint. Developing evolutionary algorithms for solving large instances and the non-linearity of the problem represent further promising avenues. Lastly, plasma donor’s motivators can be studied to increase the likelihood of a potential donor providing plasma.

CRediT authorship contribution statement

Vijaya Kumar Manupati: Conceptualization, Methodology, Formal analysis, Writing – original draft. Tobias Schoenherr: Writing – review & editing. Stephan M. Wagner: Writing – review & editing. Bhanushree Soni: Writing – review & editing. Suraj Panigrahi: Writing – review & editing. M. Ramkumar: Writing – review & editing, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

Abadi, Y.M., Hajeer, A.H., Luke, T., Raviprakash, K., Balkhy, H., Johani, S., Al-Dawood, A., Al-Quhtani, S., Al-Omari, A., Al-Hameed, F., Hayden, F.G., 2016. Feasibility of using convalescent plasma immunotherapy for MERS-CoV infection Saudi Arabia. Emerg. Infect. Dis. 22 (9), 1554.
Arcot, P.J., Kumar, K., Mukhopadhyay, T., Subramanian, A., 2020. Potential challenges faced by blood bank services during COVID-19 pandemic and their mitigative measures: The Indian scenario. Transfus. Apheres. Sci. 102077.
Beigel, J.H., Tebas, P., Elie-Turenne, M.C., Bajwa, E., Bell, T.E., Cairns, C.B., Shoham, S., Deville, J.G., Feucht, E., Feinberg, J., Luke, T., 2017. Immune plasma for the treatment of severe influenza: An open-label, multicentre, phase 2 randomised study. The Lancet Respiratory Medicine 5 (6), 500-511.
Yi, W., Ozdamar, L., 2007. A dynamic logistics coordination model for evacuation and support in disaster response activities. Eur. J. Oper. Res. 179 (3), 1177–1193.

Zeng, Q.L., Yu, Z.J., Gou, J.J., Li, G.M., Ma, S.H., Zhang, G.F., Xu, J.H., Lin, W.B., Cui, G.L., Zhang, M.M., Li, C., 2020. Effect of convalescent plasma therapy on viral shedding and survival in patients with coronavirus disease 2019. J. Infect. Dis. 222 (1).

Zhang, B., Liu, S., Tan, T., Huang, W., Dong, Y., Chen, L., Chen, Q., Zhang, L., Zheng, Q., Zhang, X., Zou, Y., 2020a. Treatment with convalescent plasma for critically ill patients with SARS-CoV-2 infection. Chest 158 (1), e9-e13.

Zhang, Q., Wang, Y., Qi, C., Shen, L., Li, J., 2020b. Clinical trial analysis of 2019-nCoV therapy registered in China. J. Medical Cirology 92 (6), 540-545.

Zhou, Y., Zheng, S., 2020. Machine learning-based multi-objective optimisation of an aerogel glazing system using NSGA-II—study of modelling and application in the subtropical climate Hong Kong. J. Cleaner Prod. 253, 119964.