CENTRALIZED PLASMA SUPPLY CHAIN NETWORK DESIGN UNDER UNCERTAIN DONOR AND RECIPIENT AVAILABILITY

By

Irij Anjum

Fall 2020-MS L&SCM-00000326893-NBS

Supervisor

Dr. Abdul Salam Khan

Department of Operations and Supply Chain

A thesis submitted in partial fulfillment of the requirements for the degree of

MS Operations & Supply Chain (MS L&SCM)

In

NUST Business School (NBS)

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THESIS ACCEPTANCE CERTIFICATE

It is certified that the final copy of the **MS L & SCM** thesis written by **Ms. Irij Anjum** Registration No. **00000326893** of **2020** has been vetted by the undersigned, found complete in all aspects as per NUST Statutes/Regulations/MS Policy, is free of plagiarism, errors, and mistakes and is accepted as fulfillment for the award of MS degree. It is further certified that necessary amendments as pointed out by GEC members and foreign/local evaluators of the scholar have also been incorporated in the said thesis.

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AUTHOR'S DECLARATION

I Irij Anjum hereby state that my MS thesis titled "Centralized Plasma Supply Chain Network Design Under Uncertain Donor and Recipient Availability" is my own work and has not been submitted previously by me for taking any degree from National University of Sciences and Technology, Islamabad or anywhere else in the country/ world.

At any time if my statement is found to be incorrect even after I graduate, the university has the right to withdraw my MS degree.

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Student Signature: _____

Date: _____

DEDICATION

In the name of Allah, the Most Gracious, the Most Merciful.

This thesis is dedicated to the unwavering support and encouragement of those who have been instrumental in my academic journey.

To my family, whose boundless love and understanding have been my anchor throughout this challenging endeavor. Your sacrifices and belief in my abilities have fueled my determination.

To my mentors and professors, who have generously shared their knowledge, guidance, and expertise. Your wisdom has shaped my understanding and inspired me to reach new heights.

To Allah, the Wisest, for granting me the strength, wisdom, and perseverance to navigate the challenges of academic pursuit. My gratitude is boundless for the opportunities and blessings bestowed upon me.

Lastly, to myself, for the perseverance and resilience that brought me to this moment. This thesis is a testament to the dedication and passion that fueled my pursuit of knowledge.

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ABSTRACT

The efficient management of the plasma supply chain network is a critical component of ensuring the availability of safe and healthy plasma units for transfusion. Plasma is an essential lifesaving component of blood and therefore plasma supply chain optimization plays a critical role in minimizing plasma waste and shortages at the time of need. In this research, a multi-objective linear programming (MOLP) model is developed for optimizing centralized plasma supply chain network design. The multifaceted challenges of network design are addressed by focusing on three key objectives: operational cost minimization, RFID-enabled traceability for healthy plasma units transfused, and the prioritization of blood type compatibility in plasma transfusion. Two-fold methodology has been employed for this study. Chance constraint programming has been implemented using the mean-variance approach to mitigate the inherent uncertainty of demand and supply of plasma due to the voluntary-donations based supply chain. It not only optimizes the supply chain network but also ensures robustness by incorporating probabilistic constraints. This approach allows for the effective management of uncertain factors, contributing to a more reliable and cost-efficient supply chain. Furthermore, we introduce an interactive multi-objective fuzzy programming technique to address the complexity of balancing the three objectives simultaneously. This approach facilitates decision-making by allowing for trade-offs and interactions among the objectives. To validate the proposed methodologies and their practical implications, a real-time case study is conducted within a region of a developing country. The findings of this study provide insights into the effectiveness of the

developed models and offer actionable recommendations for improving the efficiency and resilience of the plasma supply chain The key outcomes of this research include the minimization of operational costs, the maximization of traceability, and the prioritization of blood type compatibility, in plasma transfusion. By integrating these objectives, our approach contributes to the optimization of the centralized plasma supply chain network and enhances the overall quality and safety of plasma transfusion processes.

Keywords: Centralized Plasma Supply Chain, Uncertainty, Chance Constraint, Mean-Variance Approach, RFID Traceability, Compatibility, Multi-Objective Fuzzy Programming, Plasma Transfusion Optimization

CHAPTER 1: INTRODUCTION

In the past few years, designing the blood and blood product's supply chain network has gained much popularity among researchers worldwide. The key aspect that differentiates this specific supply chain from others is that the supply chain is service based, i.e., it is based on voluntary donations of blood and blood products (Baghbani, 2022). While the typical "business supply chains" are developed with product manufacturing, extraction, processing etc., and optimized distribution and storage system for profit boost through product consumption. On the contrary, the blood products supply chain is developed for humanitarian service only. As blood products cannot be manufactured or extracted as per requirements, being a human-based or human-resourced product, hence the supply of blood products remains uncertain or imprecise. In addition, the lack or deficiency of blood products in time of need can lead to death (Baghbani, 2022). It means that the whole healthcare industry is dependent on voluntary blood donations to satisfy the demand of crucial lifesaving products such as blood. Hence, maintaining a sufficient supply of healthy blood products is essential.

Blood is composed of four equally valuable components: red blood cells, white blood cells, platelets, and plasma. The importance of plasma specifically was emphasized during the peak outbreak of Covid-19 pandemic in 2020. Therein, the plasma of the recovered COVID-19 patient was extracted for the COVID-19 antibodies and was used in treatment of other patients. Therefore, plasma donations from the recovered patients were appealed worldwide. Antibodies obtained through plasma were injected into the then suffering patients in critical condition as per the authorization of United States Food and

Drug Administration (FDA) (Shirazi et al. 2021). It has been observed that the antibodies of the plasma have proven successful in curing the disease, as they act as a stimulus triggering the patient's own immune system to attack and kill the virus. Plasma is also used in treatments of accidental traumas, burns, electric shocks, severe liver diseases and other viruses like severe acute respiratory syndrome (SARS), Middle East Respiratory Syndrome (MERS), and many others. Hence, plasma plays a crucial role in saving human life in various scenarios. Though plasma has the longest shelf life along with the red blood cells; however, the processes of collecting blood from donors, transporting it to the blood centers, blood, and component testing processing, and again transporting to the hospital makes plasma an easily decomposing yet highly valuable component of blood; requiring a sustainable plasma supply chain so that its availability at the time of need can be ensured.

To maintain a sufficient reserve of plasma, in the healthcare industry where both the supply and demand of plasma is ambiguous, a centralized plasma supply chain needs to be optimized to support the critical plasma requirements. An optimized centralized plasma supply chain would require timely blood collection at various donation points and the collected blood transportation to the regional blood bank which would act as the pivotal and the most imperative part of the whole supply chain, where blood is to be tested for any transfusable disease such as, HIV, Hepatitis etc., and then separated into its various components. The plasma extracted at the blood bank would then be transported to the hospitals for plasma transfusions, as required. Factors such as the vitality of the blood plasma, the high cost of processing it, its short life and long transit time, are also a few issues plaguing the plasma supply chain along with the main issues of collecting, storing, and distributing plasma units (Shirazi et al. 2021). A sufficient plasma inventory also needs

to be maintained at the regional blood bank and the specific demand points to avoid any disruptions in plasma management, as any disruption leading to the lack of product availability at the time of need can lead to irreversible damage to human life (Baghbani, 2022). Hence, an accurate information and planning system is required to deal with the issues in the existing blood plasma supply chain.

Though plasma has a longer shelf life then the other components of blood (up to 1 year when frozen); however, the whole supply chain procedure of blood collection, transportation, sorting, testation, centrifugation, storage, and distribution is time consuming and can easily result in plasma decomposition before the stage of freezing, as plasma is a highly perishable blood product. Plasma needs to be frozen with twenty-four hours of donation to elongate its shelf life to up to 1 year. This has proven to be a challenge, as plasma extraction from freshly donated blood and then freezing is an extensive process with various steps in between, such as blood testing after collection and blood centrifugation into plasma and other products etc. (Kees at el., 2022) which often leads to the shortage and wastage of such valuable lifesaving resources.

Shortages and wastage of plasma are further accumulated due to the lack of proper integration of all the supply chain tiers in a decentralized system, which is the case in most of the developing countries, where each hospital has its own blood departments that process blood and plasma for themselves only. Literature focuses on various parts of plasma supply chain such as the collection point allocation, vehicle routes, and other various levels of the supply chain instead of the whole and centralized plasma supply chain (İnanç at el., 2017). It means that the whole plasma supply chain activities starting from the donated blood collection to the end where plasma units are transfused at the hospitals as per demand, is

infatuated by uncertainty, due to the lack of information related to products, especially the highly perishable ones such as plasma. The information such as the location of plasma units, the expiration date of units in various facilities, the best due date for transfusion, the number of damaged or outdated unit disposed at a specific location, when where and from whom the plasma was extracted, how long has it been frozen for, what time the plasma was frozen after initial collection, the inventory of various plasma types at various tiers of the supply chain etc., plays a crucial role in timely provision of healthy plasma units at the demand points in order to mitigate the risk of losing a human life. Embedding Radio Frequency Identification (RFID) technology in the plasma supply chain would certainly address these numerous challenges associated with the management of plasma supply chain. As RFID-enabled, centralized supply chain of plasma can significantly improve the supply of healthy plasma at the plasma transfusion points, resulting in efficiently satisfying the demand (Hajipour et al., 2021). This emerging technology solidifies one's trust in the health of the plasma used for transfusion, as it verifies the source of the plasma by tracing information at every stage of the supply chain. All the required information is easily extractable through the usage of radio frequency identification (RFID) technology, ensuring safe and healthy plasma transfusion along with demand satisfaction. This ultimately leads to reduced shortages and wastage of such valuable resources throughout the supply chain, as disposal of plasma units due to expiration would be reduced significantly.

Moreover, RFID-enabled traceability allows the central medical facilities such as blood banks to get updated on the lifetime of perishable items by tracking throughout the centralized plasma supply chain. This helps in enforcing end-to-end traceability for highly

valuable and highly perishable products as plasma. RFID also significantly enhances the transportation process's efficiency by merely taking advantage of tracking items via reading the tags attached to them. RFID enabled traceability implementation in the plasma supply chain results in reducing the perishability likelihood in the plasma units received by the endpoints of the chain, i.e., the hospitals and gradually helps in minimizing wastage throughout the network.

Although the demand of blood supply and its individual components is increasing, it has been observed that still only 5% of the total population donates blood, leading to frequent stockouts and shortages (Zahiri and Pishvaee, 2017). Moreover, the blood and plasma supply are also limited by the donor's blood types and its compatibility with the receptor. For instance, plasma and platelets extracted from AB+ blood type is the most desirable, and this blood type is compatible with all other blood types; however, only 1% of donations are made by the AB+ blood group (Shirazi et al. 2021).

Table 1.1 presents the different blood types and their compatibility with different donor blood types. The O- blood type are universal donors, and this blood type is mostly used during emergencies, hence, it is always in high demand. However, only 7% of donations made are by the O- blood types. Therefore, it can be assumed that another major problem that plagues the blood plasma supply chain in terms of uncertain demand and supply is the lack of availability of same blood type plasma for transfusions within the required time.

Table 1.1: Compatible blood types

Recipient Blood Type	Matching Donor Blood Type
A+	A+, A-, O+, O-
A-	A-, O-
B+	B+, B-, O+, O-
B-	B-, O-
AB+	Compatible with all blood types
AB-	AB-, A-, B-, O-
O+	O+, O-
O-	O-

For the purposes of proper resource usage, reduce wastage of excess plasma units of a certain blood type and to satisfy the demand of plasma transfusions, other approaches need to be utilized. Plasma "substituted-transfusions" is one such approach where the same blood type plasma transfusion is replaced with other blood type plasma that is compatible with patients' blood group (Baghbani, 2022). Although plasma transfusion of same donated blood as of the recipients' blood type is the ideal situation (Baghbani, 2022); however, in case of the lack of availability of the demanded plasma of a certain blood type in an emergency situation or otherwise, substituted-transfusions can be opted in order to save a human life. The concern for compatibility of various blood types for the demand blood type, for substituted-transfusion of plasma is at times undermined by the availability of plasma of a specific blood type in question. It means that even though a specific blood type is more compatible with the demanded plasma blood type, yet substituted-transfusion would be based on which blood type plasma is more in storage rather than which is more

compatible, causing various complication in plasma substituted-transfusion leading to compromised patient's or plasma receptor's health (Salimian and Mousavi, 2022). This can be overcome by opting priority-based substituted-transfusions. where highest, mediocre, and lowest priority is given to various compatible blood types based on industry experts' opinions (Kees at el., 2022).

In this research, a centralized plasma supply chain is designed, where the demand and the supply of the plasma is uncertain due to the voluntary donation-based nature of the product, and the regional blood bank acts as the pivotal point of centralization. Figure 1.1 illustrates the process flow of a centralized plasma supply chain network designed for this research. For economic purposes, the overall cost of the operational supply chain is considered, which includes the cost of blood collection, cost of transporting the blood units to the blood bank, cost of screening, cost of centrifugation, RFID implementation cost, disposal cost, inventory management cost and the cost of plasma transfusion etc. Moreover, the designed plasma supply chain aims to reduce the plasma shortages and wastages through implementation of RFID-enabled traceability, which allows the information flow throughout the centralized supply chain and ensures safe and healthy plasma transfusion. Furthermore, demand satisfaction with lower risk is ensured in the designed supply chain through compatibility-prioritized plasma transfusion. The ideal same blood type plasma transfusion, substituted-transfusion of compatible and prioritized plasma, and plasma outsourcing is opted, in order to satisfy the demand of recipients and save human life in time of need.

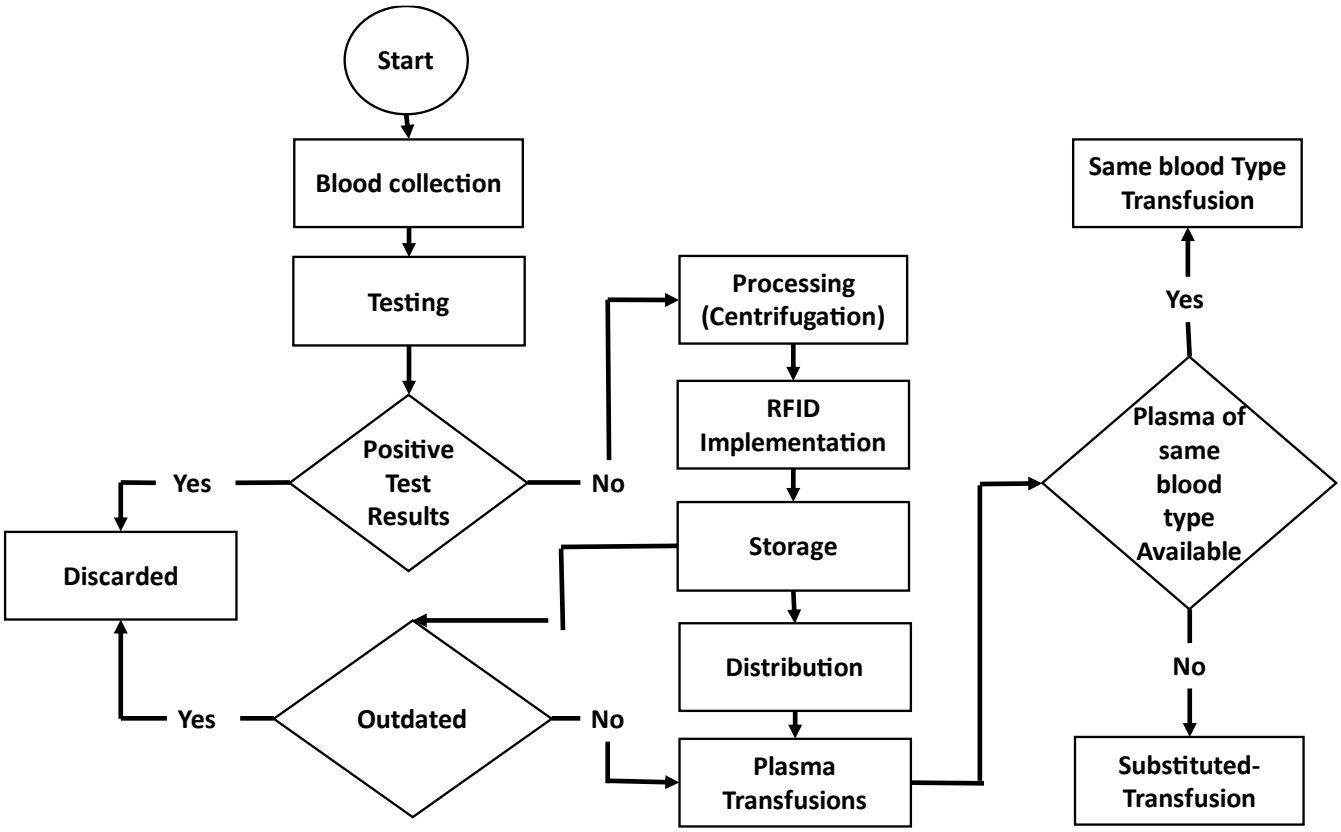

Figure 1.1: Plasma supply chain process flow chart

The supply chain network developed is multi-objective and multi-period. The first objective aims to minimize the operational cost, while the second objective aims to maximize traceability via RFID implementation in terms of the amount of health plasma units transferred and transfused at the hospitals. The third objective of this research is to maximize the compatibility-prioritized plasma transfusion to satisfy the plasma demand. To solve the proposed multi-objective model, an Interactive Multi-objective Fuzzy Programming approach is used, along with the Chance Constraint methodology to mitigate the uncertainty form the designed to a certain extent. In the first method, an objective

function is solved at a time and its value is recorded, and then this objective acts as a constraint and other objectives are optimized separately. The same process is repeated for the other objectives and finally, a pay-off table is achieved that has the extreme function values of each objective. In the chance constraint methodology, the stochastic parameters of plasma demand and supply are converted into deterministic parameters through the mean-variance approach, where mean and variance of the demand supply parameters are incorporated in the respective constraints. Finally, a real-world case study of blood plasma supply chain of the twin cities of Rawalpindi and Islamabad is studied to validate the model and the solution approaches used in this study.

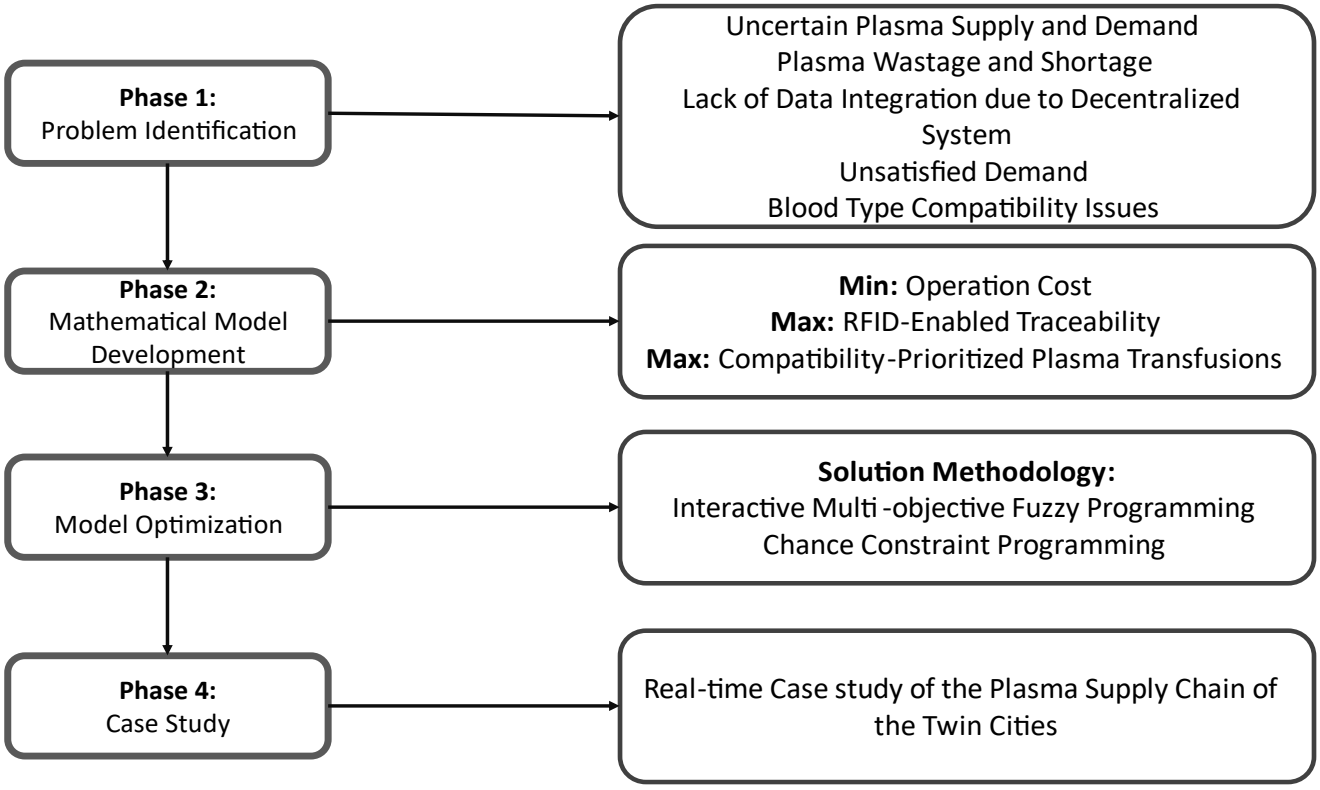

Figure 1.2: Plasma supply chain research phases

This study comprises of four research phases, as illustrated by Figure 1.2. In the first phase, we define the problem that needs to be solved through detailed review of the literature and identifying gap analysis. In the second phase, a multi-objective and multi-period linear programming model is developed for the centralized plasma supply chain network design. The third phase of the research includes the optimization and solving of the mathematical model developed using the interactive multi objective fuzzy programming and chance constraint approaches. In the last phase, a real scenario-based case study is solved to validate the results.

1.1 Problem Statement

There is a lack of research on developing an economical centralized and traceability plasma supply chain network design under uncertain donor (supply) and receptor (demand) availability with compatible-prioritized plasma transfusions. The existing supply chains are decentralized in the case of developing countries leading to wastage and shortages of plasma units at the various demand points. Implementation of new technology i.e., RFID to enhance product traceability is not considered for provision of safe and healthy plasma units for transfusion. An RFID-enabled traceability can reduce plasma wastages and shortages due to inventory expiry, along with bridging the supply chain wide-information gap.

The substituted transfusion i.e., the replacement of required blood type plasma with another compatible blood type plasma has not been discussed in the plasma demand

satisfaction, in case of the lack of the same blood type plasma availability. Due to the risks associated with substituted-transfusions such as allergic reactions etc., which can be sorted through prioritizing the compatible blood types into highest, mediocre, and lowest compatibility with a certain blood type. The compatibility-prioritized plasma transfusion can reduce the risks associated with substituted-transfusion in case same blood type plasma transfusion is not possible. Both RFID implementations and substituted-transfusion can effectively combat the issues of uncertain supply and demand of plasma, by ensuring the timely provision of healthy plasma or its substitute at the time of need, throughout the centralized supply chain.

Hence, this research focuses on minimizing the operational cost of plasma supply chain, maximizing RFID-enabled traceability, and maximizing the compatibility of prioritized plasma transfusions.

1.2 Aims And Objectives

To address the above-mentioned problems, the following aims and objectives are focused on in this research:

- To develop a multi-objective mathematical model for centralized plasma supply chain under uncertain demand and supply.
- To minimize the operational cost of the plasma supply chain designed.
- To maximize Traceability through RFID Implementation, in terms of healthy plasma units' provision.

- To maximize the Compatibility-Prioritized Plasma Transfusion at the demand points.
- To optimize the supply chain network design through Interactive Multi-Objective Fuzzy Programming and Chance Constraint Programming.
- To validate the proposed model and solution methodologies through the case study of the twin cities in Pakistan.

1.3 Research Questions

Research Question 1: How to develop an economical, low cost and efficient centralized plasma supply chain?

Research Question 2: How to reduce plasma wastage and shortages, and ensure maximum utilization of the valuable plasma resource?

Research Question 3: How to ensure safe and healthy plasma provision for transfusions.

Research Question 4: How to ensure availability of complete data and record of every single plasma unit in inventory, throughout the plasma supply chain.

Research Question 5: How to optimize the plasma supply chain with uncertain demand and supply?

Research Question 6: How to satisfy the demand of plasma with an uncertain supply?

Research Question 7: How to mitigate the risk associated with substituted-transfusion?

1.4 Chapter Summary

This chapter defines the importance of a centralized plasma supply chain network design in saving humanitarian life. It differentiates between a business supply chain and the blood and its product supply chain, along with reasoning the significance of developing a centralized plasma supply chain to ensure healthy plasma availability at the time of need. A detailed description of the supply chain network design is provided. It also defines the problems such as shortages, wastage, uncertain demand and supply, the lack of data availability and demand unsatisfaction etc., that plague the plasma supply chain. This chapter comprises of three subsections. The first section defines the problem that this study aims to optimize, while the second section provides the aims and objectives of our research. The third and the last section lists the research questions this study aims to answer.

CHAPTER 2: LITERATURE REVIEW

Over the years, it has become more and more evident that globalization has transformed the modern world and businesses to a great extent. In this transformed modern world, the supply chain has proven to be the backbone of the systems in place for any process that is in dire need of improvements and optimizations constantly, to remain efficient. For this purpose, the medical and humanitarian industry have made several attempts to design highly efficient supply chain networks; however, the gap for improvement continues to persist.

2.1 Blood Supply Chain Network

A recent study was conducted in Khalilpourazari (2019), on designing a six-echelon blood supply chain in the case of crisis, especially earthquakes. The supply chain considered the donors, blood collection centers, regional and local blood banks, and regional and local hospitals. It aimed to minimize the cost, time spent and unfulfilled demand through simulation and optimization processes, along with using neural-learning process to learn and gain knowledge from the past to avoid the worst possible scenario in case of disaster (Khalilpourazari et al. 2019). The data from the past and the experiences of human being involved during the disastrous event can be helpful in identifying the flaws in the current system and strategies of the blood supply chain (Mizutani and Dreyfus 2017; Karasözen et al. 2017; Şaylı and Yılmaz 2017). However, Khalilpourazari (2019) dismissed the factor of blood type compatibility in transfusions, which is crucial in the case

of a crisis where same blood type units might not be available due to resource constraint, and substitution would need to be opted. The study also failed to acknowledge the importance of individual components of whole blood, as whole blood transfusions are rear occurrence (Baghbani, 2022). In fact, plasma becomes the main requirement in crisis situations due to its clotting and wound healing characteristics. Moreover, the study suggested the use of helicopters for transportation of blood and critical patient, which is not really a feasible option as not only the usage of helicopters is expansive, but it also has lower capacity as compared to other typical transportation vehicles, which will eventually require more trips to be made between hospitals and blood banks, increasing the overall cost. As discussed before, the study failed to address the concept of blood compatibility between donated blood and the person receiving it, which is the main constraint when dealing with blood and blood product transfusions. In case of a disaster that leads to an expected influx of patients, the demand of blood and its individual components such as blood plasma requires emergency surgical needs and transfusion (Fahimnia et al. 2017). Hence, an urgent need of compatible blood and blood products is required, which has been proven to be a difficult task due to lack of inventory management and uncertain supply of donors of compatible blood type, that is required at the given time. Therefore, this research is focused on developing a mathematical model for an inventory managed supply chain for blood plasma.

Fahimnia et al. (2017) developed a stochastic blood supply chain network design with the objectives of transportation cost and time minimization. They studied the supply chain network design with different blood types and their compatibility in the form of a robust stochastic model. The concept of blood compatibility has also been studied by Zahiri

and Pishvaee (2017) in the form of a mathematical model. However, none of these studies considered the individual components of blood and their supply chain development. Plasma transfusion is a common practice in cases of accidents, emergencies and in routine medical procedures due its high antibodies content (Shirazi et al. 2021). Also, the models developed lacked in addressing the perishable and sensitive nature of blood and its individual components, which is the main complexity of blood and plasma supply chain.

2.2 Demand And Supply Uncertainty

The inventory management of blood supply chain and its component's supply chain has proven to be difficult task over the years, as proven by several studies. The main reasons for this are the perishable nature of blood, uncertain demand, uncertain supply, and the lack of compatible blood types in stock at time of need (Dillon et al. 2017). This concept was addressed in research conducted in 2017 where a two-stage stochastic programming model was designed for red blood cells inventory management, with the objectives of minimizing cost, blood shortage and wastage due to outdating, in terms of the perishable nature of red blood cell and their uncertain demand (Dillon et al. 2017). Optimization software was used to solve the proposed mathematical model. The research did not study the hospital and the blood banks as an integrated or centralized entity in terms of inventory management to mitigate chances of shortage in case of disasters and emergencies. Moreover, the study did not consider the uncertain supply aspect of the blood supply chain, as only 5% of the total population donates blood with no compatibility concerns for the demand of receptors.

Gunpinar and Centeno (2015) studied the concept of integrated inventory management between the hospitals and the blood banks, where an integer programming model was developed and optimized with the objective of minimizing cost and shortages. However, it was in the context of red blood cells and not blood plasma. Hence, this research will be used to propose strategies for centralization and inventory management of blood plasma, to reduce plasma wastages and shortages. The concept of blood and its component shortages has also been studied in former research, where stochastic integer programming model under demand uncertainty along the blood supply chain was studied with the objective of minimize wastage and shortage of platelets, in the context of inventory management (Rajendran, 2019).

2.3 Centralized Supply Chain

The methods of Queueing theory and Markov chain have been used to manage blood supply chains in established literature. Also, first in and first out techniques have been used by the blood banks to avoid outdating of the blood products. The approaches proved to be unsuccessful in providing the required blood type plasma or other blood component at the time of need. Moreover, as pointed out by Osorio et al. (2015), mathematical modelling and its optimization has rarely been studied, and the research that have made use of modelling and optimization focused only on problems related to location allocation, time management and vehicle routing etc. Therefore, this research focuses on developing a centralized plasma supply chain network design, with an emphasis on blood

type compatibility prioritization, in order to ensure safe and healthy plasma availability for demand satisfaction.

Moreover, research has been carried out to examine the "decision-making problem" in the context of inventory control of blood supply and its shortages within the blood supply chain (Zhou et al. 2021), where the FIFO and LIFO inventory strategies for blood demand and supply were studied. Mathematical modelling was also developed to deal with objectives of the research, i.e., blood shortages, blood outdating and shortest transportation time (Zhou et al. 2021). EWA (Estimated Withdrawal & Aging) strategy was employed for decision making which was further substantiated by a practical and numerical simulation. Both the studies contributed to the healthcare sector; however, there was an absence of acknowledgement of the separate demand and need of individual blood components and how their characteristics affect the supply chain. Also, the objectives of blood shortages, blood outdating and shorter transportation time can be easily addressed through a centralized plasma supply chain. As inventory in each supply chain entity is accessible to the others, hence, outsourcing of required product would be possible in case of a shortage. Wastage can also be reduced through optimal usage of product inventory within the centralized supply chain for combined demand satisfaction.

The concept of centralization for blood supply chain was recently studied in context of developing a multi-period mixed-integer linear programming (MILP) model for blood supply chain of a developing country with a focus on determining the appropriate dimensions and overseeing the operations of a centralized blood supply center (Kees at el., 2022). The objectives of this problem were to minimize the shortage, the total costs, and the number of substitutions. To effectively handle these multiple objectives, their uncertain

target values, and the imprecision in certain parameters, the model was restructured as a fuzzy mixed-integer goal programming model. Fuzzy goal programming methodology was used to optimize the mathematical model. Results showed that centralization in blood supply chain yields various improvements and benefits such as improved efficiency, cost savings, better quality control, and the ability to respond effectively in emergencies, ultimately enhancing the availability and safety of blood products.

2.4 Plasma Supply Chain Network

Blood and its supply have always played a vital role in the healthcare system, hence, the timely supply of blood that is not outdated, at the required time and of compatible nature has always been an important topic for researchers. Hence, numerous articles and studies are available on this topic. However, blood components such as plasma, platelets etc. are of equal importance and could be used for induvial transfusion as well, instead of whole blood as per the patient's requirements. Yet, research on individual components of blood, especially plasma, has been scarce in terms of a sufficient plasma supply chain network design. An example of such study includes a study of 2017 where research was carried out on how to enhance "blood utility" to minimize shortages and other damages (Ramezanian and Behboodi, 2017). The factors of donor's distance to blood collection center, their previous experience and advertising account etc., were considered as the social aspect affecting the blood utility. Mixed integer linear programming (MILP) optimization and robust optimization approach were used to solve the mathematical problem developed and was applied on a practical example of Tehran.

Even when the Covid-19 spread was at its peak along with the demand of plasma for the treatment of Covid-19 patients, the blood supply was still of critical importance. As evident from the study carried out by Ngo et al. (2020) addressing the ways that outbreak of Covid-19 has negatively affected the blood supply, management and distribution between the blood banks and hospital keeping the safety of the donors and receptors intact. The study defines new policies and strategies to adapt and improve the blood supply along with suggesting opting for other non-orthodox treatments, such as whole blood substitution with other products such saline and "convalescent plasma" etc., to avoid extreme blood loss and the patient going into Hypovolemic shock. This shock occurs when the body begins to shut down due to the loss of large amounts of blood or fluid. Hence, the study suggests blood substitutes such as saline to make up for the lost blood for the time being. However, Substituted-transfusion of compatible blood type plasma is not discussed as the next best alternative for extreme blood loss situations. Pasma is known for its high antibodies and blood clotting characteristics, which can effectively reduce bleeding and overall blood loss.

The few studies that include the research on plasma are mostly in medical terms and deal with medicinal benefits of plasma and its role in treatments of several diseases, accidents, traumas and burns, etc. Such as the research conducted by Catteeuw and DiNubile (2021) where, the "rhu-pGSN" protein found in blood plasma is studied, as this protein is what allows the "Convalescent plasma (CP) therapy" by reducing inflammation caused by the virus.

However, since the outbreak of Covid-19 pandemic, plasma has been studied and researched upon more than before, due its involvement in treatment of patients that are

severely affected by the virus. One such research has been carried out in India, where after the second and the most devastating wave of Covid-19 the “Convalescent plasma (CP) therapy” was approved to aid the huge amount of affected people (Datta and Chakrabarty, 2021). However, CP therapy was then evoked, and this research was conducted to study the reasons and challenges associated with CP therapy for it to be discontinued.

Another research was carried out based on contradictory results of CP therapy as there were indications that CP therapy can prove more efficient when plasma transfusions are made in a certain time-period (Ateş et al. 2021). Hence, the results of patients undergoing the CP therapy with plasma transfusion to made in firsts three and seven days of showing symptoms of virus contraction will be compared with patients who received CP therapy after seven days and more of showing the virus symptoms. Results showed that patients who received plasma transfusion with 7 days of showing symptoms had significantly less inflammation, risk, hospital stay and faster recovery rate. Hence, the value of a developing effective plasma supply chain network design was further highlighted in this research.

2.5 Compatible Plasma Substitution

The importance of blood plasma is evident through the recent study carried out in 2021 were a four-echelon supply chain was designed to “locate the blood collection centers, allocations of temporary or permanent plasma-processing facilities and determining the allocation of the temporary and permanent facilities to hospitals”, in terms of blood plasma in the case of Covid19 outbreak (Shirazi et al. 2021). Simulation approach

and optimization techniques were used to simulate the increase in demand of plasma after the pandemic outbreak. The objective of the research was to reduce the supply chain costs and the "plasma flow time" i.e., the time it took for the plasma units to reach the demand points after initial collection of blood. A bi-objective model was proposed and solved through the ε-constraint method. The factor of blood substitutability was also studied to improve the timely availability of plasma. The study's prime focus was on allotting and allocating the different entities of the supply chain within the defined area; in order to reduce the overall cost incurred along with reducing the plasma transportation time. However, the process of allotting and allocating, that is the actual construction of the supply chain entities according to the devised supply chain network, would definitely be more cost incurring and a wastage of the already limited resources of the healthcare sector. Instead, centralizing the existing plasma and blood supply chain entities and their resources can prove to be more financially beneficial. Centralization can ensure resource sharing and demand satisfaction through readily available plasma units within the supply chain (Baghbani, 2022). Moreover, no aspect of inventory management and strategies for mitigation of the possible failure of the plasma cold stores, stockouts and expiry of same or compatible blood types of etc. has been studied. Neither, the main constraint of blood transfusion, that is lack of compatible blood plasma was addressed.

Furthermore, in (Baghbani, 2022), a multi-leveled plasma supply chain mathematical model was developed in the context of COVID-19 with the objectives of minimizing cost and optimizing the plasma transportation or provision rate. Fuzzy programming solution methodology was opted to deal with the uncertainty element of the model. The primary activities within the blood supply chain commence with the donors

and conclude with the recipients. This process entails dealing with uncertainties, notably concerning supply and demand, which significantly impact economic performance within the supply chain. Considering these uncertainties, it becomes imperative to establish an effective network for the provision of sufficient blood and blood products to ensure equitable regulation of supply and demand. This can be achieved through adopting substituted-transfusion of compatible blood type plasma, even though the ideal situation for a blood transfusion is for the donor's blood type to be the same as the recipient's.

2.6 RFID-Enabled Traceability

In the sector of healthcare, product demand satisfaction is directly or indirectly proportional to the optimization of its supply chain (Sadri et al., 2021). Therefore, efficient, and traceable plasma supply chain is the key element of healthy and safe plasma demand satisfaction. Even though the traceability concept is rarely implemented in the healthcare sector, recent research (Sadri et al., 2021) studied the traceability in donation-based blood supply chain. It studied the implementation of traceability in the plasma supply chain through Blockchain adoption. Results proved that blockchain based traceability was efficient for a decentralized system and 'peer-to-peer' distribution technology allows safe end-to-end traceability and overall security throughout the supply chain. However, the concept of traceability through RFID was not considered, even though RFID implementation is excellent for real-time tracking as it provides location and identification data as items move through a network of readers (Thakur, 2020). Moreover, RFID can be more cost-effective for tracking items at scale, and it is more commonly used in retail and

logistics due to its scalability (Thakur, 2020). In a traceable plasma supply chain, information must be traceable at every stage of the supply chain, for every unit of plasma, starting from the time it was collected till the time of transfusion or consumption. For this purpose, RFID is ideal as it provides real-time tracking and identification (Thakur, 2020). Traceability in a centralized plasma supply chain can be achieved through RFID Implementation. RFID-enabled traceability in plasma can ensure safety in process and storage of the product, i.e., the testing, storage, and distribution phases while keeping intact the privacy of the donors.

The concept of traceability in the context of blood supply chain can be further explored through research conducted on “Indonesian Red Cross Society”. It focused on designing a “blood traceability system” to maximize the accessibility of optimal quality blood bags at the time of need, for demand satisfaction (Vanany et al., 2015). Major blood collecting and storage entities of the supply chain collaborated in the traceability system, continuing the existing blood supply chain process. Traceability for this study was implemented through barcode technology, for data integration in the traceability system designed. To capture information, a barcode scanner or reader must be physically pointed at the barcode, and it requires a direct line of sight to scan accurately, meaning that the process of scanning barcodes is typically manual and one item at a time. Therefore, RFID implementation is more suitable for blood supply chain as RFID tags contain electronic information and can be read wirelessly using RFID readers or antennas (Thakur, 2020). It also allows for batch scanning or simultaneous reading of multiple tags within the reader's range, making it a faster and more efficient method for tracking multiple items at once,

along with allowing data management without the need for constant connectivity to a central database (Thakur, 2020).

The concept of RFID enabled traceability was recently studied for a disaster relief supply chain network where a bi-objective nonlinear mathematical model was developed (Hajipour, 2021). In this research, RFID technology was utilized for the objective of maximizing the quantity of undamaged items received by demand points. The study found that RFID implementation provides instant access to comprehensive and crucial product information such as the real-time location of items, product expiration dates, optimal replenishment dates, and the quantity of damaged items at specific locations. Results of the study suggested the usage of RFID tracking system to stay informed about the shelf life of perishable items and ensure provision of unspoiled medications.

Based on the literature reviewed, it can be perceived that no study so far has been conducted on centralized plasma supply chain network design under demand and supply uncertainty that is inventory managed. Neither the objectives of compatibility prioritized blood plasma transfusion have been studied so far. Substituted transfusion of plasma or even whole blood have never been considered as an approach for demand satisfaction, to mitigate the element of same blood type plasma unavailability. Plasma health has also never been a point of concern, as timely provision of the desired product remains an issue. In addition, an economical, cost friendly yet integrated and centralized blood plasma supply chain has been studied. Therefore, after observing the importance of blood plasma in the healthcare system and its currently increasing demand after the outspread of Covid-19, this research examines a centralized plasma supply chain with inherent uncertainty in its demand and supply, with the objective of minimizing the operational cost, ensuring

provision of safe and healthy plasma through implantation of RFID-enabled Traceability throughout the supply chain and maximizing the demand satisfaction through blood type compatibility-prioritized plasma transfusion and substituted transfusions.

2.7 Contribution Table

Table 2.1 shows the literature contribution table for the existing literature on blood and plasma supply chain network design for the objective of minimizing the operational cost, maximizing RFID-enabled Traceability, and maximizing blood type compatibility-prioritized plasma transfusion and substituted transfusions within the centralized system and under uncertain demand and supply.

Apparent from the literature review and the literature contribution Table 2.1, the blood component of plasma, which is an essential lifesaving, human, voluntary-donations based product; lacks research in the context of plasma supply chain optimization. Moreover, blood type compatibility has always acted as a constraint in blood supply chain research, and no study so far has worked upon optimizing this significant problem of the blood and plasma supply chain. While, in our research, blood type compatibility prioritization plays a major role in plasma supply chain optimization. As, along with same blood type plasma units, the compatibility-prioritized blood types are used for substituted-transfusion of the plasma units, in order to satisfy the demand of the plasma at the demand points; and to optimize our third research objective of "Compatibility-Prioritized Plasma transfusions." This concept has not been explored till date for compatibility prioritized transfusions and demand fulfillment, as shown in Table 2.1.

The concept of traceability in the healthcare sector has recently evolved; and as illustrated through Table 2.1, no research has been done on inclusion of RFID-enabled traceability within the plasma supply chain. Therefore, the second objective of the research focuses on optimizing the plasma supply chain through maximizing the usage of RFID-enabled traceability. As, RFID tracking system ensures provision of reliable information regarding the shelf life and the health of plasma units throughout the supply chain and at every stage, eventually guaranteeing availability of healthy plasma units at the demand point, within the given time frame.

Resource Scarcity in the healthcare sector is a worldwide problem, however the situation in developing countries is even more unpleasant. Therefore, a centralized plasma supply chain is designed to ensure resource sharing of essential resources of blood plasma. Centralization ensures improved efficiency, cost savings, better quality control, and the ability to respond effectively in emergencies, ultimately enhancing the availability and safety of blood products. So far only Baghbani (2022) has studied centralized plasma supply chain as shown in Table 2.1, however the research was in a very different context than ours.

Furthermore, the two-fold methodology selected for this research is unique. As implementation of the Chance Constraint Programming effectively diminishes the element of inherent uncertainty from the plasma supply chain. No prior research has aimed it mitigating the uncertainty from the demand and supply constraints of the plasma supply chain before, as presented through the Table 2.1. While the Interactive multi-objective fuzzy programming yields the optimal function values along with the satisfaction level of each objective function, within their respective upper and lower bound of solution values.

As evident from the contribution table below, this combination of methodologies has not been implemented before for plasma supply chain optimization.

Table 2.1: Literature contribution table

Author	Plasma Supply Chain	Centralization	Demand and Supply Uncertainty	Blood Type Compatibility	Cost	RFID-Enabled Traceability	Compatibility-Prioritized Transfusions	Demand Satisfaction	Traceability in Healthcare	Methodology
(Khalilpourazari, et al., 2019)					✓			✓		Lexicographic weighted Tchebycheff
(Dillon, 2017)			✓	✓	✓					Modified Stochastic Genetic Algorithm
(Baghbani, 2022)	✓	✓	✓	✓	✓			✓		Fuzzy Chance-Constrained Programming
(Ramezanian and Behboodi, 2017)	✓		✓		✓					Robust OptimizationApproach
(Shirazi et al., 2021)	✓		✓	✓	✓					ε-constraint method, SPEA-II), (NSGA-II), (MOGWO), and (MOIWO) approaches
(Kees et al., 2022)		✓			✓		✓			Fuzzy mixed-Integer Goal Programming
(Vanany et al., 2015).			✓					✓	✓	UML approach
(Hajipour, 2021)					✓	✓			✓	Vibration Damping Optimization
Proposed Research	✓	✓	✓	✓	✓	✓	✓	✓	✓	Chance Constraint Programming and Modified Interactive Fuzzy Optimization

2.8 Chapter Summary

In this chapter, an in-depth analysis of the existing literature review is presented. In summary, the literature review highlights the existing gaps in research regarding centralized plasma supply chain network design under demand and supply uncertainty. The proposed research will aim to address these gaps by developing a centralized plasma supply chain network that incorporates RFID-enabled traceability, prioritizes blood type compatibility, and considers substituted transfusions to ensure safe and healthy plasma availability for demand satisfaction, along with cost minimization. The contribution table is developed based on the literature review, and the defined objectives will be optimized using two-fold methodology of Chance Constraint Programming and Interactive Multi-objective Fuzzy Programming technique.

CHAPTER 3: DEVELOPMENT OF MATHEMATICAL MODEL

This section provides a detailed view of the problems within the existing plasma supply chain, the proposed mathematical model designed to address these problems, and the notations, decision variables, parameters, objective functions, and constraints.

3.1 Problem Description

This research aims to develop and optimize a centralized plasma supply chain network. The “centralized” plasma supply chain network developed is motivated by real case scenario of a developing country. The supply of blood and blood products to the demand points is through a decentralized supply chain system; each hospital or demand point in the supply chain system is responsible for fulfilling its own demand for blood and blood related products such as plasma (Kees at el., 2022). A decentralized supply chain has proven to give rise to unsatisfied demand, product shortage and wastage of extremely invaluable resources of blood products, considering the lack of product traceability and complete information within a decentralized plasma supply chain (Hajipour, et al., 2021). A generic framework of the blood or blood product’s supply chain designed is present through Figure 3.1.

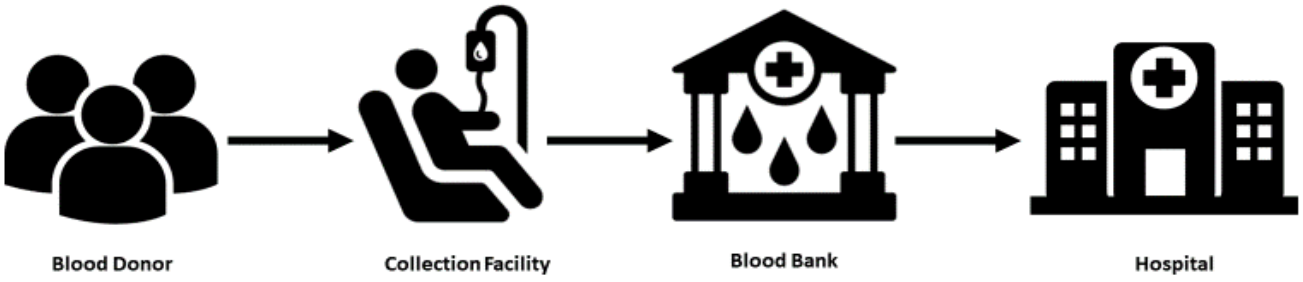

Figure 3.1: Generic plasma supply chain representation

Moreover, irrespective of the consolidation or disassociation of each tier of a supply chain, the plasma supply chain remains plagued with uncertainty in supply (uncertain number of donations in each time) and demand of plasma due to the voluntary-based nature of blood and plasma supply chain (Shokouhifar & Ranjbarimesan, 2022). Hence, demand satisfaction remains a key challenge for the plasma supply chain.

Apart from the issues of lack of centralization and uncertainty in demand and supply, another key obstacle faced by of the plasma supply chain is the perishable nature of blood products. Even though plasma has a longer shelf life when frozen, i.e., up to a year as compared to other blood products, yet it remains a highly perishable blood product. Plasma needs to be frozen with twenty-four hours of donation to elongate its shelf life to up to 1 year. This has proven to be a challenge, as plasma extraction from freshly donated blood and then freezing is an extensive process with various steps in between, such as blood testing after collection and blood centrifugation into plasma and other products etc. (Kees at el., 2022).

Plasma transfusion is limited to same blood group transfusion mostly due to the blood group type compatibility concerns, leading to unsatisfied demand, as substituted-transfusions are not considered to be an optimal option. The concern for compatibility of various blood types for the demand blood type, for substituted-transfusion of plasma is at times undermined by the availability of plasma of a specific blood type. Even though a specific blood type is more compatible with the demanded plasma blood type, yet substituted-transfusion would be based on which blood type plasma is more in storage rather than which is more compatible, causing various complication in plasma substituted-transfusion leading to compromised patient's or plasma receptor's health (Salimian and Mousavi, 2022).

The supply chain network developed for this research is based on a four-echelon centralized plasma supply chain consisting of donor blood groups, blood collection facilities, blood centers and hospitals. The proposed model of the plasma centralized supply chain for this research is presented in Figure 3.2. The multi-tiers supply chain model includes various blood types donated by voluntary donors, which are collected at the temporary and permanent collection facility, i.e., at the mobile collection facilities and collection facilities. Blood collection of different blood types is also carried out at the blood bank, through direct blood donations in a centralized system.

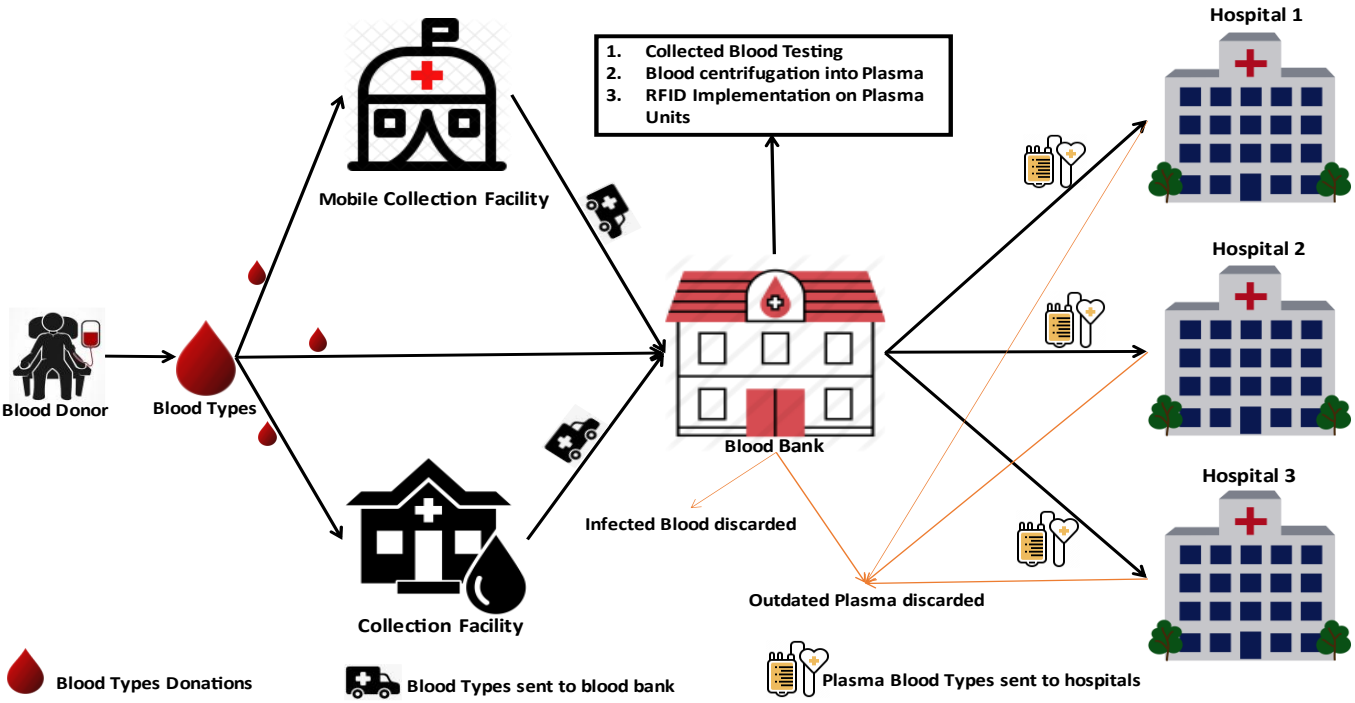

Figure 3.2: Proposed centralized plasma supply chain network framework.

The collected blood units of various blood types are then transported from the mobile collection and collection facilities to the central or the regional blood bank. Compared to other collection facilities, the blood bank plays a crucial role in centralizing and optimizing the whole supply chain. Once the blood units are transported to the blood bank, they are screened for diseases and infections that are transmissible through blood transfusion and the infected units are then disposed of. The screened blood units are then separated into various blood products such as red blood cells, platelets, and plasma etc., through the process of centrifugation.

The centrifuged plasma units of various blood types are then implemented with RFID tags. RFID enabled traceability allows for the long-term plasma lifetime traceability

and can also help in reducing the various risks of contamination at different stages of the product's life (Hajipour et al., 2021). Moreover, RFID Implementation bridges the information gap between the various supply chain tiers. Hence, allowing supply chain wide access to the crucial data of the plasma inventory at the designated storage points (i.e., blood bank and hospitals). The information shared via RFID includes quantity, quality, remaining lifetime, and the blood type of plasma available at the blood bank and the hospitals, available to other entities of the centralized supply chain upon shortage or in emergency situations. Therefore, a RFID enabled, centralized supply chain of plasma can significantly improve the supply of healthy plasma at the plasma transfusion points, resulting in efficiently satisfying the demand. This emerging technology solidifies one's trust in health of the plasma used for transfusion, as it verifies the very source of the plasma by tracing information at every stage of the supply chain (Hajipour et al., 2021).

The blood centers are responsible for Inventory management and distribution of the plasma units. Plasma of various blood types is transported from the blood bank to the demand point or hospitals as per their projected demand, and the lack of blood type units of plasma required at the hospital. To satisfy the demand of patients at the hospital plasma substituted-transfusion along with standard plasma transfusion are opted. Outsourcing of plasma units of various blood types is also made by hospitals in case of emergencies, from the other hospitals and the blood bank of the centralized system. A certain amount of inventory is also maintained by the hospitals. The Plasma units in storage that exceed their healthy lifetime are discarded by both the blood bank and the hospitals, based on the data gathered through RFID Tags.

The multi-objective mathematical model is developed such that the first objective function minimizes the total operational cost of the plasma supply chain network designed. The second objective function of the model focuses on maximizing the plasma supply chain traceability through RFID implementation. Here traceability employed is in terms of undamaged product received by the demand point, or to be more specific, the healthy plasma units received and transfused only at the hospitals. The third objective function maximizes the Compatibility-Prioritized Plasma Transfusions using the Compatibility Prioritization Substitution Index. Where Priority is defined in three levels i.e., "s=1" has the highest substitution priority, "s=2" has intermediate substitution priority and "s=3" has the lowest substitution priority.

The objectives of maximizing RFID-enabled Traceability and Compatibility-Prioritized Plasma Transfusions with the plasma supply chain correlates with 3rd and 12th Sustainable Development Goals (SDG) of the United Nations (UN) General Assembly 2030 Agenda. In September 2015, the United Nations General Assembly adopted the 2030 Agenda, envisioning a significant shift towards achieving a more sustainable future by the year 2030 (UN, 2015). This agenda comprises 17 comprehensive sustainable development goals (SDGs), accompanied by 169 associated targets and over 230 indicators for monitoring progress (Bennich 2t al., 2020). The 2030 Agenda is applicable to all nations and stakeholders globally, irrespective of their current economic status or sustainability challenges (Bennich et al., 2020).

Both our objectives relate to the 3rd SDG i.e. Good Health and Well-Being (Bennich et al., 2020). As, Ensuring the traceability of undamaged plasma units received and transfused at hospitals is crucial for maintaining the quality and safety of blood

transfusions. This directly supports SDG 3, which aims to achieve universal health coverage, including access to safe and affordable blood products. While, prioritizing plasma transfusions based on compatibility contributes to improving healthcare outcomes and reducing potential complications. It also aligns with SDG 3 by ensuring access to safe and effective medical treatments, including blood transfusions. To summaries, our research objectives significantly contribute to SDG 3 by enhancing the efficiency, safety, and quality of the plasma supply chain and transfusion process, ultimately supporting the broader goal of achieving good health and well-being for all.

The research objectives of RFID-enabled Traceability and Compatibility-Prioritized Plasma Transfusions also relate to the 12th SDG i.e. Responsible Consumption and Production (Bennich et al., 2020). As, maximizing plasma supply chain traceability through RFID implementation can help in reducing wastages by ensuring that the undamaged plasma units are efficiently tracked and utilized. This aligns with the SDG 12 target, which aims to halve per capita global food waste and reduce food losses along production and supply chains. Also, both the objectives of the model, which include maximizing plasma supply chain traceability and prioritizing plasma transfusions, contribute to minimizing shortages. By optimizing the compatibility-prioritized plasma transfusions, the system is better equipped to meet the demand for plasma units, reducing the likelihood of shortages. This aligns with the SDG 12 target as well, which aims to achieve the sustainable management and efficient use of natural resources. In summary, the research aligns with SDG 12 by promoting responsible consumption and production through the reduction of wastages and shortages in the plasma supply chain.

3.2 Model Assumptions

- ABO-RH compatibility of each plasma and blood unit is taken into consideration.
- All Eight types of Blood are considered.
- Types and capacity of vehicles used in the network for transportation are not considered.
- The capacity of the blood collection facilities, blood centers and the hospitals are limited.
- Impact of time spent during transfer of blood units from mobile collection facility and collection facility to blood banks and plasma units from blood bank to hospitals is considered for remaining healthy lifetime of plasma.
- Returns of plasma units to the blood bank are not allowed.
- Exceptional cases such as natural disasters or infectious diseases that massively impact and increase historical demand rates and decrease blood donations are excluded from this research.
- All costs are deterministic and fixed.
- Only the Operational Cost of the model is considered.
- Any donor can donate to the collection facilities.
- Each blood donor has a maximum blood supply capacity of 1 unit.
- Storage is not possible in mobile collection and collection facilities and only blood banks and hospitals can hold inventory.

- The value of plasma units frozen and in storage do not degrade till expiration, i.e., linear value of plasma units in inventory.
- All the processes involved between the blood collection till its conversion to plasma and freezing are to be carried out within 1 days' time.
- Whole blood units are processed to produce red blood cells, Plasma, and Platelets
- Plasma donation or the Apheresis method of plasma collection is not considered.
- RFID Tags are implemented on plasma and other blood components after centrifugation and at the blood bank only.
- Locations of entities involved in the model are fixed and known.

3.3 Model Notations

This section presents the necessary notations used in parameters, decision variables Objective functions and the constraints of the proposed Multi objective and Multi period plasma supply chain model.

3.3.1 Sets of Mathematical Model

The sets for the mathematical model formulation are shown below:

b	Blood types	$b=1,2,3,....,B$
c	Collection facility	$c=1,2,3,....,C$
m	Mobile collection facility	$m=1,2,3,....,M$
k	Blood bank	$k=1,2,3,....,K$
h	Hospitals	$h=1,2,3,....,H$
p	Plasma blood types	$p=1,2,3,....,P$
t	Time period	$t=1,2,3,....,T$
r	RFID Tags	$r=1,2,3,....,R$
s	Compatibility Prioritized Substitution Index	$s=1,2,3,....,S$

s = {high (s=1), medium (s=2), low (s=3)}

3.3.2 Parameters of Mathematical Model

The Parameters for the mathematical model formulation are shown in below:

C_{bct} Cost of Blood type "b" collection at the Collection facility "c" at Time period "t" ($/unit)

C_{bmt} Cost of Blood type "b" collection at the Mobile collection facility "m" at Time period "t" ($/unit)

C_{bkt} Cost of Blood type "b" collection at the Blood bank "k" at Time period "t" ($/unit)

C^t_{bck} Cost of transporting Blood type "b" from the Collection facility "c" to the Blood bank "k" at time period "t" ($/km)

C^t_{bmk} Cost of transporting Blood type "b" from the Mobile collection facility "m" to the Blood bank "k" at time period "t" ($/km)

C^t_{pkh} Cost of transporting Plasma blood type "p" from the Blood bank "k" to the Hospitals "h" at Time period "t" ($/km)

C^t_{Tbk} Cost of Blood type "b" screening and testing process at the Blood bank "k" at time period "t" ($/unit)

C^t_{bpk} Cost of centrifuging Blood type "b" into Plasma blood type "p" at the Blood bank "k" at Time period "t" ($/unit)

C_{pht} Cost of total Plasma blood type "p" transfusions at the Hospital "h" at Time period "t" ($/unit)

C^{t}_{Dbk} Cost of discarding the infected Blood type "b" at the Blood bank *"k"* at Time period *"t"* ($/unit)

C^{t}_{Dpk} Cost of discarding the outdated Plasma blood type "p" at the Blood bank *"k"* at Time period *"t"* ($/unit)

C^{t}_{Dph} Cost of discarding the outdated Plasma blood type "p" at the Hospitals *"h"* at Time period *"t"* ($/unit)

C_{pkt} Plasma blood type "p" holding cost at the Blood bank *"k"* at Time period *"t"* ($/unit)

C_{pht} Plasma blood type "p" holding cost at the Hospitals *"h"* at Time period *"t"* ($/unit)

C^{t}_{rpk} Cost of RFID Tags "r" implemented on the units of Plasma blood type "p" at the blood bank *"k"* at Time period *"t"*($/unit)

C^{ht}_{pok} Cost of outsourcing Plasma blood type "p" from Blood bank *"k"* for transfusion at the Hospitals *"h"* at Time period *"t"*($/unit)

ϑ_{ck} Distance between the Collection facility *"c"* to the Blood bank *"k"* (km)

ϑ_{mk} Distance between the Mobile collection facility *"m"* to the Blood bank *"k"* (km)

ϑ_{kh} Distance between the Blood bank *"k"* to the Hospitals *"h"* (km)

π^{t}_{dbk} Disposal rate of infected Blood type "b" at the Blood bank *"k"* at Time period *"t"* (unit less)

π^{t}_{dpk} Disposal rate of discarding the outdated Plasma blood type "p" at the Blood bank *"k"* at Time period *"t"*(unit less)

π^t_{dph} Disposal rate of discarding the outdated Plasma blood type " p " at the Hospitals *" h "* at Time period *" t "* (unit less)

R^t_{bpk} Rate of converting blood type " b " into Plasma blood type " p " at the Blood bank " k "at Time period *" t " (%)*

D_{hpt} Demand of Hospitals *" h "* for donated Plasma blood type " p " at Time period *" t "* (unit)

D^t_{pph} Demand of donated Plasma blood type " p " for transfusion with Plasma blood type " p " at Hospitals *" h "*at Time period *" t "* (unit)

θ^t_{shp} Binary Compatibility Matrix for different blood group types

$$\begin{cases} 1 & \text{If donated Plasma blood type "}p\text{" can be subsituted for demand Plasma blood type "}p\text{"} \\ & \text{by patient at the Hospitals "}h\text{" at Time period "}t\text{"} \\ 0 & \text{otherwise,} \end{cases}$$

P^t_{shp} Plasma Substitution prioritization Index of the Compatibility Matrix blood types at hospital *" h "* for Plasma blood type " p " at time period *" t "* (unit less)

ξ^t_{sph} Compatibility Prioritized Substitution Index " s " used for substituted-transfusion of donated Plasma blood type " p " at Hospitals " h "at Time period *" t "* (unit less)

S^t_{sph} Supply of donated Plasma blood type " p " for substituted-transfusion based on Compatibility Prioritized Substitution Index " s " at Hospitals *" h "*at Time period *" t "* (unit)

Ω_{ct} Maximum storage capacity of collection facility *" c "* at Time period *" t "* (unit)

Ω_{mt} Maximum storage capacity of Mobile collection facility *" m "* Time period " t " (unit)

Ω_{kt} Maximum storage capacity of Blood bank " k "at Time period *" t "* (unit)

Ω_{ht} Maximum storage capacity of Hospitals "h"at Time period "t" (unit)

Ω^{t}_{Tbk} Maximum Blood type "b" Testing and Screening capacity of Blood bank "k" at Time period "t" (unit)

Ω^{t}_{bpk} Maximum Centrifugation Capacity of the Blood bank "k" to convert Blood type "b" capacity of Plasma blood type "p" at Time period "t" (unit)

B_t The total budget to be spent the Plasma Supply Chain at time period "t" ($)

L^{t}_{pkh} The remaining healthy lifetime of Plasma blood type "p" sent from the Blood bank "k" to the Hospitals "h" Time period "t" (weeks)

L_{pht} The remaining healthy lifetime of Plasma blood type "p" at the Hospitals "h" Time period "t" (weeks)

L^{ht}_{pok} The remaining healthy lifetime of Plasma blood type "p" outsourced from Blood bank "k" for transfusion at the Hospitals "h" at Time period "t" (weeks)

R_{pt} Rate of deteriorating health of Plasma blood type "p" after RFID Implementation at Time period "t" (%)

∂_{bct} Imprecise Number of Blood type "b" donations made at the Collection facility "c" at Time period "t" (unit)

∂_{bmt} Imprecise Number of Blood type "b" donations made at the Mobile collection facility "m" at Time period "t" (unit)

∂_{bkt} Imprecise Number of Blood type "b" donations made at the Blood bank "k" at Time period "t" (unit)

3.3.3 Decision Variables of Mathematical Model

The decision variables for the mathematical model formulation are shown below:

Q_{bct} Quantity of Blood type "b" donated at the Collection facility "c" at Time period "t

Q_{bmt} Quantity of Blood type "b" donated at the Mobile collection facility "m" at Time period "t"

Q_{bkt} Quantity of Blood type "b" donated at the Blood bank "k" at Time period "t"

Q^t_{bck} Quantity of Blood type "b" transported from Collection facility "c" to Blood bank "k" at Time period "t"

Q^t_{bmk} Quantity of Blood type "b" transported from Mobile collection facility "m" to Blood bank "k" at Time period "t"

Q^t_{pkh} Quantity of Plasma blood type "p" transported from Blood bank "k" to the Hospitals "h" at Time period "t"

Q^t_{Tbk} Quantity of Blood type "b" screened and tested at the Blood bank "k" at Time period "t"

Q^t_{bpk} Quantity of Blood type "b" centrifuged into Plasma blood type "p" at the Blood bank "k" *at* Time period "t"

Q_{pht} Quantity of total Plasma blood type "p" transfused at hospital "h" at time period "t"

Q^{t}_{pph} Quantity of donated Plasma blood type " p " available for transfusion for the demanded Plasma blood type " p " at hospital " h " at time period *"t"*

Q^{ht}_{spp} Quantity of donated Plasma blood type " p " available for substituted-transfusion for the demanded Plasma blood type " p " at Hospital *"* h *"* for transfusion at time period *"t"*

Q^{ht}_{pok} Quantity of Plasma blood type " p " outsourced from Blood bank *"* k *"* for transfusion at the Hospitals *"* h *"* at Time period *"t"*

Q^{t}_{dbk} Quantity of infected Blood type "b" discarded at the Blood bank *"* k *"*after failing screening and testing process at Time period *"t"*

Q^{t}_{dpk} Quantity of outdated Plasma blood type " p " discarded at the Blood bank *"* k *"* at Time period *"t"*

Q^{t}_{dph} Quantity of outdated Plasma blood type " p " discarded at the Hospital *"* h *"* at Time period *"t"*

I_{pkt} Inventory of Plasma blood type " p " stored at the Blood bank *"* k *"* at Time period *"t"*

I_{pht} Inventory of Plasma blood type " p " stored at the Hospital *"* h *"* at Time period *"t"*

$I_{pk(t-1)}$ Remaining Inventory of previous time period of Plasma blood type " p " at the Blood bank *"* k *"* at Time period *"t"* ($/unit)

$I_{ph(t-1)}$ Remaining Inventory of previous time period of Plasma blood type " p " at the Hospitals *"* h *"* at Time period *"t"* ($/unit)

Io_{pkt} Initial Inventory of Plasma blood type " p " stored at the Blood bank *"* k *"* at Time period *"t"*

Io_{pht} Initial Inventory of Plasma blood type " p " stored at Hospital *" h "* at Time period *"t"*

Q^{t}_{rpk} Quantity of RFID Tags " r " implemented on the units of Plasma blood type " p " at the blood bank *" k "* at Time period *"t"*

3.4 Mathematical Model

3.4.1 Total Operational Cost Minimization

In terms of above-mentioned notation, the proposed mathematical model is formulated as follows as the first Objective Function:

$$MinTC = \left[\sum_{b=1}^{B}\sum_{c=1}^{C}\sum_{t=1}^{T}(Q_{bct}.C_{bct}) + \sum_{b=1}^{B}\sum_{m=1}^{M}\sum_{t=1}^{T}(Q_{bmt}.C_{bmt}) + \sum_{b=1}^{B}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q_{bkt}.C_{bkt}) \right. \tag{3.1}$$

$$+\sum_{b=1}^{B}\sum_{c=1}^{C}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q_{bck}^{t}.C_{bck}^{t}.\vartheta_{ck}) + \sum_{b=1}^{B}\sum_{m=1}^{M}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q_{bmk}^{t}.C_{bmk}^{t}.\vartheta_{mk}) + \sum_{p=1}^{P}\sum_{k=1}^{K}\sum_{h=1}^{H}\sum_{t=1}^{T}(Q_{pkh}^{t}.C_{pkh}^{t}.\vartheta_{kh})$$

$$+\sum_{b=1}^{B}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q_{Tbk}^{t}.C_{Tbk}^{t}) + \sum_{b=1}^{B}\sum_{p=1}^{P}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q_{bpk}^{t}.C_{bpk}^{t})$$

$$+\sum_{b=1}^{B}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q_{dbk}^{t}.C_{dbk}^{t}) + \sum_{p=1}^{P}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q_{dpk}^{t}.C_{dpk}^{t}) + \sum_{p=1}^{P}\sum_{h=1}^{H}\sum_{t=1}^{T}(Q_{dph}^{t}.C_{dph}^{t})$$

$$+\sum_{p=1}^{P}\sum_{k=1}^{K}\sum_{t=1}^{T}(I_{pkt}.C_{pkt}) + \sum_{p=1}^{P}\sum_{h=1}^{H}\sum_{t=1}^{T}(I_{pht}.C_{pht})$$

$$+\sum_{p=1}^{P}\sum_{h=1}^{H}\sum_{t=1}^{T}(Q_{pht}.C_{pht}) + \sum_{p=1}^{P}\sum_{k=1}^{K}\sum_{h=1}^{H}\sum_{t=1}^{T}(Q_{pok}^{ht}.C_{pok}^{ht})$$

$$\left. +\sum_{r=1}^{R}\sum_{p=1}^{P}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q_{rpk}^{t}.C_{rpk}^{t}) \right]$$

The first objective function as shown in equation (3.1), minimizes the total operational cost of the plasma supply chain network designed. The Operational cost consists of various factors such as cost of blood collection, cost of transporting the blood units to the blood bank, cost of screening, cost of centrifugation, RFID Implementation cost etc. To be specific the first-three terms of equation (3.1) minimize the overall cost of blood collection, where the terms $\sum_{b=1}^{B}\sum_{c=1}^{C}\sum_{t=1}^{T}(Q_{bct}.C_{bct})+\sum_{b=1}^{B}\sum_{m=1}^{M}\sum_{t=1}^{T}(Q_{bmt}.C_{bmt})+\sum_{b=1}^{B}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q_{bkt}.C_{bkt})$ represents the cost of blood collection at the collection facility, mobile collection facility, and the blood bank respectively. While the next three terms of the mathematical model as follow; $\sum_{b=1}^{B}\sum_{c=1}^{C}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q_{bck}^{t}.C_{bck}^{t}.\vartheta_{ck})+\sum_{b=1}^{B}\sum_{m=1}^{M}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q_{bmk}^{t}.C_{bmk}^{t}.\vartheta_{mk})+\sum_{p=1}^{P}\sum_{k=1}^{K}\sum_{h=1}^{H}\sum_{t=1}^{T}(Q_{pkh}^{t}.C_{pkh}^{t}.\vartheta_{kh})$ displays the cost of transporting blood units from the collection and mobile collection facility to the blood bank and then transporting the plasma units from the blood bank to the hospital. Moving on, $\sum_{b=1}^{B}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q_{Tbk}^{t}.C_{Tbk}^{t})+\sum_{b=1}^{B}\sum_{p=1}^{P}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q_{bpk}^{t}.C_{bpk}^{t})$ term presents the cost of screening the blood collected along with the cost of centrifuging blood into plasma units in the equation (1).

The next term $\sum_{b=1}^{B}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q_{dbk}^{t}.C_{dbk}^{t})+\sum_{p=1}^{P}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q_{dpk}^{t}.C_{dpk}^{t})+\sum_{p=1}^{P}\sum_{h=1}^{H}\sum_{t=1}^{T}(Q_{dph}^{t}.C_{dph}^{t})$ shows the cost of blood disposal after screening at the blood bank, along with the cost of outdated plasma units disposal at the blood bank and at the hospitals respectively. Moreover, the cost of holding inventory at both the blood bank and the hospital is involved in the equation (3.1) through the following terms

$\sum_{p=1}^{P}\sum_{k=1}^{K}\sum_{t=1}^{T}(I_{pkt}.C_{pkt})+\sum_{p=1}^{P}\sum_{h=1}^{H}\sum_{t=1}^{T}(I_{pht}.C_{pht})$. The next two terms of the first objective function include the cost of plasma transfusion along with the cost of plasma outsourcing presented as $\sum_{p=1}^{P}\sum_{h=1}^{H}\sum_{t=1}^{T}(Q_{pht}.C_{pht})+\sum_{p=1}^{P}\sum_{k=1}^{K}\sum_{h=1}^{H}\sum_{t=1}^{T}(Q_{pok}^{ht}.C_{pok}^{ht})$. The last term of the model formulated shows the inclusion of the cost of RFID implementation on the Plasma units at the blood bank and is presented as $\sum_{r=1}^{R}\sum_{p=1}^{P}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q_{rpk}^{t}.C_{rpk}^{t})$ in the equation (3.1) of the first objective function.

3.4.2 Traceability via RFID Maximization

In terms of notation mentioned above, the proposed mathematical model is formulated as follows as the second Objective Function for centralized plasma supply chain network designed:

$$MaxTrace=\left[\sum_{P=1}^{P}\sum_{k=1}^{K}\sum_{h=1}^{H}\sum_{t=1}^{T}\left(\begin{array}{c}\left(\left(1-e^{-(L_{pkh}^{t}.R_{pt})}\right).Q_{pkh}^{t}\right)+\left(\left(1-e^{-(L_{pht}^{t}.R_{pt})}\right).Q_{pht}\right)\\ +\left(\left(1-e^{-(L_{pok}^{ht}.R_{pt})}\right).Q_{pok}^{ht}\right)\end{array}\right)\right] \quad (3.2)$$

The equation (3.2) above is employed to maximize the number of undamaged items that received by demand points, i.e., in more specific terms the equation (3.2) maximizes the quantity of healthy or "undamaged" plasma units of various blood types received by and transfused at the hospitals; through the usage of radio frequency identification (RFID) technology enabled traceability. Hence, Traceability via RFID Maximization is employed specifically in terms of healthy items received by demand points.

RFID enabled traceability allows the central medical facilities such as blood banks to be able to get updated on the lifetime of perishable items by tracking throughout the centralized plasma supply chain. Enforcing end-to-end traceability for highly valuable and highly perishable products as plasma (Hajipour et al., 2021). RFID also significantly enhances the transportation process's efficiency by merely taking advantage of tracking items via reading the tags attached to them. RFID enabled traceability implementation in the plasma supply chain would definitely result in reducing the perishability likelihood in the plasma units received by the endpoints of the chain, i.e., the hospitals; gradually minimizing wastage throughout the network.

The concept of traceability in our model concerns only the remaining lifetime of items. It is used to maximize the number of healthy plasma units transported to and transfused at the hospitals. Here, the concept of both; the regular transportation of plasma units to the hospitals and outsourcing of the plasma units from the blood bank to hospitals at the times of emergency, are considered. By accessing the remaining healthy lifetime

plasma units, as the input of the lifetime exponential function, one can calculate the number of healthy items transported and transfused at the demand points within levels.

The terms $\left(1-e^{-(L^{t}_{pkh}.R_{pt})}\right)$ and $\left(1-e^{-(L^{ht}_{pok}.R_{pt})}\right)$ used in the equation (3.2), gives us the rate by which the plasma units would stay unexpired during the processes of transportation and outsourcing from the blood bank to the hospitals, in a given time period. While the term $\left(1-e^{-(L^{t}_{pht}.R_{pt})}\right)$ gives us the rate by which the plasma units would stay unexpired in storage of the hospitals, till the time of transfusion process to be carried out, in a given time period. Thus, multiplication of these terms with their specified Quantities, would calculate the number of unexpired or healthy plasma units that are received by and transfused at the hospitals, as shown through the equation (3.2).

To be explicit, the term $\left(\left(1-e^{-(L^{t}_{pkh}.R_{pt})}\right).Q^{t}_{pkh}\right)$ calculates the number of unexpired or healthy plasma units transported from the blood bank to the hospitals in a given time period. Similarly, the term $\left(\left(1-e^{-(L^{ht}_{pok}.R_{pt})}\right).Q^{ht}_{pok}\right)$ calculates the number of unexpired or healthy plasma units outsourced from the blood bank by the hospitals in a given time period, in case plasma units of same or compatible blood types are not available at the hospitals. Lastly, the term $\left(\left(1-e^{-(L^{t}_{pht}.R_{pt})}\right).Q_{pht}\right)$ is used to calculate the number of unexpired or healthy plasma units transfused at the hospital in a given time period. The addition of above-mentioned three terms presents the maximization of the quantity of

healthy or “undamaged” plasma units of various blood types received by and transfused at the hospitals: through the usage of radio frequency identification (RFID) technology.

Traceability is one of the crucial actions recently applied to supply chain network design problems because all the information related to products, especially the highly perishable ones such as plasma, could be reached immediately. For instance, the location of plasma units, the expiration date of units in various facilities, the best due date for transfusion, and the number of damaged or outdated unit disposed at a specific location are all easily extractable, through the usage of radio frequency identification (RFID) technology.

3.4.3 Compatibility-Prioritized Plasma Transfusion Maximization

The proposed mathematical model formulated as the third objective is presented by the below equation (3.3) and is used to maximize the Compatibility-Prioritized plasma transfusions. Where the term $\left(Q_{pph}^{t}\right)$ in equation (3.3) implies the transfusion of donated Plasma Blood type “ p ” units available in the hospital storage with same Plasma Blood type “ p ” that is demanded. However, in case same Plasma Blood type is not available, the next course of action would be to substitute units of other compatible Plasma Blood types for transfusions, based on Prioritization Substitution Index “ s ”. Which is presented through the term $\left(\sum_{s=1}^{S}\sum_{p=1}^{P}\sum_{h=1}^{H}\sum_{t=1}^{T}\left(\xi_{sph}^{t}.Q_{spp}^{ht}\right)\right)$ of equation (3.3). Where highest priority plasma is chosen for substituted-transfusion, in case same blood type plasma is not

available for transfusion. In case highest priority plasma blood type is also not available then intermediate priority and lowest priory plasma blood type would be opted for substituted-transfusion, respectively. Priority based Substituted-transfusion of plasma insures safer demand fulfillment, reduces wastage and shortage of required product; in a system where the supply or availability and the demand of plasma is uncertain. As donations of various blood types are based on the commonality of the blood type plasma required, e.g., O+ is the most common blood type in the overall population; however, AB- is the least common. Hence, naturally the availability of O- would not be an issue in transfusion, while substituted-transfusion is more likely to be opted for AB-, due to lower availability.

$$MaxCPT = \left[\begin{array}{c} \left(\sum_{p=1}^{P} \sum_{h=1}^{H} \sum_{t=1}^{T} \left(Q_{pph}^{t} \right) \right) \\ + \\ \left(\sum_{s=1}^{S} \sum_{p=1}^{P} \sum_{h=1}^{H} \sum_{t=1}^{T} \left(\xi_{sph}^{t} . Q_{spp}^{ht} \right) \right) \\ + \\ \left(\sum_{p=1}^{P} \sum_{k=1}^{K} \sum_{h=1}^{H} \sum_{t=1}^{T} \left(Q_{pok}^{ht} \right) \right) \end{array} \right] \tag{3.3}$$

Prioritization Substitution Index "s" set employed here, is driven through the usage of the equation (3.4) as shown below. Which is a product of Binary Compatibility Matrix $\left(\theta_{shp}^{t}\right)$ for compatible Plasma substitution and Plasma Substitution prioritization Matrix $\left(P_{shp}^{t}\right)$ obtained through a survey of various experts' opinion regarding the must

compatible blood types of plasma for substituted-transfusion with a specific blood type. The product of equation (3.4) is then categorized into a priority-based index for substituted-transfusion, referred to as the set "Prioritization substitution Index" presented as " s ".

$$\left(\theta_{shp}^{t}.P_{shp}^{t}\right) \tag{3.4}$$

The Prioritization Substitution Index is presented through Table 3.1. Where " $s=1$ " Plasma blood type has the Highest Substitution Priority, " $s=2$ "has intermediate substitution priority and " $s=3$ " has the lowest substitution priority for a specific plasma blood type; and would be substituted accordingly in case same type of plasma is not available for substitution, as mentioned above in explicit details.

Table 3.1: Prioritization Substitution Index

Plasma Blood Type / Priority	**High (s=1)**	**Medium (s=2)**	**Low (s=3)**
AB+	AB-	A+	O-
AB-	A-	B-	O-
A+	A-	O+	O-
A-	O-		
B+	B-	O+	O-
B-	O-		
O+	O-		
O-			

Moreover, Plasma Blood type, that is compatible with the demanded plasma blood type but falls lower then "$s=3$", is not included in the Prioritization Substitution Index i.e., it is not considered for substituted-transfusion. In addition, the next course of action would be to outsource the same Plasma Blood type "p" that is demanded at the hospital as presented through the term $\left(\sum_{p=1}^{P}\sum_{k=1}^{K}\sum_{h=1}^{H}\sum_{t=1}^{T}\left(Q_{pok}^{ht}\right)\right)$, in case the units of same Plasma Blood type and its substitute Plasma Blood type as per Prioritization substitution Index is not available in a specific scenario as shown in equation (3.3).

3.4.4 Constraints

Capacity Constraints:

$$\sum_{c=1}^{C} Q_{bct} \leq \Omega_{ct} \qquad \forall_b \quad \forall_t \qquad (3.5)$$

$$\sum_{m=1}^{M} Q_{bmt} \leq \Omega_{mt} \qquad \forall_b \quad \forall_t \qquad (3.6)$$

$$\sum_{k=1}^{K} Q_{bkt} \leq \Omega_{kt} \qquad \forall_b \quad \forall_t \qquad (3.7)$$

$$\sum_{h=1}^{H} Q_{pkh}^{t} \leq \Omega_{ht} \qquad \forall_k \quad \forall_p \quad \forall_t \qquad (3.8)$$

The constraints from equation (3.5) - (3.8) Defines the capacity of each entity involved in the plasma supply chain network designed. Where the constraint (3.5) defines that the amount of blood collected at the collection facility should be either less than or equal to the overall collection capacity of collection facility. Same senior is implied by constraint (3.6) for mobile collection facility. The constraints (3.7) and (3.8) represent the capacity constraint for the collection and transportation of blood units to the blood bank and transportation of the plasma units to the hospitals respectively, which should be less than and equal to the storage capacity of both the entities in question.

Demand Constraint:

$$\sum_{h=1}^{H} Q_{pkh}^{t} \geq D_{hpt} \qquad \forall_k \quad \forall_p \quad \forall_t \qquad (3.9)$$

The constraint (3.9) is the overall demand constraint, defining that the quantity of plasma units transferred to the hospitals from the blood bank should be sufficient to satisfy the demand of plasma units at the hospitals in a given time period.

Transshipment Constraints:

$$\sum_{k=1}^{K} Q_{bck}^{t} \geq \sum_{k=1}^{K} Q_{pkh}^{t} \qquad \forall_b \quad \forall_c \quad \forall_p \quad \forall_h \quad \forall_t \qquad (3.10)$$

$$\sum_{k=1}^{K} Q_{bmk}^{t} \geq \sum_{k=1}^{K} Q_{pkh}^{t} \qquad \forall_b \quad \forall_m \quad \forall_p \quad \forall_h \quad \forall_t \qquad (3.11)$$

Constraints (3.10) and (3.11) are related to transshipment, defining the transportation process of blood collected at collection facility and mobile collection facility respectively, and transported to blood bank; from there on plasma units are then transported to hospitals after conversion in a given time period as shown in constraint (3.11).

Supply Constraints:

$$\sum_{k=1}^{K} Q_{bck}^{t} \leq \Omega_{kt} \qquad \forall_c \quad \forall_b \quad \forall_t \qquad (3.12)$$

$$\sum_{k=1}^{K} Q_{bmk}^{t} \leq \Omega_{kt} \qquad \forall_m \quad \forall_b \quad \forall_t \qquad (3.13)$$

$$\sum_{h=1}^{H} Q_{pkh}^{t} \leq \Omega_{ht} \qquad \forall_k \quad \forall_p \quad \forall_t \qquad (3.14)$$

The constraints from equation (3.12) – (3.14) are employed to specify the supply of blood and plasma units. The constraints (3.12) and (3.13) define that the amount of blood units supplied by the collection facility and the mobile collection facility respectively, should be as per the capacity of the blood bank. While the constraints (3.14) limit the supply of plasma units from the blood bank to the hospital, according to the demand and capacity of the hospital.

Plasma Conversion Constraint:

$$\sum_{k=1}^{K} Q_{pkh}^{t} \leq \left[\left(\sum_{k=1}^{K} Q_{bck}^{t} + \sum_{k=1}^{K} Q_{bmk}^{t} + \sum_{k=1}^{K} Q_{bkt} \right) . \left(R_{bpk}^{t} \right) \right] \qquad \forall_b \quad \forall_c \quad \forall_m \quad \forall_p \quad \forall_h \quad \forall_t \qquad (3.15)$$

The Plasma conversion constraint as presented through equation (3.15) determines that a certain percentage denoted by R_{bpk}^{t}, of the total blood collected at all three collection points would be converted into plasma. Hence, the amount of plasma transported to the hospital from the blood bank would that less than or equal to that certain percentage denoted by R_{bpk}^{t}; of the whole blood collected.

Plasma Transfusion Constraint:

$$\sum_{h=1}^{H} Q_{pht} \leq \left[\left(\sum_{h=1}^{H} Q_{pkh}^{t} \right) + \left(\sum_{h=1}^{H} I_{pht} \right) \right] \qquad \forall_k \quad \forall_p \quad \forall_t \qquad (3.16)$$

The constraint (3.16) defines that the amount of plasma transfusion that take place at the hospitals in each time period; would be the sum of the initial inventory of plasma units stored at the hospital along with the amount of plasma unit transported from the blood bank to the specific hospital.

Disposal Constraints:

$$\sum_{k=1}^{K} Q_{dbk}^{t} \leq \left[\left(\sum_{k=1}^{K} Q_{bck}^{t} + \sum_{k=1}^{K} Q_{bmk}^{t} + \sum_{k=1}^{K} Q_{bkt} \right) . \left(\pi_{dbk}^{t} \right) \right] \qquad \forall_c \quad \forall_b \quad \forall_m \quad \forall_t \qquad (3.17)$$

$$\sum_{k=1}^{K} Q_{dpk}^{t} \leq \left[\left(\sum_{k=1}^{K} I_{pkt} \right) . \left(\pi_{dpk}^{t} \right) \right] \qquad \forall_p \quad \forall_t \qquad (3.18)$$

$$\sum_{h=1}^{H} Q_{dph}^{t} \leq \left[\left(\sum_{h=1}^{H} I_{pht} \right) . \left(\pi_{dph}^{t} \right) \right] \qquad \forall_p \quad \forall_t \qquad (3.19)$$

Blood and plasma disposal constraints are presented by the equations (3.17) – (3.19). Where the equation (3.17) presents the amount of infected disposed at the blood bank after screening the total blood collected at the blood bank. While the constraints (3.18)

and (3.19) define the total amount of outdated plasma units discarded from the total inventories held at the blood bank and the hospitals, respectively.

Inventory and Safety Stock Constraints:

$$\sum_{k=1}^{K} I_{pkt} = \left[\left(\sum_{k=1}^{K} I_{pk(t-1)} \right) + \left(\left(\sum_{k=1}^{K} Q_{bck}^{t} + \sum_{k=1}^{K} Q_{bmk}^{t} + \sum_{k=1}^{K} Q_{bkt} \right) . \left(R_{bpk}^{t} \right) \right) - \left(\sum_{h=1}^{H} Q_{pkh}^{t} \right) \right] \quad \forall_b \quad \forall_c \quad \forall_m \quad \forall_p \quad \forall_h \quad \forall_t \tag{3.20}$$

$$\sum_{h=1}^{H} I_{pht} = \left[\left(\sum_{h=1}^{H} I_{ph(t-1)} \right) + \left(\sum_{h=1}^{H} Q_{pkh}^{t} \right) - \left(\sum_{h=1}^{H} Q_{pht} \right) \right] \quad \forall_p \quad \forall_t \tag{3.21}$$

$$\sum_{k=1}^{K} I_{pk(t-1)} = \left[\left(\sum_{k=1}^{K} I_{pkt} \right) - \left(\sum_{h=1}^{H} Q_{pkh}^{t} \right) \right] \quad \forall_p \quad \forall_h \quad \forall_t \tag{3.22}$$

$$\sum_{h=1}^{H} I_{ph(t-1)} = \left[\left(I_{pht} \right) - \left(\sum_{h=1}^{H} Q_{pht} \right) \right] \quad \forall_p \quad \forall_t \tag{3.23}$$

The equations (3.20) and (3.21) both are the inventory constraints. Where the constraint (3.20) determines the overall plasma inventory at the blood bank; which is equal to the amount of plasma transported to the hospital from the blood bank subtracted from the total amount of blood collected at the blood bank; along with the addition of the plasma inventory of the precious period at the blood bank. In the case of the plasma inventory held

at the hospitals, it would be equal to the sum of plasma units sent by blood bank for the hospitals and the previous period's plasma inventory held at the hospitals; subtracted from the amount of plasma used for transfusion, as shown through constraint (3.21). While the constraint (3.22) and (3.23) determines the value of previous period's inventory held at the blood bank and the hospitals respectively. Which are equivalent to the initial inventory held at both the blood bank and the hospital, after the reduction of the amount of plasma units transferred to the hospitals from blood bank for constraint (3.22) and the consumption of plasma units for transfusion at the hospital for Constraint (3.23)

Budgetary Constraint:

$$TC \leq B_t \qquad \forall_t \tag{3.24}$$

$$TC = \left[\sum_{b=1}^{B}\sum_{c=1}^{C}\sum_{t=1}^{T}(Q_{bct}.C_{bct}) + \sum_{b=1}^{B}\sum_{m=1}^{M}\sum_{t=1}^{T}(Q_{bmt}.C_{bmt}) + \sum_{b=1}^{B}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q_{bkt}.C_{bkt}) \right. \tag{3.25}$$

$$+\sum_{b=1}^{B}\sum_{c=1}^{C}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q^t_{bck}.C^t_{bck}.\vartheta_{ck}) + \sum_{b=1}^{B}\sum_{m=1}^{M}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q^t_{bmk}.C^t_{bmk}.\vartheta_{mk}) + \sum_{p=1}^{P}\sum_{k=1}^{K}\sum_{h=1}^{H}\sum_{t=1}^{T}(Q^t_{pkh}.C^t_{pkh}.\vartheta_{kh})$$

$$+\sum_{b=1}^{B}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q^t_{Tbk}.C^t_{Tbk}) + \sum_{b=1}^{B}\sum_{p=1}^{P}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q^t_{bpk}.C^t_{bpk})$$

$$+\sum_{b=1}^{B}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q^t_{dbk}.C^t_{dbk}) + \sum_{p=1}^{P}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q^t_{dpk}.C^t_{dpk}) + \sum_{p=1}^{P}\sum_{h=1}^{H}\sum_{t=1}^{T}(Q^t_{dph}.C^t_{dph})$$

$$\left. +\sum_{p=1}^{P}\sum_{k=1}^{K}\sum_{t=1}^{T}(I_{pkt}.C_{pkt}) + \sum_{p=1}^{P}\sum_{h=1}^{H}\sum_{t=1}^{T}(I_{pht}.C_{pht}) \right]$$

$$+\sum_{p=1}^{P}\sum_{h=1}^{H}\sum_{t=1}^{T}(Q_{pht}.C_{pht})+\sum_{p=1}^{P}\sum_{k=1}^{K}\sum_{h=1}^{H}\sum_{t=1}^{T}(Q_{pok}^{ht}.C_{pok}^{ht})$$

$$+\sum_{r=1}^{R}\sum_{p=1}^{P}\sum_{k=1}^{K}\sum_{t=1}^{T}(Q_{rpk}^{t}.C_{rpk}^{t})\Bigg]$$

The (3.25) constraints define that the total operation cost for the whole supply chain designed is equal to Total operational cost objective function. While the constraint (3.24) is the budgetary constraint according to which the overall operational cost of the plasma supply chain should be lower than the budgetary amount defined for a specific time period.

Uncertainty Constraints:

$$\sum_{c=1}^{C} Q_{bct} \leq \partial_{bct} \qquad \forall_b \quad \forall_t \qquad (3.26)$$

$$\sum_{m=1}^{M} Q_{bmt} \leq \partial_{bmt} \qquad \forall_b \quad \forall_t \qquad (3.27)$$

$$\sum_{k=1}^{K} Q_{bkt} \leq \partial_{bkt} \qquad \forall_p \quad \forall_t \qquad (3.28)$$

The constraints from (3.26) – (3.28) are incorporated into the mathematical model to define the element of uncertainty. The equations (3.26), (3.27) and (3.28) suggests the amount of blood collected at the collection facility, mobile collection facilities and the

blood bank specifically is through imprecise or uncertain number of donations made; meaning that blood supply is uncertain for the model developed.

Blood Testing capacity Constraint:

$$\sum_{k=1}^{K} Q_{Tbk}^{t} \leq \Omega_{Tbk}^{t} \qquad \forall_p \quad \forall_t \qquad (3.29)$$

The constraint (3.29) limits the process of screening and testing the blood units collected and transported from collection and mobile collection facilities, limitation is defined as the screening and testing capacity of the central blood bank.

Plasma conversion capacity Constraint:

$$\sum_{k=1}^{K} Q_{bpk}^{t} \leq \Omega_{bpk}^{t} \qquad \forall_b \quad \forall_p \quad \forall_t \qquad (3.30)$$

Constraint (3.30) limits the process of blood conversion into plasma at the blood bank, which should not be more than the conversion capacity of the blood bank in a given time period.

Demand for Plasma Transfusion Constraint:

$$\sum_{p=1}^{P} CPT \geq D_{pph}^{t} \qquad \forall_h \quad \forall_t \qquad (3.31)$$

$$MaxCPT = \left[\begin{array}{c} \left(\sum_{p=1}^{P} \sum_{h=1}^{H} \sum_{t=1}^{T} \left(Q_{pph}^{t} \right) \right) \\ + \\ \left(\sum_{s=1}^{S} \sum_{p=1}^{P} \sum_{h=1}^{H} \sum_{t=1}^{T} \left(\xi_{sph}^{t} . Q_{spp}^{ht} \right) \right) \\ + \\ \left(\sum_{p=1}^{P} \sum_{k=1}^{K} \sum_{h=1}^{H} \sum_{t=1}^{T} \left(Q_{pok}^{ht} \right) \right) \end{array} \right] \qquad (3.32)$$

The constraint (3.31) is used to address the demand of various blood types of plasma for transfusion with a specific blood type of plasma at the hospitals. The demand is satisfied through Compatibility-Prioritized plasma transfusions or CPT as shown in equation (3.32). Where same blood type plasma transfusions, substituted-transfusions and outsourced transfusions are made to satisfy the demand of hospitals for plasma units in a given time period.

Supply for Plasma Transfusion Constraint:

$$\sum_{p=1}^{P} Q_{spp}^{ht} \leq \sum_{p=1}^{P} S_{sph}^{t} \qquad \forall_s \quad \forall_h \quad \forall_t \qquad (3.33)$$

$$\sum_{p=1}^{P} Q_{pph}^{t} \leq \sum_{p=1}^{P} \Omega_{ht} \qquad \forall_h \quad \forall_t \qquad (3.34)$$

$$\sum_{p=1}^{P} Q_{pok}^{ht} \leq \sum_{p=1}^{P} \Omega_{kt} \qquad \forall_k \quad \forall_h \quad \forall_t \qquad (3.35)$$

The constraints (3.33) - (3.35) define the supply constraint for Plasma transfusion at the hospitals at a given rime period. The equation (3.33) limits the supply of various Plasma types required for substituted-transfusion based on Compatibility prioritized index; which should be equivalent to the expected supply of required plasma types at the hospital, at a given time. Moreover, the equations (3.34) and (3.35) limit the supply of a specific plasma type required by the hospital for same blood type and outsourced transfusion, at a given time to inventory holding capacity of the Hospital and the supply capacity of blood bank in case of outsourcing.

Plasma Outsourcing Capacity Constraint:

$$\sum_{k=1}^{K} Q_{pok}^{ht} \leq I_{pkt} \qquad \forall_p \quad \forall_h \quad \forall_t \qquad (3.36)$$

The last constraint (3.36) Limits the amount of plasma units outsourced from the blood bank by the hospital for required transfusions, which should not be more than the inventory of plasma units held by the blood bank at a given period.

3.5 Chapter Summary

In this chapter, a multi-objective & multi-period mathematical model is developed for centralized plasma supply chain network design under uncertain donor and recipient availability. This chapter is comprised of four sections. The first section explains the problem within the plasma supply chain and who those problems can be curbed with the supply chain network that is designed in this research. The second section defines the assumptions made while developing the model. The third section consists of the notations used in mathematical sub-divided into the sets, parameters, and decision variables respectively. The last or the fourth section is where the mathematical model is developed, consisting of three objectives to be optimized. The first objective of the model is to minimize the operational cost of the plasma supply chain network designed. The second objective aims to maximize the maximizes the quantity of healthy or "undamaged" plasma units of various blood types received by and transfused at the hospitals; through the usage of RFID-enabled traceability. The last objective is developed to maximize the blood type Compatibility-Prioritized plasma transfusions, within the supply chain; through same blood type plasma transfusions, substituted-transfusions and outsourced plasma transfusions. The fourth section also explains the constraints for the model developed in detail.

CHAPTER 4: RESEARCH METHODOLOGY

This section discusses in detail the methodology opted for the multi-objective and multi-period plasma supply chain network designed.

4.1 Methodology Justification and Comparison

4.1.1 Chance Constraint Approach

The plasma supply chain developed is under uncertain demand and supply due to the voluntary donation-based nature of blood and blood products. Therefore, to mitigate the uncertainty of the demand and supply parameters of the developed mathematical mode, Chance constraint (CC) (Charnes and Cooper, 1959) methodology is opted. Solving chance-constrained optimization problems can be computationally challenging and various techniques such as Monte Carlo simulation, sample average approximation, and Mean-variance approach can be used for chance constraint optimization.

As mentioned, demand and supply of the plasma is uncertain in the modeled supply chain, making both the parameters stochastic in nature. The parameters are converted into deterministic parameters by employing the chance constraint methodology through the mean-variance approach which has been opted for our research. This method was first employed by Charnes and Cooper (1959), and it was found to follow the constraints of the problem (Li et al., 2008). In the mean-variance method, the mean or expected value

(average) and the variance (risk) of both demand and supply parameters are incorporated into their specific constraints; significantly reduce the uncertainty of the mathematical model.

Chance constraint is an operation research method of dealing with stochastic or fuzzy parameters or objectives of a mathematical model (Li et al., 2008). Through chance constraint stochastic variables are converted into deterministic ones, by incorporating the average and standard deviation of the said parameters into the model. Chance constraint programming appropriate for optimization planning problems where demand is uncertain, as reliability and optimality is ensured through incorporation of mean and variance of the uncertain parameters (Li et al., 2008). Centralized plasma supply chain model developed for this study is the optimal example of a planning problem, where various entities are to be unified to ensure plasma demand satisfaction. And the uncertain nature of donor and recipient of the plasma or blood supply chain is a well-known fact. Hence, chance constraint programming is opted to mitigate the uncertain eliminate of this study. This method was first employed by Charnes and Cooper (1959), and it was found to follow the constraints of the problem (Li et al., 2008).

Trapezoidal Membership Functions is another methodology that can be used to deal with uncertainty in a mathematical model. Trapezoidal membership functions are commonly used in fuzzy logic, where uncertainty is represented as linguistic variables (e.g., "high," "medium," "low") (Imran et la. 2018). Meaning that trapezoidal membership function, does not explicitly provide probabilities but rather capture the degree to which a variable belongs to a particular fuzzy set, which can be a drawback when precise risk assessment is necessary. While chance constraint on the other hand provides, precise

probabilistic risk assessment and is optimal for solving complex and computationally intensive problems to find robust solutions that are less sensitive to parameter variations (Liu and Kakuzo, 1998).

Moreover, research often involves making decisions or recommendations based on data, which is inherently uncertain. Chance constraint programming allows researchers to explicitly account for this uncertainty by modeling it through probabilistic constraints (Liu and Kakuzo, 1998). This helps in making more robust decisions. This methodology promotes robust optimization, meaning that solutions are not overly sensitive to variations in input parameters. This is vital when making decisions based on uncertain data, as it reduces the risk of poor outcomes due to unforeseen variations. Overall, chance constraint programming is a well-suited method for addressing complex, dynamic problems with uncertain data (Liu and Kakuzo, 1998) and has proven to be effective in these domains, hence it is ideal for methodology for minimizing the uncertain nature of plasma supply chain designed for this study.

4.1.2 Interactive Multi-Objective Fuzzy Programming Approach

Moreover, there are two kinds of “core” approaches used for solving a multi-objective model. The first approach makes use of “Aggregation Functions” such as, goal programming, lexicographic ordering, weighted sum method, min-max weighted method, e-constraint approach and interactive fuzzy programming. However, these methods of aggregation functions used for solving a multi-objective model; do not provide the “Pareto

Optimal Front" i.e., a range or set of solutions (Imran et la. 2018); instead, they generate a single but exact solution that is known as the "Global Optimum".

The second approach that can be used to solve the developed multi-objective and multi-period model is "Evolutionary Heuristics". This methodology generates the pareto front, when employed. Genetic algorithm (GA) and Non-Dominated sorting (NSGA-II) are examples of the methodologies used for multi-objective optimizations, grouped as Heuristics (Imran et la. 2018). This approach allows the simultaneous optimization and evaluation of all the objective functions of the developed model; and the "Pareto Optimal Front" is plotted. Hence, provide a range of solutions for the objective function, while satisfying all the constraints of the model (Imran et la. 2018). However, the global optimum is not generated or achieved through the Heuristic approaches, as the solution sets often gets whirled in the local optimums. Also, the Heuristics approach, being quite complicated to implement, is more preferred and opted for "Non-linear Multi-objective Program" optimizations. It also fails to prioritize the objective functions according to value to human life.

Therefore, the core methodology opted for this research is "Interactive Multi-Objective Fuzzy Programming" (IMOFP) (Imran et la. 2018). The methodology was first developed and used by Mr. Zimmermann (Zimmermann, 1978), and in case of the Healthcare industry this methodology was used by Dr. Imran (2018) for the optimization of medicine Supply Chain. As, the model plasma supply chain network designed is linear in nature, consisting of three important objectives, i.e., the optimization of the centralized plasma supply chain's Operational Cost, the RFID-Enabled Traceability, and the Compatibility-Prioritized Plasma Transfusion. However, Compatible plasma transfusion

that is save due to traceability at each stage of products life is of more value to the healthcare industry than the overall cost; hence, this methodology is comparatively more suitable option.

For the computational aspect of interactive multi-objective Fuzzy programming methodology, acquiring the optimal and satisfactory solution is comparatively easier, in case of linear programming problems (El-Wahed et al., 2006). This methodology is optimal for multi-objective problems where comparative tradeoffs are required. The diverse development of the said programming methodology allows efficient application on real-world scenarios such as transportation and production problem etc., both of which are an exemplary part of supply chain process (Werners, 1987).

Moreover, using a fuzzy approach to represent information and requirements through fuzzy sets, particularly their membership functions, is often more suitable for addressing real-world situations. Fuzzy mathematical programming models are capable of handling multiple objectives and accommodating flexible regions of feasible solutions. One significant benefit of this method is that, under specific conditions, it allows the formulation of equivalent crisp models that can be solved using readily available software efficiently (Werners, 1987).

Furthermore, the approach presented in interactive fuzzy linear programming is tailored to specific problems and dependent on user input (Lai and Hwang, 1992). It considers a wide range of scenarios that a decision maker might encounter when modeling and solving linear programming problems. Interactive fuzzy linear programming offers an effective and methodical method for addressing the specified linear programming problem,

presenting the outcomes (including solutions and resource utilization) to the decision maker. The decision maker may find the solution acceptable or opt to adjust certain parameters or alter the original model based on their preferences. The process is continued till a satisfactory solution is generated by the decision maker and the problem is solved (Lai and Hwang, 1992).

Interactive Multi-Objective Fuzzy Programming (IMOFP) plays a significant and essential role in the study of "Centralized Plasma Supply Chain Network Design under Uncertain Demand and Supply". As, one of the primary objectives of the study is to simultaneously optimize multiple conflicting objectives (Sakawa, 2000), including operational cost minimization, RFID-enabled traceability maximization, and blood type compatibility-prioritized plasma transfusion maximization. IMOFP is crucial because it provides a systematic and interactive approach to address these multiple objectives, allowing decision-makers to explore the trade-offs and preferences between them (El-Wahed et al., 2006). This is particularly important in healthcare logistics, where achieving a single objective often comes at the expense of others, and decision-makers need to strike a balance. Moreover, the research context involves uncertain demand and supply conditions, which are common in healthcare logistics. IMOFP is valuable because it can accommodate imprecise or fuzzy information, allowing for the inclusion of uncertain data in the optimization process. IMOFP also allows for active stakeholder involvement through an interactive decision-making process (Sakawa, 2000), hence aligning the solution with the unique needs and priorities of the healthcare system.

Interactive Multi-Objective Fuzzy Programming (IMOFP) is a valuable tool for decision-makers facing multi-objective problems with uncertain or imprecise information

(Imran et la. 2018). When comparing IMOFP with other linear methodologies such as Goal Programming, Robust Optimization, and Epsilon Constraint, several key differences and considerations can be pointed out in its favor:

In terms of ***Objective Handling***, IMOFP allows decision-makers to interactively explore trade-offs between multiple objectives (El-Wahed et al., 2006). It accommodates fuzzy objectives, which can capture imprecise information, and decision-makers can adjust their preferences during the decision-making process. While Goal Programming aims to minimize deviations from predefined target values for each objective and might not be able handle imprecise or uncertain objectives as effectively as IMOFP. As for Robust Optimization, it focuses on ensuring that a solution remains feasible and provides certain performance guarantees under uncertainty. It doesn't explicitly address multiple objectives but is used to find a single robust solution that performs well under various scenarios. Lastly, in terms of objectives optimization, the Epsilon Constraint converts a multi-objective problem into a single-objective problem by treating one objective as primary and others as constraints. This approach doesn't explicitly allow for interactive exploration of trade-offs between objectives (El-Wahed et al., 2006).

For the ***Treatment of Uncertainty***, the IMOFP explicitly incorporates fuzzy or uncertain information in the decision-making process (Imran et al., 2018). It allows for subjective input and adaptation during the exploration of solutions, making it suitable for handling varying degrees of uncertainty. While Goal Programming can handle imprecise objectives to some extent, it does not inherently provide a systematic way to address uncertainties. It relies on predefined target values for objectives. As for Robust Optimization, it focuses on ensuring feasibility under uncertainty rather than explicitly

modeling and managing uncertain objectives. The Epsilon Constraint doesn't really provide a comprehensive framework for handling uncertainties in the same way as IMOFP (El-Wahed et al., 2006).

For ***Decision-Maker Involvement***, the IMOFP encourages active involvement of decision-makers. They can adjust their preferences and objectives during the interactive process, making it a suitable choice for problems where stakeholder input is crucial (Sakawa, 2000). While Goal Programming typically involves decision-makers setting predefined goals and target values and does not accommodate real-time adjustments and preferences as effectively as IMOFP. Robust does not provide decision-makers with a platform for active involvement in exploring trade-offs between multiple objectives, and the Epsilon Constraint requires the selection of a primary objective, which limits the flexibility for decision-makers to adapt and interact with the optimization process.

However, in terms of ***Complexity***, the interactive nature of IMOFP can make it more complex and time-consuming (Sakawa, 2000) compared to non-interactive methods. Yet, the involvement from decision-makers eventually leads to well-informed and adaptable decisions, Goal Programming is generally less complex than IMOFP since it involves setting and optimizing against predefined objectives and targets. Robust Optimization does not address multiple objectives directly and focuses on finding a single, robust solution; hence this methodology is not a viable option for multi-objective problems. Epsilon Constraint has always been utilized for simplified problems only.

To summaries, in comparison of Goal Programming, Robust Optimization, Epsilon Constraint methodologies etc., the IMOFP stands out for its ability to handle imprecise

information, involve decision-makers interactively, and address multiple objectives in uncertain environments. However, it is more complex and time-consuming compared to non-interactive linear methodologies.

Conclusively, Two-fold methodology is opted for this research as illustrated through Figure 4.1, where the core methodologies opted for optimization is “Interactive Multi-Objective Fuzzy Programming” combined with “Chance Constraint Approach” to eliminate uncertainty of the model. Figure 5 illustrates the Two-fold methodology framework. The combination of the two methodologies would lead to more robust results and would provide advantages such as reducing the computational shortcomings of each individual methodologies (El-Wahed et al., 2006). For instance, Interactive Multi-Objective Fuzzy Programming will be able to provide the optimal solution values with high confidence levels for all the objective functions, however the results will be afflicted with stochastic, imbalance and vague result that is highly sensitive to slight changes. However, when combined with chance constraint optimization, the uncertainty eliminate of the model will be marginalized, by employing of mean-variance approach for the fuzzy parameters of model i.e., demand and supply and converting them into deterministic parameters. Hence, providing more robust and precise results.

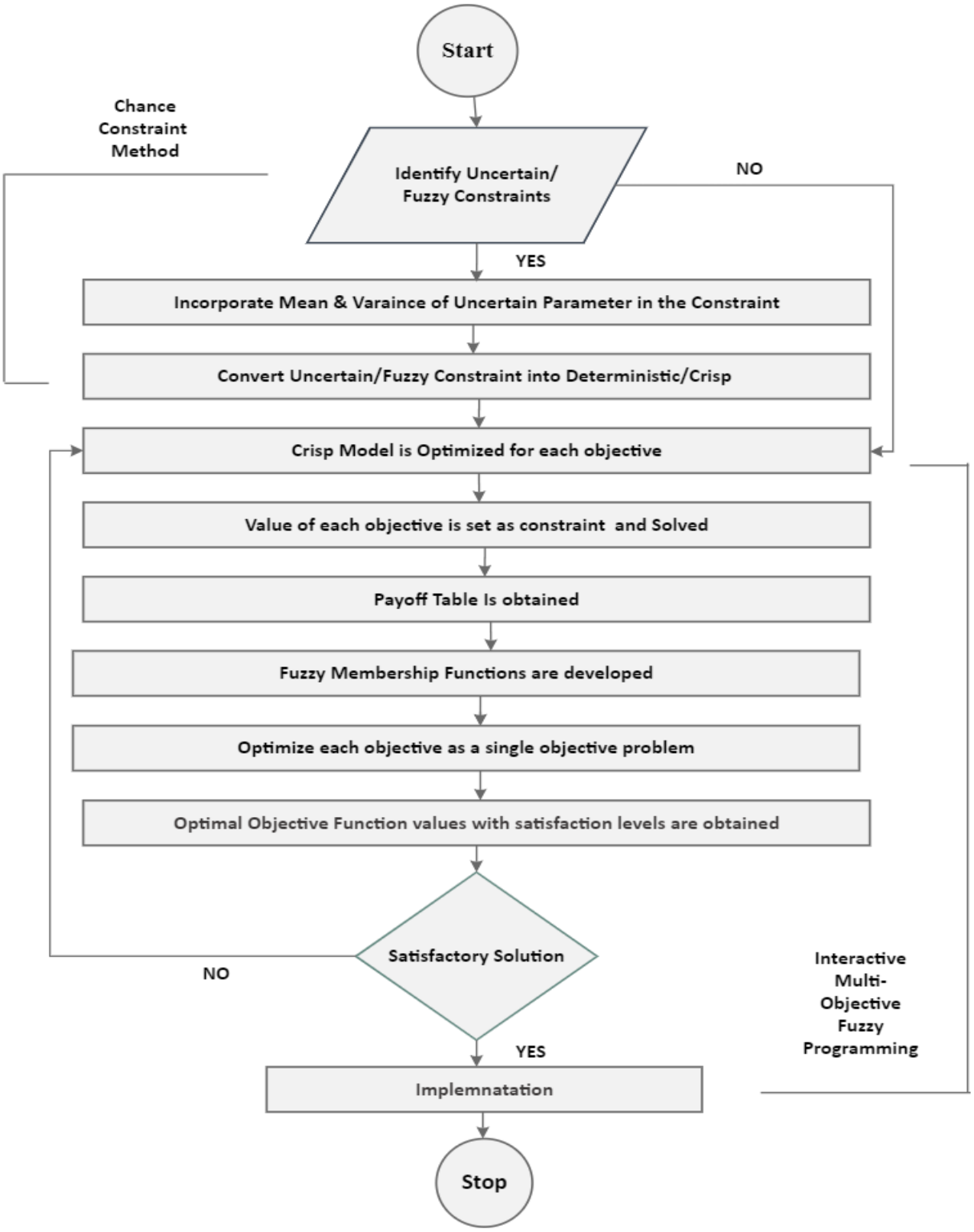

Figure 4.1: Two-fold methodology flowchart

4.2 Chance Constraint Implementation

Chance constraint programming is a mathematical optimization technique used when dealing with uncertain parameters or variables in decision-making problems (Baghbani, 2022). In the context of supply chain network designed, it can be applied to handle uncertainties in donor and recipient availability in a plasma supply chain in order to mitigate the uncertainty in the mathematical model. Moreover, the mean-variance approach is opted for chance constraint optimization, as it significantly reduces the element of uncertainty in the model, by incorporating the mean (average) and the variance (risk) of a specific parameter in its defined constraint.

In the context of plasma supply chain network design, uncertainty can arise due to factors such as fluctuations in donor turnout, changes in recipient demand, transportation delays, or unexpected events like natural disasters. Therefore, as the demand and supply of the plasma supply chain are uncertain in the developed plasma supply chain, both the parameters are stochastic in nature. The parameters are converted into deterministic parameters by employing the chance constraint methodology (Baghbani, 2022), through the usage of mean-variance approach. Then the deterministic parameters of the demand and supply are incorporated into their specific constraints. The mean or expected value of a random variable represents its average value. While the variance measures the spread or risk associated with the random variable. It quantifies how much the actual outcomes might deviate from the mean. Lower variance indicates lower risk, while higher variance implies higher risk. By adjusting both the demand and supply constraints in terms of their specific

mean and variance, decision-makers can find solutions that strike an optimal balance between risk and reward.

Hence, to cope with uncertainty, the chance-constrained approach is used. And the deterministic equivalent of the proposed uncertain constraints of; overall plasma demand at the hospitals as i.e., the constraint (3.9) and the overall plasma supply to the hospitals i.e., the constraint (3.14) is as follows:

4.2.1 Deterministic Demand Constraint

In Constraint (3.9) the demand parameter D_{hpt} is uncertain and stochastic, following Normal distribution (Jagannathan, 1974). Hence the following steps are followed to make the parameter deterministic:

$$\sum_{h=1}^{H} Q_{pkh}^{t} \geq D_{hpt} \qquad \forall_k \quad \forall_p \quad \forall_t \qquad (4.1)$$

Chance Constraint Optimization when D_{hpt} on the right side is random variable:

$$P\left\{ D_{hpt} \leq \sum_{h=1}^{H} Q_{pkh}^{t} \right\} \geq \alpha \qquad (4.2)$$

Assuming that normal distribution is followed with $E\left\{D_{hpt}\right\}$ *and* $Var\left\{D_{hpt}\right\}$:

$$h_i = \sum_{h=1}^{H} Q_{pkh}^{t} \tag{4.3}$$

$$P\left\{ D_{hpt} \le \sum_{h=1}^{H} Q_{pkh}^{t} \right\} \ge \alpha \tag{4.4}$$

Putting the values of equation (4.3) in equation (4.4):

$$P\left\{ D_{hpt} \le h_i \right\} \ge \alpha \tag{4.5}$$

$$P\left\{ \frac{D_{hpt} - E\left\{D_{hpt}\right\}}{\sqrt{Var\left\{D_{hpt}\right\}}} \le \frac{h_i - E\left\{D_{hpt}\right\}}{\sqrt{Var\left\{D_{hpt}\right\}}} \right\} \ge \alpha \tag{4.6}$$

$$K_D = P\left\{ \frac{D_{hpt} - E\left\{D_{hpt}\right\}}{\sqrt{Var\left\{D_{hpt}\right\}}} \right\} \tag{4.7}$$

K_D introduced in equation (4.7) is the pre-defined “constant confidence level”.

$$P\left\{ K_D \le \frac{h_i - E\left\{D_{hpt}\right\}}{\sqrt{Var\left\{D_{hpt}\right\}}} \right\} \ge \alpha \tag{4.8}$$

$$\frac{h_i - E\left\{D_{hpt}\right\}}{\sqrt{Var\left\{D_{hpt}\right\}}} \geq K_D \tag{4.9}$$

$$h_i \geq \left(K_D \cdot \sqrt{Var\left\{D_{hpt}\right\}} \right) + E\left\{D_{hpt}\right\} \tag{4.10}$$

Substituting the original values of equation (4.3) in equation (4.10):

$$\sum_{h=1}^{H} Q_{pkh}^{t} \geq \left(K_D \cdot \sqrt{Var\left\{D_{hpt}\right\}} \right) + E\left\{D_{hpt}\right\} \tag{4.11}$$

New Deterministic Demand Constraint is as follows:

$$\sum_{h=1}^{H} Q_{pkh}^{t} \geq \left(K_D \cdot \sqrt{Var\left\{D_{hpt}\right\}} \right) + E\left\{D_{hpt}\right\} \qquad \forall_k \quad \forall_p \quad \forall_t \tag{4.12}$$

Hence, the new deterministic demand Constraint is presented through the Constraint (48), which includes the mean and variance of the total plasma demanded by the hospitals, for the designed centralized plasma supply chain. The constraint (4.12) would replace the former demand constraint (3.9) for onwards solution optimization.

4.2.2 Deterministic Supply Constraint

In Constraint (3.14) the supply parameter Q_{pkh}^{t} is uncertain and stochastic, following Normal distribution (Jagannathan, 1974). Hence the following steps are followed to make the parameter deterministic:

$$\sum_{h=1}^{H} Q_{pkh}^{t} \leq \Omega_{ht} \qquad \forall_k \quad \forall_p \quad \forall_t \tag{4.13}$$

Chance Constraint Optimization when Q_{pkh}^{t} on the left side is random variable:

$$P\left\{\sum_{h=1}^{H} Q_{pkh}^{t} \leq \Omega_{ht}\right\} \geq 1-\alpha \tag{4.14}$$

Assuming that normal distribution is followed with $E\left\{Q_{pkh}^{t}\right\}$ *and* $Var\left\{Q_{pkh}^{t}\right\}$:

$$h_i = \sum_{h=1}^{H} Q_{pkh}^{t} \tag{4.15}$$

$$P\left\{\sum_{h=1}^{H} Q_{pkh}^{t} \leq \Omega_{ht}\right\} \geq 1-\alpha \tag{4.16}$$

Putting the values of equation (4.15) in equation (4.16):

$$P\left\{h_i \le \Omega_{ht}\right\} \ge 1-\alpha \tag{4.17}$$

$$P\left\{\frac{h_i - E\left\{h_i\right\}}{\sqrt{Var\left\{h_i\right\}}} \le \frac{\Omega_{ht} - E\left\{h_i\right\}}{\sqrt{Var\left\{h_i\right\}}}\right\} \ge 1-\alpha \tag{4.18}$$

$$K_Q = P\left\{\frac{h_i - E\left\{h_i\right\}}{\sqrt{Var\left\{h_i\right\}}}\right\} \tag{4.19}$$

K_Q introduced in equation (4.19) is the pre-defined "constant confidence level".

$$P\left\{K_Q \le \frac{\Omega_{ht} - E\left\{h_i\right\}}{\sqrt{Var\left\{h_i\right\}}}\right\} \ge 1-\alpha \tag{4.20}$$

$$K_Q \le \frac{\Omega_{ht} - E\left\{h_i\right\}}{\sqrt{Var\left\{h_i\right\}}} \tag{4.21}$$

$$E\left\{h_i\right\} + \left(K_Q \cdot \sqrt{Var\left\{h_i\right\}}\right) \le \Omega_{ht} \tag{4.22}$$

Substituting the original values of equation (4.15) in equation (4.22):

$$\sum_{h=1}^{H}\left(E\left\{Q_{pkh}^t\right\}\right) + \sum_{h=1}^{H}\left(K_Q \cdot \sqrt{Var\left\{Q_{pkh}^t\right\}}\right) \le \Omega_{ht} \tag{4.23}$$

New Deterministic Supply Constraint is as follows:

$$\sum_{h=1}^{H}\left(E\left\{Q_{pkh}^{t}\right\}\right)+\sum_{h=1}^{H}\left(K_{Q}\cdot\sqrt{Var\left\{Q_{pkh}^{t}\right\}}\right)\leq\Omega_{ht} \qquad \forall_k \quad \forall_p \quad \forall_t \qquad (4.24)$$

Hence, the new deterministic supply Constraint is presented through the Constraint (4.24), which includes the mean and variance of the total plasma supply to the hospitals, for the designed centralized plasma supply chain. The constraint (4.24) would replace the former supply constraint (3.14) for onwards solution optimization.

4.3 Interactive Multi-Objective Fuzzy Programming Implementation

Following are the steps of the core Solution approach adopted:

4.3.1 α−extreme Solutions

Two different methods can be opted for obtaining the α-extreme solution, both of the methods are as follow:

1. In this first approach, the maximum and minimum values of all three objective functions are known for decision making. The minimum and maximum values are treated as the lower and upper bounds of each specific objective function. The objective functions are solved within the pre-set lower and upper bounds, along with constraints defined for each objective function. As a result, a pay-off table is generated, which is then used to further linearize the model after confining it to a single objective function. The issue arises in this method when the preset lower and upper bounds contradict or violate the constraints of the model. Therefore, the solution might be feasible, but the optimality of the solution remains unconfirmed.

2. For the second approach, each objective function is solved separately with its specific defined constraints, and the resulting solution values of each objective function are noted down. The solved objective functions are considered as the new added constraints for each objective function, and then are solved and optimized

separately again. This step is repeated for all 3 objective functions of the mathematical model. A payoff table is then developed based on the values obtained through the above-mentioned procedure, defined as the α-extreme values for each objective function. In this approach, the multi-objective & mixed-integer linear programming is made use of to obtain the lower and upper bounds of the objective functions. Hence, the lower and upper bounds, along with the constraints of the model are always satisfied during the mathematical model optimization. Therefore, this approach is opted for the optimization of our developed mathematical model, in order to ensure generation of the global optimal solution.

4.3.2 Linearization using the fuzzy membership function.

The second method as discussed in the previous section is used as the proposed Interactive Fuzzy Programming methodology. To linearize the objective functions, a fuzzy membership function is utilized (Imran et la. 2018). The triangular membership function is employed for the linearization of the objective functions. The equation (34) represents the generic form of triangular membership function utilized, where f_o^{a-lb} and f_o^{a-ub} are the extreme function values of function "o".

$$u_o = \begin{cases} \dfrac{f_o^{a-ub} - f}{f_o^{a-ub} - f_o^{a-lb}} & {}_i f \ f \geq f_o^{a-lb} \\ & {}_i f \ f_o^{a-lb} < f < f_o^{a-ub} \\ & {}_i f \ f \leq f_o^{a-ub} \end{cases} \tag{4.25}$$

4.4 Chapter Summary

This chapter explains the solution methodologies used to optimize the model. A detailed review for both CCP and IMOFP is provided, along with their comparison with various methodologies of the same nature. Firstly, the chance constraint methodology is used to mitigate the uncertainty in the mathematical model developed. Demand and supply of the plasma supply chain are uncertain, making both the parameters stochastic in nature. The parameters are converted into deterministic parameters by employing the chance constraint methodology, through the usage of mean-variance approach. Then the deterministic parameters of the demand and supply are incorporated into their specific constraints. Furthermore, the interactive fuzzy programming approach is used as the core solution methodology. In this method one objective function is solved at a time and its value is recorded, and then this objective is defined as the constraint for other objective functions, which are then solved and optimized separately. The same process is repeated for the other objectives and finally, a pay-off table is achieved that has the α-extreme function values of each objective.

CHAPTER 5: CASE STUDY

In this section, a real-time case study has been opted for the implementation of the mathematical model developed in the third chapter. Therefore, the case of blood and plasma supply chain of the twin cities of Rawalpindi, Islamabad and their suburbs has been selected for the developed mathematical model implementation and results have been analyzed. The supply chain model has been designed based on international industry frameworks of blood supply chain, along with catering the real-time problems within the decentralized blood supply chain of a developing country such as Pakistan. The country's present blood supply chain system is far from ideal, decentralized, and inefficient in demand satisfaction. The current supply chain system of the two major cities of the developing country of Pakistan is plagued with plasma and blood shortages due to insufficient blood and plasma supply, uncertain donor availability, uncertain demand, and due to wastage because of product expiry. Therefore, data set for several supply chain entities such as the regional blood bank etc., that do not currently exist in the system is adopted from the literature of same problem size. Most of the data is collected from the existing entities such as collection centers, hospitals, etc. and through market research. Relevant data sets used in the formulation of mathematical model are given in appendix.

The 4-echelon blood plasma supply chain network of the twin cities and suburbs consists of donated plasma of all eight blood types, four potential mobile collection centers dispersed throughout the defined region, two main collection centers of both the cities of Islamabad and Rawalpindi, a single regional blood bank catering to the twin cities and their

suburbs. Lastly, the three selected hospitals, which are the demand points of the supply chain, are of different functionality and capacity. The hospital selected are of differing nature and capacity, hence acting as an appropriate sample of the demand of plasma for the twin cities. The selected hospital includes a major government facilitated hospital, a medium level private hospital and a larger private hospital of the twin cities. The geographical location of the concerned facilities and demand point is illustrated through Figure 5.1.

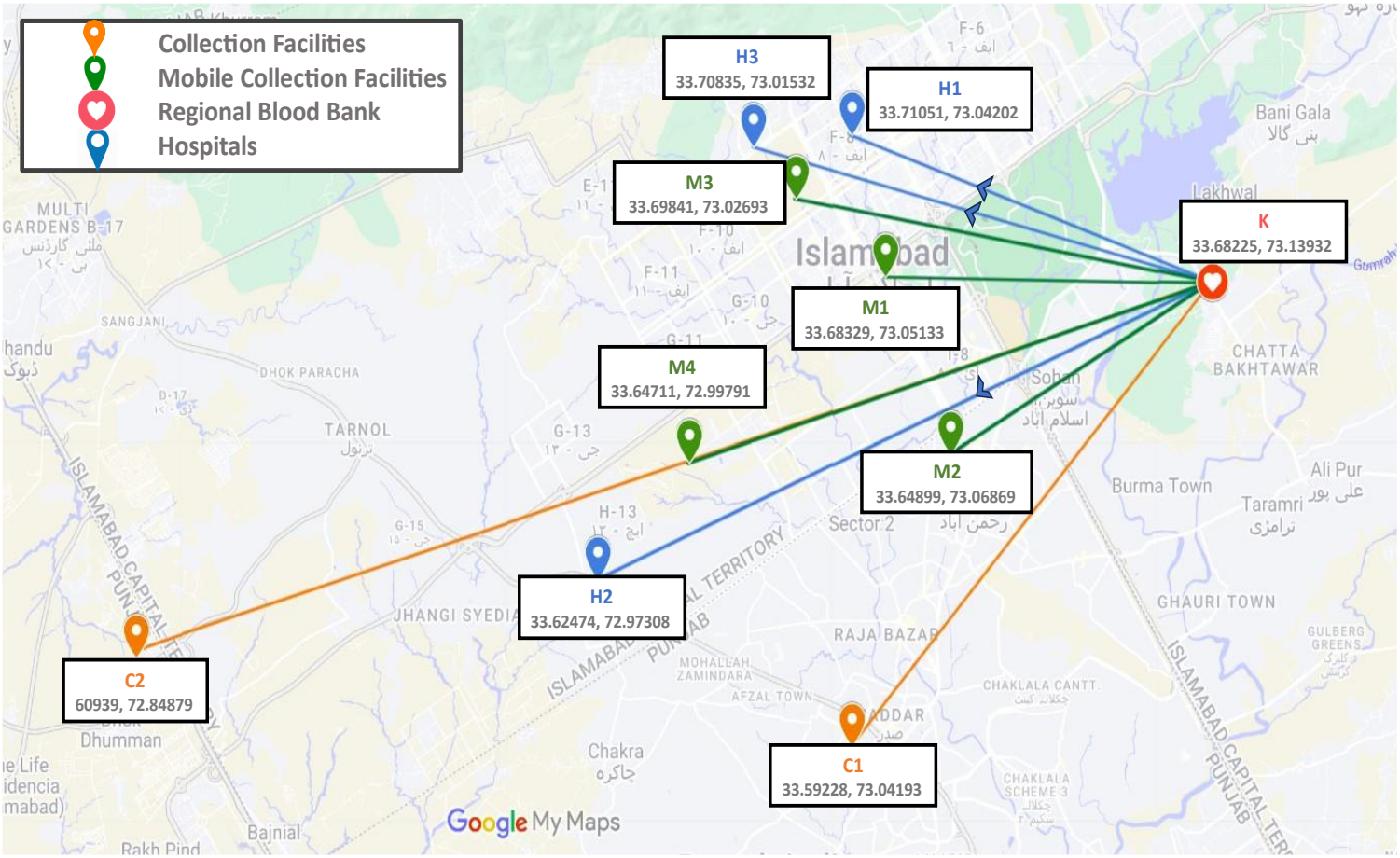

Figure 5.1: Geographical location of concerned facilities and demand point

The flow of plasma within the supply chain is initiated through the donation of all the blood types at the mobile collection facility, collection facility and at the blood bank at times. The collected blood is then transported to the blood bank, where blood is screened for transmissible diseases, plasma is extracted, and RFID tags are implemented to ensure provision of healthy plasma units and traceability. Plasma inventory is maintained at the blood bank as well as plasma units are transported to the hospitals as per their projected demand. The hospital is the last entity of plasma supply chain where plasma is consumed via transfusions. Disposal is a two-stage process where blood is initially disposed at the blood bank after testing, if found to be infected. The second disposal occurs when plasma expires in storage at both the blood bank and the hospitals. The centralized plasma supply chain for case study of twin cities is illustrated through Figure 5.2.

Moreover, plasma transfusion is prioritized in the mathematical model implemented, where same blood type plasma transfusions is the go-to option. However, in cases where same plasma transfusions are not possible, substituted-transfusion is opted, and the top three prioritized compatible blood type plasma is transfused based on availability in storage and level of plasma type prioritization (i.e. High, medium and low priority). In case if neither same blood type plasma nor the top three prioritized and compatible blood type plasma is available in storage, the last resort opted for demand satisfaction is outsourcing the same blood type plasma from the blood bank. Hence, satisfying the objective of developing and optimizing a centralized plasma supply chain by ensuring demand satisfaction and reducing wastage and shortages of life saving, human-based resource of plasma.

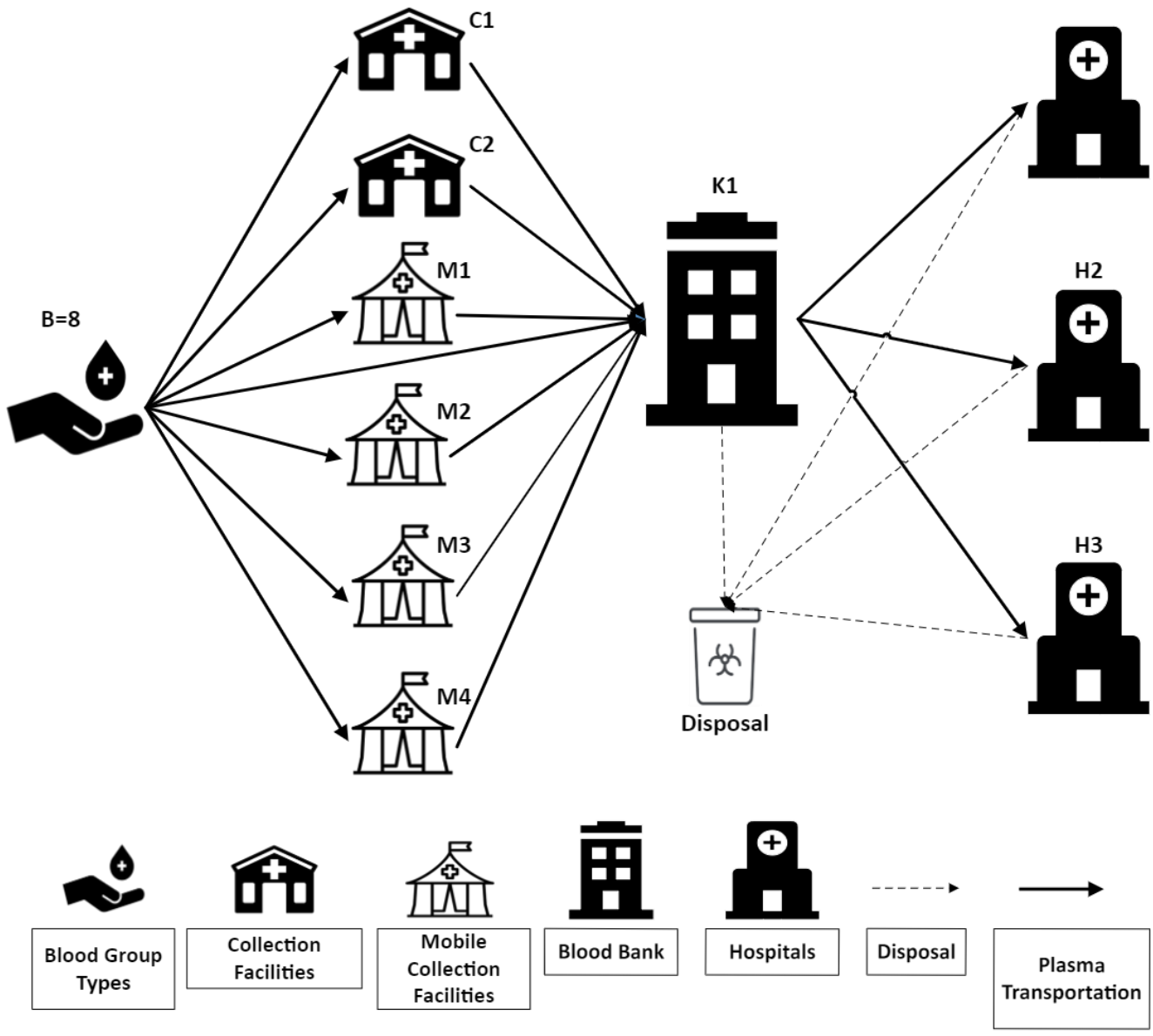

Figure 5.2: Centralized plasma supply chain framework for case study

5.1 Chapter Summary

This chapter elaborates on the real-time case study that is used to validate the developed mathematical model of centralized plasma supply chain. The case of the twin cities of Islamabad and Rawalpindi (Pakistan) is selected for the implementation of the designed centralized plasma supply chain. The 4-echelon blood plasma supply chain network of the twin cities and suburbs consists of donated plasma of all eight blood types, four potential mobile collection centers dispersed throughout the defined region, two main collection centers of both the cities of Islamabad and Rawalpindi, and a single regional blood bank catering to the twin cities and their suburbs. Along with the demand points of the supply chain that are the three hospitals selected for this specific study, which are of differing functionality and capacity in order to ensure heterogeneity in selection.

CHAPTER 6: RESULTS AND DISCUSSION

6.1 Numerical Example

The numerical results were derived using MATLAB (R2022b) on a personal computer with 16 GB RAM, Gen Intel(R) Core (TM) i7 and 2.20 GHz processor. The branch and bound algorithm are used for the solution. The solution of the case study consists of the following steps.

1. The crisp model is solved for all the objectives to obtain the payoff values as given in Table 6.1. The bound of each objective were obtained using linear programming. To generate the payoff table, the objective functions are first optimized separately. And then their values are set as an equality constraint in order to optimize the other objective turn wise. For example, in the case of operational cost, the value of the cost in the first column and first row of Table 6.1, is the optimal value of the cost function which would be set as constraint for the optimization of other functions:

    - **Step 1**: Minimize Objective Cost F1

      Subject to all the constraints and F1 = $ 3,023,973

      Once the optimal value is obtained of the cost function is obtained, we set this function as a constraint and optimized the second objective. The value of second objective (F2) of Traceability is obtained through this method in the second column of the first row.

- **Step 2:** Maximize Traceability F2

  Subject to constraints all the constraints and F2 = 31,078,000 units

  The optimal value of the traceability function obtained is used as a constraint to optimize the first objective. The value of cost function (F2) is obtained through this method in the first column of the second row.

These are employed for all the objectives until the payoff table obtained as shown in Table 6.1.

Table 6.1: Payoff table for cost and traceability objective function

Payoff Table		
	F1 ($)	F2 (Units)
F1- Operational Cost	3,023,973	159,080,000
F2- Traceability	9,029,564	31,078,000

2. Next step is to develop fuzzy membership functions for each objective to get satisfaction level. The fuzzy membership is calculated using the equation (4.25) mentioned in methodology section. Below given equations (6.1) to (6.2) are the satisfaction of the Operational Cost and the RFID-enabled Traceability, respectively. Note that slightly more weight is given to other objective functions than the Operational Cost. Results are shown in.

$$u_1 = \left\{ \begin{array}{c} 0 \\ \dfrac{9,029,564 - F1}{9,029,564 - 3,023,973} \\ 1 \end{array} \middle| \begin{array}{l} F1 \geq 3{,}023{,}973 \\ 3{,}023{,}973 < F1 < 9{,}029{,}564 \\ F1 \leq 9{,}029{,}564 \end{array} \right\} \quad (6.1)$$

$$u_2 = \left\{ \begin{array}{c} 0 \\ \dfrac{159,080,000 - F2}{159,080,000 - 31,078,000} \\ 1 \end{array} \middle| \begin{array}{l} F2 \geq 31{,}078{,}000 \\ 31{,}078{,}000 < F2 < 159{,}080{,}000 \\ F2 \leq 159{,}080{,}000 \end{array} \right\} \quad (6.2)$$

Multi-objective interactive fuzzy programming was used to solve the numerical example of the real-time case study of the plasma supply chain of the twin cities of Islamabad and Rawalpindi. The method requires conversion of a multi-objective mathematical model into a single objective problem by linearizing the problem defined and assigning weights. The optimal solution of the problem was found within the Elapsed time of 524.7 seconds. The finalized values of the objective functions after the application of the multi-objective interactive fuzzy programming; are given in Table 6.2. Where the optimal function values and the satisfaction level of each objective function of the model is specified. The specified satisfaction levels of each objective function measure the "relative percentage deviation of achieved function value" from their respective upper and lower bound values obtained as solution of the objective function as defined in Equation (6.1-6.2).

Table 6.2: Optimal objective function value with satisfaction level

Objectives	**Satisfaction level**	**Objective function value**
Operational Cost ($)	95%	3,343,624
Traceability (units)	100%	8,000,000

In order to better understand the imperative value and the computation of the satisfaction levels defined, the equation (6.1) and Table 6.2 is taken into consideration. The optimal function value of the operational cost objective is $ 3,343,624 as defined in the Table 6.2, which when put in the equation (6.1), replacing F1 results in equation (6.3) as below:

$$u_1 = \left(\frac{9,029,564 - 3,343,624}{9,029,564 - 3,023,973} \right) = 0.946 \; or \; 95\% \tag{6.3}$$

Apparent from the equation (6.3) that the optimal value of $ 3,343,624 is between the lower and upper bound values of the operational cost objective function. If F1 is supposed to be $ 9,029,564 then as per the equation (6.3) the optimal value of the cost objective function is 0. While, if the value of F1 is supposed as $ 3,023,973 then as per the equation (64) the optimal value of the cost objective function is 100. Based on this, it can be concluded that the closer the optimal value is to the lower bound, the higher is the level

of satisfaction for the solution generated. Therefore, as the optimal value of $ 3,343,624 of operational cost objective function is closer to its lower bound value of $ 3,023,973, hence the satisfaction level is computed to be 95%, as shown in equation (6.3). Also, the satisfaction level of the Traceability Objective function is computed in the same manner as described with an optimal value of 8,000,000 Healthy plasma units provided to the demand points with a confidence level of 100%: for the case study of the centralized plasma supply of the Twin cities of Pakistan.

Moreover, MATLAB (R2022b) function "intlinprog" was used to solve, optimizeand Maximize the linear programming problem of Compatibility-Prioritized plasma transfusion with integer constraints. The objective function Compatibility-Prioritized plasma transfusion can be rephrased as plasma demand satisfaction through Compatibility-Prioritized transfusion, the process of which is explained in detail in the 3.4.3. section of the third chapter. Upon solving the linear objective function, optimal objective Value was computed to be 477,000 units of Compatibility-Prioritized plasma transfused at the demand points with a confidence level of 100%; for the case study of the centralized plasma supply of the Twin cities of Pakistan, as presented through the Table 6.3. Meaning that the objective function has been maximized to this value of 477,000 plasma units, while satisfying all constraints.

Table 6.3: Optimal value of compatibility-prioritized transfusion objective

Objective	**Objective function value**
Compatibility-Prioritized Transfusion (units)	477,000

During the computation Compatibility-Prioritized Transfusion objective function, the “intlinprog” problem solver stopped at the root node, meaning that the optimal solution was achieved quickly and exploring further nodes in the branch-and-bound algorithm was not required. Also, the optimal objective value generated was within the small “gap tolerance” of the optimal value, hence very close to the optimal solution. The “gap tolerance” is a measure of how close the solver is to the true optimal solution. The smaller the gap tolerance, the closer is the solution to the true optimal solution, and the higher is the satisfaction level. Therefore, for Compatibility-Prioritized Transfusion objective function the optimal objective Value of 477,000 units was calculated with zero gap tolerance, justifying the satisfaction level of 100%, as shown in Table 6.3. To summarize, the optimal solution generated for this objective was very close to the true optimal value with quite a high degree of confidence in solution quality.

The Table 6.4 below presents the total computed cost of transporting Plasma of all eight Blood Types to the various Hospitals of our model and case study after Processing, the processing here includes the cost of collection, transportation to the blood bank, cost of screening and blood centrifugation into plasma, the cost of RFID implementation and the cost of transportation of processed plasma to the hospitals for consumption. Hence, the result Table 6.4 represents the total cost incurred till a batch of units of plasma reaches the hospital or the demand point, after going through the whole centralized supply chain.

Table 6.4: Cost of transporting plasma to the hospitals after processing

Hospitals	H1		H2		H3	
Periods	t1	t2	t1	t2	t1	t2
AB+	$ 36.0	$ 43.0	$ 53.0	$ 64.0	$ 71.0	$ 78.0
AB-	$ 36.0	$ 43.0	$ 53.0	$ 64.0	$ 71.0	$ 78.0
A+	$ 36.0	$ 43.0	$ 53.0	$ 64.0	$ 71.0	$ 78.0
A-	$ 36.0	$ 43.0	$ 53.0	$ 64.0	$ 71.0	$ 78.0
B+	$ 36.0	$ 43.0	$ 53.0	$ 64.0	$ 71.0	$ 78.0
B-	$ 36.0	$ 43.0	$ 53.0	$ 64.0	$ 71.0	$ 78.0
O+	$ 36.0	$ 43.0	$ 53.0	$ 64.0	$ 71.0	$ 78.0
O-	$ 36.0	$ 43.0	$ 53.0	$ 64.0	$ 71.0	$ 78.0

Three hospitals (H1, H2, and H3) and two periods (t1 and t2) are considered in our case study of the twin cities, and the computed cost values are specified for each combination of blood type, hospital, and period. For example, if we look at the cost of transporting AB+ blood type plasma to H1 during t1, it is $ 36 in Table 6/4. However, if you look at the same blood type but for H2 during t2, the cost is $ 43. Also, it seems that the costs generally increase for each blood type and hospital from period t1 to t2. Hence, the structure of the table allows for easy comparison between the costs associated with transporting plasma of different blood types to different hospitals during different periods, as illustrated through Figure 6.1.

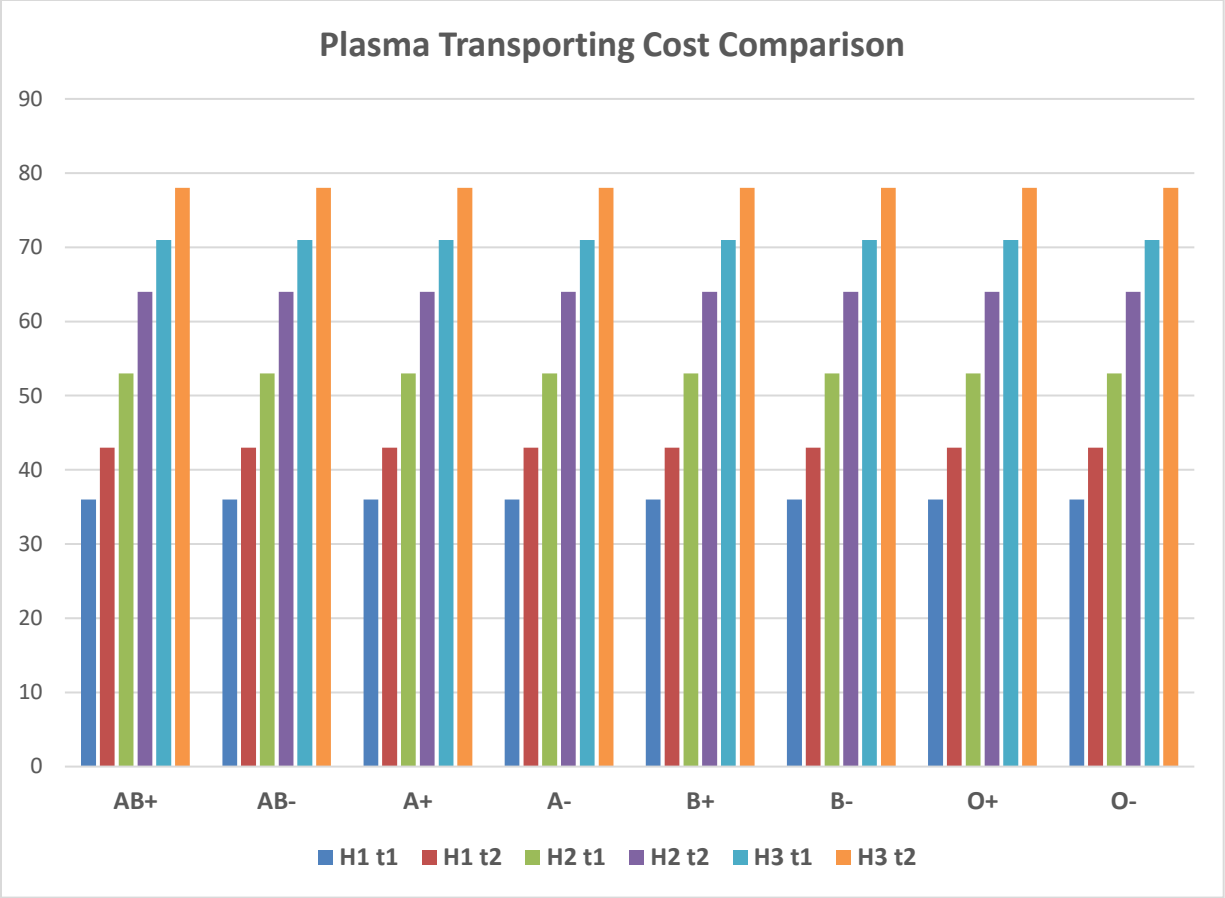

Figure 6.1: Plasma transportation cost comparison

Similarly, Table 6.5 below presents the total cost computed for the transfusion of plasma of all eight blood types at the various Hospitals of our model. The provided table provides the cost in US Dollars ($) that is associated with plasma transfusion for various blood types at different hospitals during two periods, t1 and t2. Also, like the previous Table 6.4, it includes three hospitals (H1, H2, and H3) and two time periods. The Hospitals are the demand point of the supply chain where plasma is consumed through plasma transfusion of various blood types.

Table 6.5: Cost of plasma transfusion of all blood types at the hospitals

Hospitals	H1		H2		H3	
Periods	t1	t2	t1	t2	t1	t2
AB+	$ 18.0	$ 21.0	$ 27.0	$ 32.0	$ 36.0	$ 43.0
AB-	$ 18.0	$ 21.0	$ 27.0	$ 32.0	$ 36.0	$ 43.0
A+	$ 18.0	$ 21.0	$ 27.0	$ 32.0	$ 36.0	$ 43.0
A-	$ 18.0	$ 21.0	$ 27.0	$ 32.0	$ 36.0	$ 43.0
B+	$ 18.0	$ 21.0	$ 27.0	$ 32.0	$ 36.0	$ 43.0
B-	$ 18.0	$ 21.0	$ 27.0	$ 32.0	$ 36.0	$ 43.0
O+	$ 18.0	$ 21.0	$ 27.0	$ 32.0	$ 36.0	$ 43.0
O-	$ 18.0	$ 21.0	$ 27.0	$ 32.0	$ 36.0	$ 43.0

If we look at the cost of plasma transfusion in Table 6.5 for AB+ blood type at H1 during t1, it is $ 18. And, if you look at the same blood type but for H2 during t2, the cost is $ 21. Now, this significant cost difference is not only due to the obvious reason of different time periods but can be also attributed to different type of the hospitals considered in our case study. As, it's a known fact that cost of medical care and procedures are quite lower in government hospitals as compared to private once. Figure 6.2 is the graphical representation of the comparison of transfusion cost incurred at the hospitals with varying time periods.

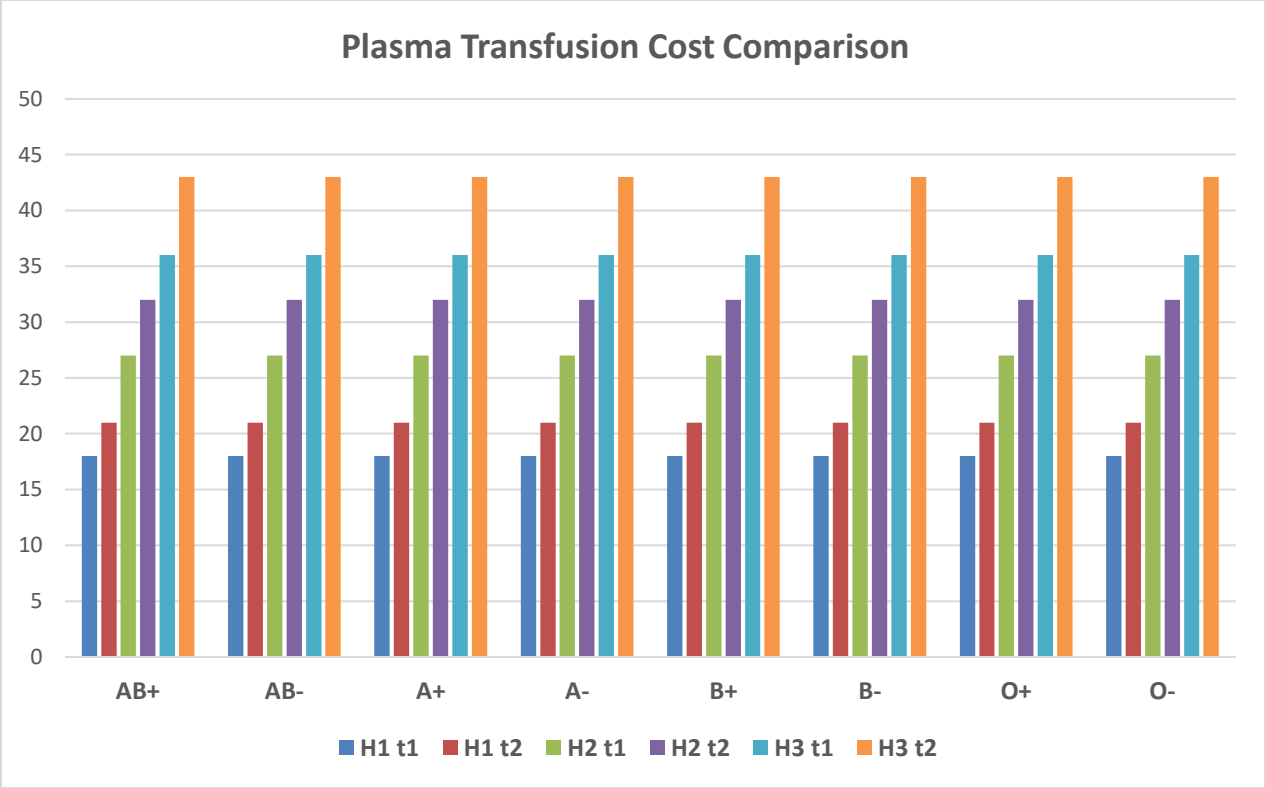

Figure 6.2: Plasma transfusion cost comparison

Comparing the Table 6.5 with the previous Table 6.4, it seems that the costs associated with plasma transfusion are generally lower than the costs of transporting plasma to hospitals after processing Reasonably so, as the processing of the whole supply chain is involved till plasma is transported to the hospital, hence a higher cost is expected, comparing to the single process of plasma transfusion.

Table 6.6 below represents the computed quantity of safe and healthy plasmas units that are transported to the demand points i.e. the hospitals, during two time periods, t1 and t2. The units are specified for each blood type i.e. AB+, AB-, A+, A-, B+, B-, O+, O-. The health of plasma units is ensured by the implementation of RFID technology, as the last

step of processes carried out at the regional blood Bank. The implementation of RFID technologies enables the centralized supply chain to efficiently trace the product in real-time.

RFID-enabled traceability allows the central medical facilities such as blood banks to be able to get updated on the lifetime of perishable items by tracking throughout the centralized plasma supply chain. Enforcing end-to-end traceability for highly valuable and highly perishable products as plasma (Hajipour et al., 2021). RFID also significantly enhances the transportation process's efficiency by merely taking advantage of tracking items via reading the tags attached to them. Hence, ensure provision of safe and healthy plasma units.

Table 6.6: Units of health plasma transported to demand points.

	t1	t2
AB+	3,000,000	1,000,000
AB-	2,000,000	3,000,000
A+	3,000,000	3,000,000
A-	3,000,000	2,000,000
B+	2,000,000	1,000,000
B-	2,000,000	2,000,000
O+	3,000,000	3,000,000
O-	3,000,000	1,016,591

Table 6.6 provides a snapshot of the quantity of health plasma units distributed to meet demand during the specified time periods for each blood type. The values in the table indicate how the distribution varies across different blood types and time periods, offering insights into the changing demands for health plasma over time. For example, during t1, 3,000,000 units of AB+ plasma are transported to demand points, while during t2, only 1,000,000 units are transported. This high variation in quantity of healthy AB+ plasma transported to the hospitals can be attributed to both the varying demand in a given time and the availability of the specific blood type plasma, in a given time period.

Similarly, Table 6.7 below provides the computed quantity of safe and health plasma units transfused the demand points i.e. the hospitals, during two time periods, t1 and t2. The units are specified for each blood type i.e. AB+, AB-, A+, A-, B+, B-, O+, O-. This table provides insights into the actual usage or consumption of health plasma units at demand points in the form of plasma transfusion, showing how the transfusion quantities vary across different blood types and time periods. The health of plasma units is ensured by the implementation of RFID technology, as the last step of processes carried out at the regional blood Bank. And the implementation of RFID technologies enables the centralized supply chain to efficiently trace the product in real-time.

Table 6.7: Units of health plasma transfused at demand points.

	t1	t2
AB+	2,955,000	955,000
AB-	1,955,000	2,955,000
A+	2,955,000	2,955,000
A-	2,955,000	1,955,000
B+	1,955,000	955,000
B-	1,955,000	1,955,000
O+	2,955,000	2,955,000
O-	2,955,000	971,591

Comparing Table 6.7 with the previous Table 6.6, you can observe the quantities transported and the quantities transfused, helping to assess the efficiency of the distribution system and the responsiveness to changing demand over time. The comparison as illustrated through Figure 6.3 allows us to assess the quantity of already scarce resource of plasma units wasted at the hospitals, due to outdating. For example, during t1, 3,000,000 units of AB+ plasma were transported to demand points, while only 2,955,000 units of AB+ plasma were transfused there. Similarly, during t2, only 1,000,000 units were transported to the hospitals, however only 955,000 units of plasma were transfused.

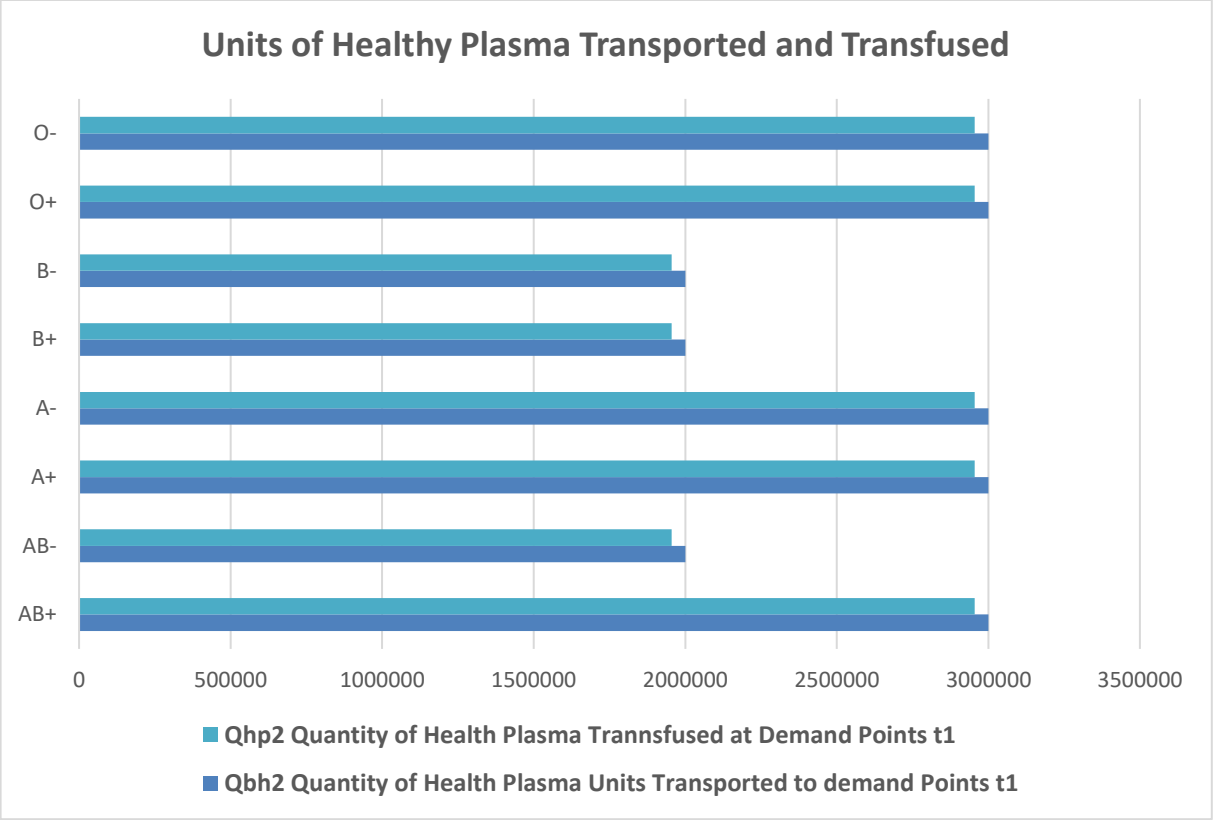

Figure 6.3: Comparison of healthy plasma units transported and transfused.

This shows the varying demand and supply of plasma of a specific blood type between the two periods. But more importantly, this comparison allows us to establish a threshold of the percentage of wastage of plasma units due to outdating at the demand points. For instance, during t1, 1.5% of AB+ plasma units were wasted; while during t2, 4.5% of AB+ plasma units were wasted. Meaning that an average of 3% AB+ plasma units were wasted. Based on these calculations, a maximum threshold of 5% of plasma units of various blood types should be expected to be wasted at the demand points due to outdating.

6.2 Sensitivity Analysis

6.2.1 Cost Sensitivity Analysis

Figure 6.4 illustrates the impact of ascending rate of plasma outsourcing on the operational cost of the supply chain with different outsourcing percentages. The Impact on operation cost is analyzed with 5%, 8%, 10%, 12%, and 15% increasing in plasma outsourcing practices within the supply chain, And the impact is observed on the operational cost values i.e. the financial expenditure associated with running the plasma supply chain at each respective outsourcing percentage.

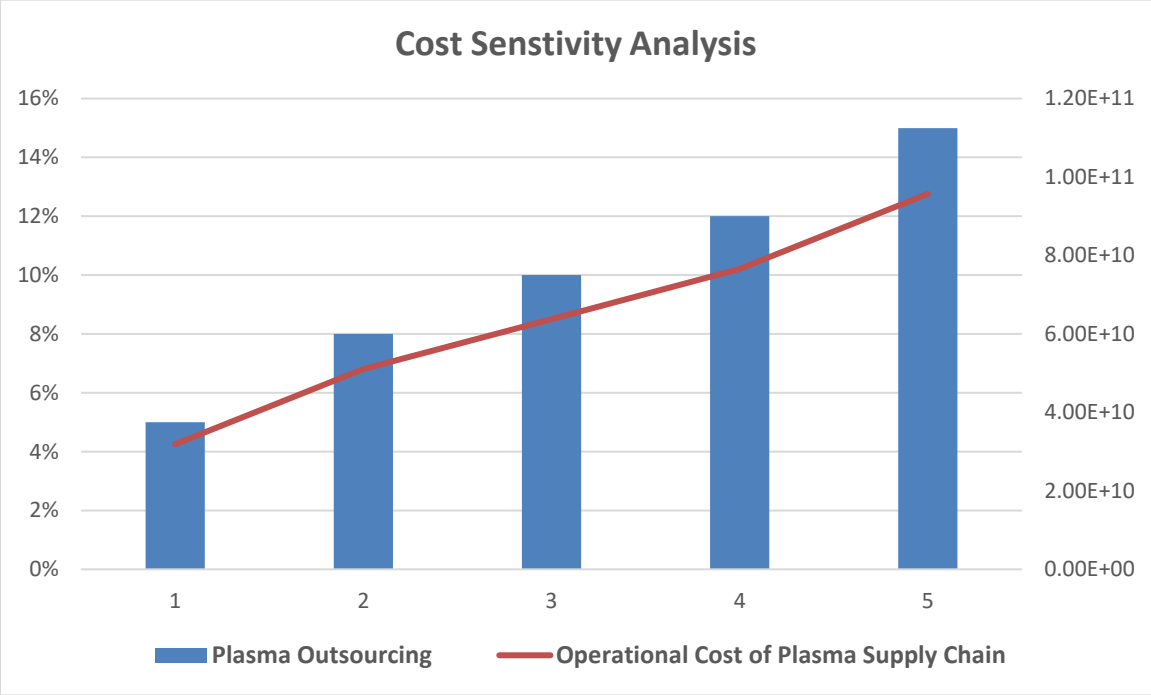

Figure 6.4: Impact of outsourcing plasma on supply chain operational cost

Apparent from Figure 6.4, as the outsourcing percentage increases, the operational cost of the plasma supply chain also increases. This suggests that outsourcing a higher proportion of plasma is associated with higher operational expenses. Even though several elements of operational cost were analyzed for the impact on the total cost, however variation in plasma outsourcing has the most significant and higher impact on the overall cost. This can be contributed to the fact that outsourcing of a single unit or batch of plasma concurs the cost that is equivalent to procuring a truck load. Hence, increased outsourcing practice leads to higher overall supply chain operational costs and should be opted for extreme lifesaving situations only.

The relationship between outsourcing percentage and operational cost may not be strictly linear. For example, the operational cost at 10% outsourcing is higher than a simple linear extrapolation from the 8% and 12% values. This indicates that there may be factors or costs that do not increase proportionally with the outsourcing percentage. The trend line indicates the economies of scale, where the cost per unit decreases as the volume of outsourced plasma increases up to a certain point. However, beyond that point, there may be diseconomies of scale, leading to increased costs per unit. However, the impact on operational cost should be interpreted in the context of overall supply chain efficiency. While outsourcing may lead to increased costs, it might also improve efficiency, reduce certain operational burdens, or enhance focus on core activities.

6.2.2 Plasma deterioration Analysis

The sensitivity analysis pertains to understanding the impact of variations in the plasma health deterioration rate on the quantity of healthy plasma units transfused at hospitals. Figure 6.5 showcases how different rates of deterioration influence the number of healthy plasma units being transfused. The objective is to assess how alterations in the rate of plasma health deterioration affect the quantity of healthy plasma units transfused at hospitals. The graph below demonstrates the changes in the quantity of healthy units transfused corresponding to varying deterioration rates of 1%, 2%, 5%, and 8%.

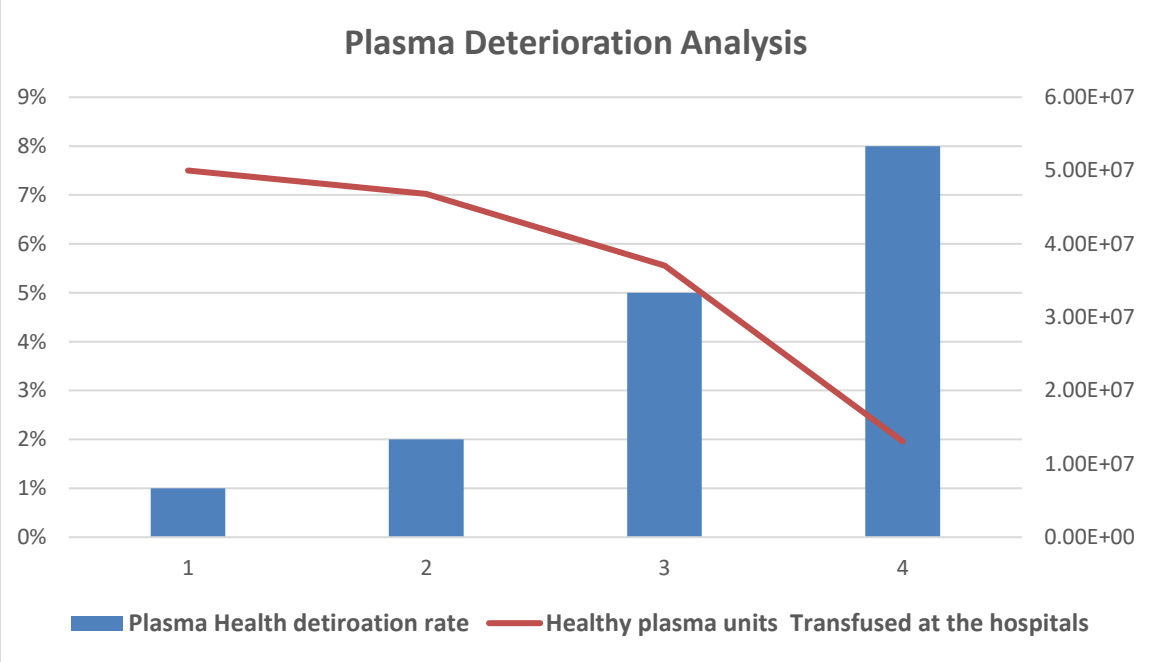

Figure 6.5: Impact of deterioration rate on quantity of healthy plasma transfused.

Apparent from Figure 6.5, with Deterioration Rate 1%, the Transfusion of Healthy Plasma Units is 5.00E+07 i.e., 50 million units. While, at a 2% Deterioration Rate the Transfusion of Healthy Plasma Units is reduced to 46.8 million units. A further decrease in results is observed when the number of transfusions is reduced to 37.1 million units only, at a 5% Deterioration Rate. Which is Substantially reduced to 13.1 million units with a Deterioration Rate of 8%

The analysis indicates a notable decrease in healthy plasma units transfused as the deterioration rate escalates. Higher deterioration rates lead to a significant reduction in the available healthy plasma for transfusion, directly impacting the capacity to provide transfusion services at hospitals. Therefore, to eliminate this significant impact of plasma deterioration rate on overall transfusion, a RFID-enabled traceable supply chain of plasma is necessary. As, RFID technology would ensure provision of healthy plasma units for transfusion, with lower deterioration rate, through providing real-time data with the centralized supply chain. Understanding the sensitivity between deterioration rates and available healthy plasma is critical for healthcare resource planning. It underscores the importance of minimizing plasma health deterioration to maintain an adequate supply of healthy plasma for transfusion purposes. Highlighting the necessity for strategies to mitigate plasma health deterioration, ensuring a consistent supply of healthy plasma units for medical treatments. Understanding the sensitivity between plasma health deterioration rates and the availability of healthy plasma for transfusion at hospitals is crucial for maintaining a robust and reliable healthcare system.

6.2.3 Prioritized Blood Type Plasma Analysis

The Impact of fluctuations in the volume availability of a High Priority Blood Type i.e. AB-, for substituted-transfusion with the demanded blood type plasma i.e. AB+ and the overall transfusions is presented through Figure 6.6. The AB+ blood type is known as the universal recipient. However, based on the prioritization substitution index developed in this research AB- is the 1st priority substitute blood group, in case of unavailability of same blood type plasma.

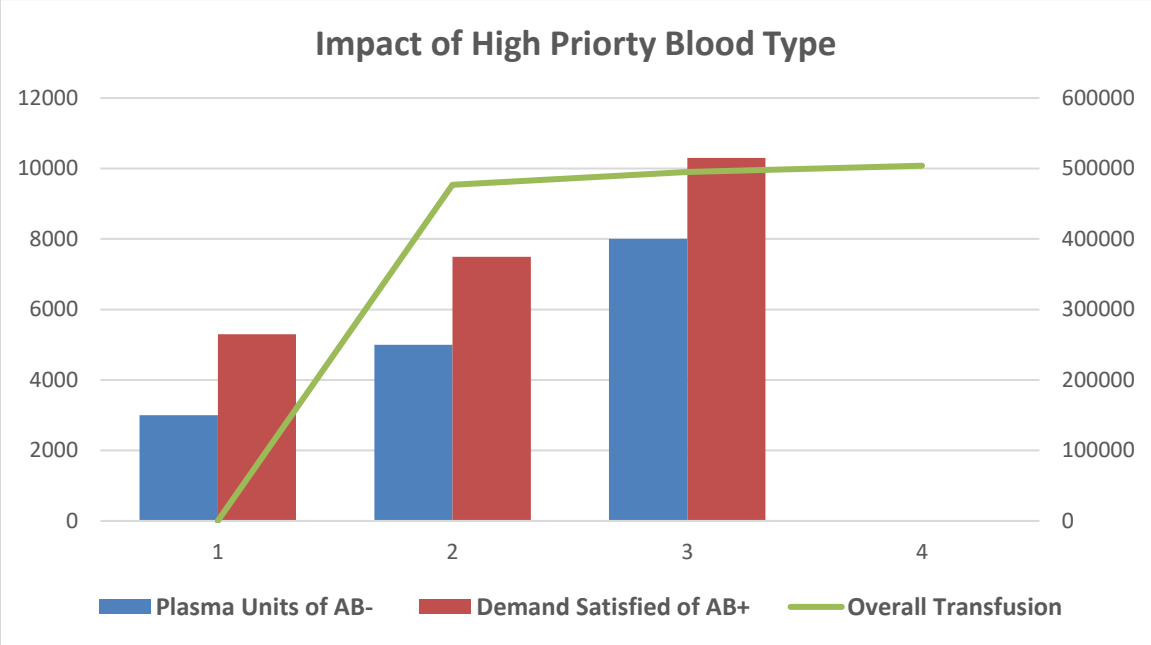

Figure 6.6: Impact of high priority blood type

The Figure 6.6 showcases transfusion scenarios where the use of AB- blood type plasma is used to meet the demand for AB+ blood type plasma, ensuring a more efficient utilization of available resources, The availability of AB- plasma in varying quantities in each scenario helps meet the demand for AB+ plasma, potentially reducing shortages and

ensuring a more flexible and adaptable transfusion system. Evidently, as the availability of AB-, the 1st priority blood type plasma surges, the satisfaction of AB+ blood type plasma demand significantly improves as well, through prioritized plasma substituted-transfusion.

However, the overall transfusion rate is mildly impacted, and an only lower rate of increase in overall transfusion process could be observed. Hence, the "Overall Transfusion" trend line reflects the total number of units transfused, highlighting the effectiveness of the strategy in meeting overall demand while considering the availability of both AB+ and AB- plasma. In summary, the table illustrates a transfusion strategy where AB- plasma serves as a high-priority substitute for AB+ plasma, contributing to the efficient and flexible management of the overall plasma supply and demand.

Moreover, the Impact of a low Priority Blood Type i.e. the plasma of O- blood group is observed on the overall substituted-transfusion rates. The O- blood type is a universal donor, meaning that the blood type is suitable for substituted-transfusion with all 8 blood types. Therefore, as illustrated through table 3, the O- blood type plasma is the last or lowest priority of almost all the blood groups. The impact of the increase in the volume of O- plasma availability on the overall transfusion rate is presented through Figure 6.7.

Apparently, from the “Overall Transfusion” tend line, a sharp increase in transfusion rate was observed initially, with an increase in O- plasma availability. However, a steady rate of rise in transfusion rate was developed with increased availability of O- plasma, soon after. This was eventually followed by a halt in the Overall Transfusion rate, and the trend line became static for further surges in the O- plasma availability.

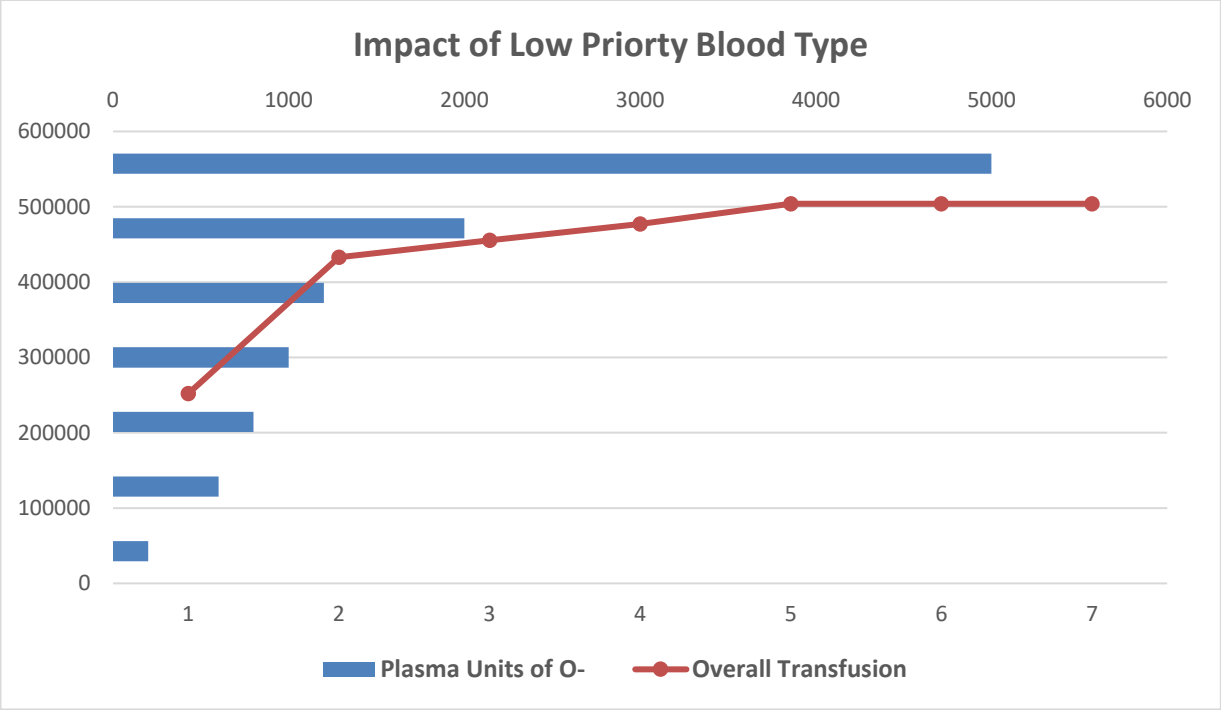

Figure 6.7: Impact of low priority blood type

In summary, the overall transfusion trend indicates a capacity to meet increasing demands for O- plasma up to a certain point, beyond which the system reaches a saturation or optimization point where further increases in demand do not lead to a proportional increase in overall transfusion. A possible reason for this case is the low priority given to O- blood type plasma, which makes it the last choice for substituted-transfusions, in case high and mediocre priority plasma types are unavailable. Hence, surge in availability of O- blood type plasma can only improve the overall transfusion and demand satisfaction rate up to a certain point only. While a more significant increase in demand satisfaction could be observed upon increased availability of 1st priority blood type plasma, as presented through figure 10; where a steady increasing trend of overall transfusion rate and demand satisfaction was established upon increasing availability of AB- blood type plasma.

6.3 Analysis of Compatibility-Prioritized Transfusion

Analysis of the impact of Compatibility-Prioritized Transfusion on the overall plasma demand satisfaction is carried out; by comparing the amount of plasma transfused in three separate scenarios. Hence, comparison of the demand satisfaction in scenarios with different transfusion strategies of; compatibility-prioritized transfusion, plasma transfusions without substituted-transfusion, and plasma transfusion without plasma outsourcing and substituted-transfusion.

As illustrated through Figure 6.8, the first scenario represents the total demand satisfaction of plasma by utilizing the compatibility-prioritized plasma transfusion strategy. Where same blood type plasma transfusion, along with substituted-transfusion of compatible blood type plasma categorized into High, mediocre and low priority blood groups for transfusion, and outsourcing of same blood type plasma from the regional blood bank is carried out; in order to satisfy the plasma transfusion demand at the hospital. In this approach, transfusions are carried out with priority given to compatible blood types. This strategy allows maximum utilization of available yet highly scares resources of various plasma units with different blood types; resulting in maximum demand satisfaction and reduced wastage of life save health care product of plasma. A total of 477000 plasma units are used for transfusion with Compatibility-Prioritized Transfusion as illustrated by Figure 6.8, which is the highest level of demand satisfaction comparatively.

In the second scenario, the element of prioritized substitute-transfusion of compatible blood type plasma is not considered. And the demand of plasma is satisfied

through same blood type plasma transfusions and outsourced same blood type plasma only. As a result, comparing to the first scenario of compatibility-prioritized plasma transfusion strategy, amount of plasma transfused is almost reduced by half and only 252000 units of plasma were used for transfusion, as presented through Figure 6.8. Hence, this scenario reflects the demand satisfaction when substituted-transfusion is not employed. Substituted-transfusion typically involves using blood or plasma from compatible blood types when the requested type is not readily available. This result signifies the importance of substituted-transfusion for plasma supply chain with uncertainty and constrained demand and supply of the required blood type plasma as substitution-transfusions comprises of half of the total transfusion in the first scenario.

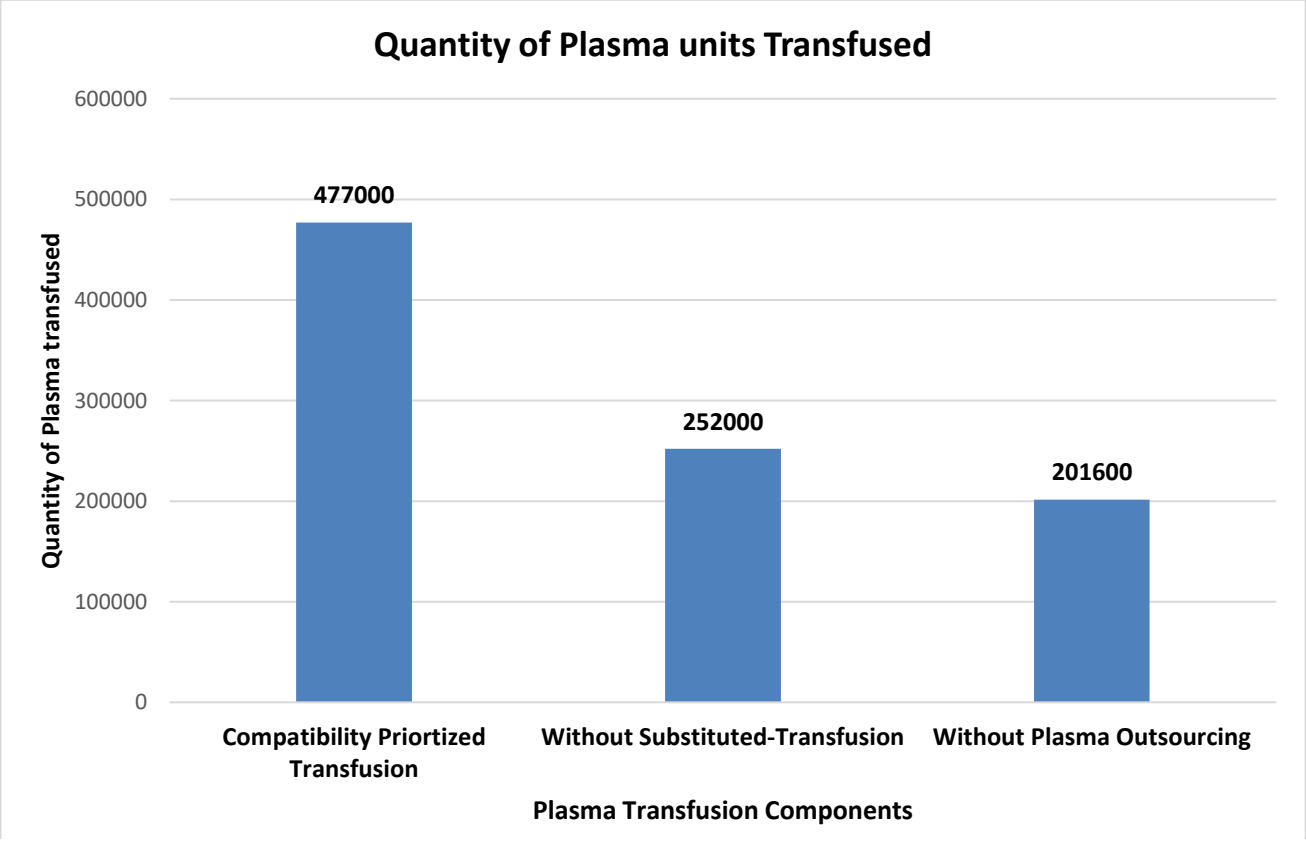

Figure 6.8: Impact of compatibility-prioritized transfusion on demand satisfaction

The last scenario is where only the available same blood type plasma is utilized for demand satisfaction, and the element of outsourcing and substituted-transfusions both are not considered. Plasma outsourcing involves obtaining plasma from regional blood bank to meet the demand. And without this strategy, the total demand satisfaction further plummeted although slightly and a total of 201600 units of same blood type plasma are transfused. The lack of a more significant impact on the quantity of plasma transfused in the absence of the element of outsourcing might be the assumption that we limit outsourcing of plasma units to 20% of overall transfusions only. Due to the high cost of the outsourcing process, the time it consumes, and its ability to highly alter the overall cost of the whole supply chain, as discussed in section 6.2 and presented through Figure 6.4. Hence, outsourcing of plasma should be kept to a minimum and for extreme cases only.

To summaries, Compatibility Prioritized Transfusion approach seems to result in the highest level of demand satisfaction, indicating that prioritizing compatibility in transfusions is an effective strategy for meeting the demand for blood or plasma units. And Without Substituted-Transfusion the demand satisfaction is lower compared to compatibility-prioritized transfusion. This implies that in scenarios where the requested blood type is not readily available, not employing substituted-transfusion may limit the ability to meet the overall demand. Moreover, the lowest demand satisfaction is observed when plasma outsourcing is not utilized. This suggests that incorporating external sources for plasma, likely with different blood types, is crucial for achieving higher overall demand satisfaction. Hence, the results highlight the importance of compatibility prioritized transfusion and the strategic use of substituted-transfusion and plasma outsourcing in optimizing the transfusion process to meet the demand for blood or plasma units. These

strategies can enhance flexibility, improve efficiency, and maximize the overall satisfaction of demand for different blood types.

6.4 Analysis of RFID-Enabled Healthy Plasma Transfusions

The impact of RFID-enabled traceability technology on the healthy plasma demand satisfaction is analyzed by comparing the amount of safe and healthy plasma units, that reached hospitals and is transfused there, with and without the use of RFID-enabled traceability technology.

Evident from Figure 6.9, in scenario where RFID technology is used to trace and centralize the plasma supply chain, 8,000,000 units of healthy plasma units were successfully transported and transfused at the demand points, with the assistance of RFID (Radio-Frequency Identification) technology. RFID technology allows for the tracking and monitoring of plasma units throughout the supply chain, ensuring that only healthy products that were traceable at every stage of their life, are used for transfusion.

RFID enabled traceability allows the central medical facilities such as blood banks to be able to get updated on the lifetime of perishable items by tracking throughout the centralized plasma supply chain. Enforcing end-to-end traceability for highly valuable and highly perishable products as plasma (Hajipour et al., 2021). RFID also significantly enhances the transportation process's efficiency by merely taking advantage of tracking items via reading the tags attached to them. RFID enabled traceability implementation in the plasma supply chain would result in reducing the perishability likelihood in the plasma

units received by the endpoints of the chain, i.e., the hospitals; gradually minimizing wastage throughout the network.

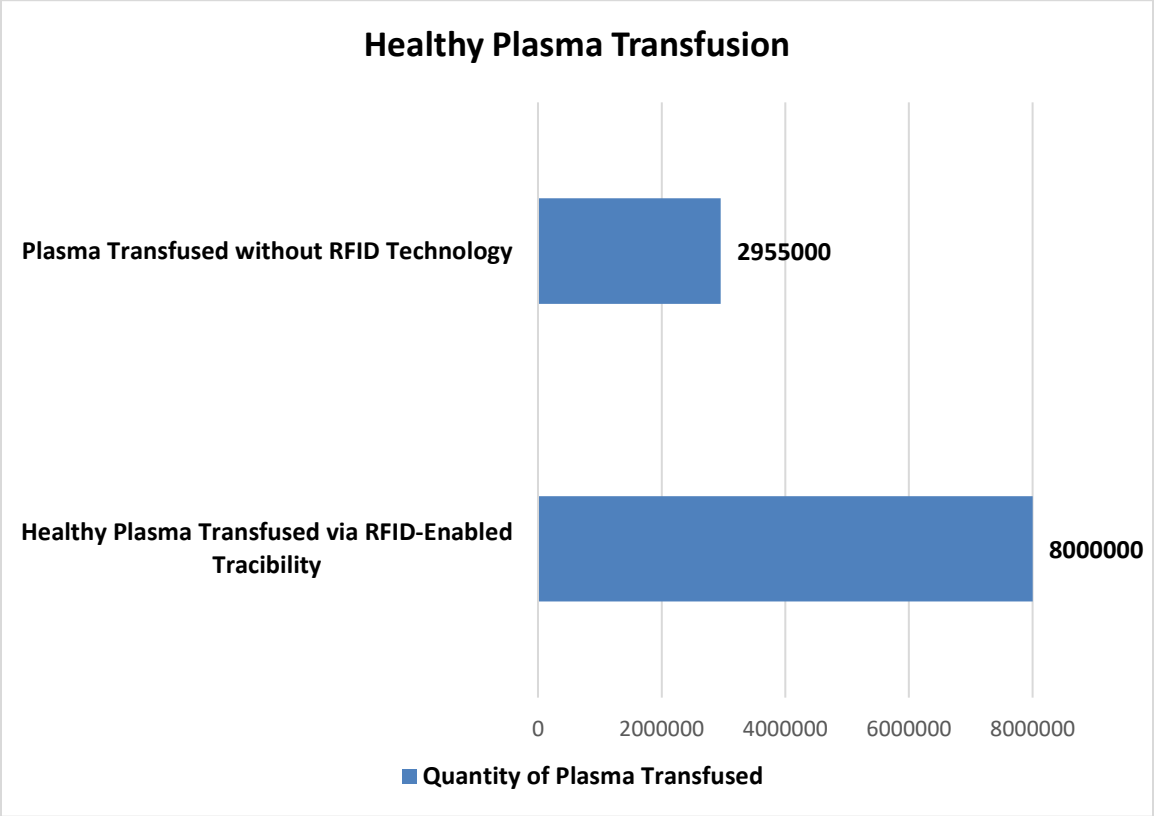

Figure 6.9: Impact of RFID implementation on healthy plasma transfusions.

Compared to the first scenario, a significantly lower number healthy plasma units reaches hospitals without the use of RFID technology for traceability. As, the absence of RFID technology results in a lack of real-time tracking and monitoring capabilities, and the overall number of healthy plasma units that reached hospitals in this scenario is 2,955,000, as illustrated through Figure 6.9. The amount of 2,955,000 plasma units is approximately 60% lower than the amount of healthy plasma units transferred to hospitals and transfused with RFID-enabled tracible plasma supply chain system.

To summarize, the higher number of healthy plasma units transfused using RFID-enabled traceability suggests that this technology has been effective in ensuring a larger quantity of safe products reaching hospitals. RFID allows for better visibility and control over the entire supply chain, reducing the risk of errors, contamination, or mishandling. While the lower number of healthy plasma units in this scenario where RFID is not involved indicates potential challenges or limitations in ensuring the traceability and safety of products without the aid of RFID technology. Without real-time tracking, the risk of errors or uncertainties in the supply chain may lead to a reduced number of safe products reaching hospitals.

The comparison underscores the importance and impact of RFID-enabled traceability technology in ensuring the safe and efficient transfusion of healthy plasma units. The higher number in the RFID-enabled scenario suggests that the technology contributes to improved supply chain management, reducing risks, and enhancing the overall safety and traceability of blood products reaching hospitals.

6.5 Practical Implications

This section specifies the practical implication of the research carried out, as summarized below:

- The incorporation of RFID-enabled traceability provides practical benefits for monitoring and tracking plasma units throughout the supply chain. This traceability will not only ensure the integrity and quality of plasma units but will also aid in rapid identification of healthy units, reducing the risk of transfusion errors.
- The result of const analysis suggest that outsourcing should be the last option for saving life and demand satisfaction, as the increasing Outsourcing practices has a significant and proportional impact the on overall operational cost.
- The research's focus on maximizing plasma transfusions with a priority on blood type compatibility has significant implications for improving patient outcomes. Healthcare facilities can implement this prioritization strategy to minimize the risk of adverse transfusion reactions and optimize plasma utilization.
- The ability to minimize operational costs through the developed methodologies directly impacts the financial sustainability of plasma supply chain operations. Implementing cost reduction strategies can free up resources for investment in other critical areas of healthcare.
- The real-time case study conducted in a developing country offers valuable insights that can be directly applied to similar regions facing resource constraints and healthcare challenges. These insights may guide local governments, non-governmental organizations, and healthcare providers in improving their plasma supply chain management practices.

- Overall, the research contributes to the resilience and reliability of the healthcare system by ensuring a stable and efficient supply of plasma components, which are essential for life-saving medical interventions.
- The methodologies proposed in this research offer practical tools for decision-makers in centralized plasma supply chain management. As the organizations can optimize the allocation of resources, such as plasma collection, storage, and distribution, based on varying and uncertain demand and supply conditions.

In conclusion, the practical implications of this research extend to a wide range of stakeholders involved in plasma supply chain management, offering strategies to address uncertainty, enhance traceability, and optimize resource allocation, ultimately improving healthcare outcomes in developing countries and beyond.

6.6 Managerial Insights

This section provides the managerial insights of the research carried out, as summarized below:

- The optimal operational cost of $ 3,343,624 represents a cost-efficient supply chain design. Managers can use this insight to allocate resources effectively, reduce unnecessary expenses, and streamline their budgeting processes.
- The high satisfaction level of 95% for operational costs indicates that the supply chain design is financially sustainable. Managers can be confident that the cost optimization strategy is robust, ensuring long-term financial stability.
- The optimal value of 8,000,000 units for traceability (RFID-enabled) suggests a high degree of traceability in the plasma supply chain. This insight can be leveraged to

strengthen traceability measures further, enhance product tracking, and improve quality control.

- The high traceability value aligns with the central focus on patient safety in healthcare logistics. Managers can use this result to assure stakeholders and regulatory bodies of the supply chain's commitment to maintaining product quality and patient well-being.
- The satisfaction levels provide managers with a clear, quantifiable way to evaluate the supply chain's performance. Decision-makers can use these levels as KPIs to monitor the supply chain's effectiveness over time and make informed decisions accordingly.
- The high satisfaction levels in operational cost, traceability, and Compatibility-Prioritized Transfusion suggest that the supply chain is effectively utilizing resources. This insight can guide resource allocation decisions and justify investments in technology and infrastructure to maintain these high standards.
- The incorporation of RFID-enabled traceability systems is a managerial imperative. Managers should invest in and deploy RFID technology to enhance traceability, thereby improving the overall quality and safety of the plasma supply chain.
- The research emphasizes the importance of prioritizing blood type compatibility during plasma transfusions. Managers should establish and enforce policies and procedures that prioritize the matching of donor plasma with recipient blood types, reducing the risk of adverse reactions.
- Establish key performance indicators (KPIs) that reflect the objectives of cost minimization, traceability maximization, and blood type compatibility prioritization. Regularly monitor and report on these metrics to gauge the success of supply chain operations.

- For organizations in developing countries, the real-time case study can provide valuable insights and serve as a reference point for improving their own plasma supply chain systems, tailored to their specific circumstances.

Incorporating these managerial implications into the plasma supply chain management framework can help organizations enhance their operations, reduce costs, and improve patient outcomes while navigating the challenges of uncertain demand and supply in the healthcare sector.

6.7 Theoretical Implications

The theoretical insight of this research is summarized as below:

- The research provides a theoretical framework for managing uncertainty in centralized plasma supply chains. This framework, which includes chance constraint programming and interactive multi-objective fuzzy programming, contributes to the broader field of operations research and supply chain management by addressing the challenge of uncertain demand and supply.
- The utilization of the mean-variance approach within chance constraint programming has theoretical implications for risk management in supply chains. It extends the understanding of how this approach can be used to ensure the robustness and reliability of supply networks, which can be applied beyond plasma supply chains.
- The concept of Pareto-optimal solutions in interactive multi-objective fuzzy programming contributes to the theoretical understanding of decision-making under multiple, often conflicting, objectives. It offers a practical approach to exploring and identifying optimal solutions within the context of complex supply chain systems.

- The incorporation of RFID technology for traceability has theoretical implications for the fields of logistics and healthcare. It demonstrates the potential of advanced technologies in enhancing traceability and ensuring the quality and safety of healthcare products, which can be generalized to other supply chain contexts.
- The research emphasizes the theoretical significance of prioritizing blood type compatibility in healthcare logistics. It underlines the importance of aligning product characteristics with recipient needs, promoting patient safety, and minimizing adverse events in the context of supply chain theory.
- The application of the theoretical framework in a real-time case study in a developing country enriches the theoretical underpinnings of the research. It demonstrates the practical feasibility and adaptability of theoretical models in diverse, real-world settings.

In summary, the theoretical implications of this research span various domains, including operations research, multi-objective decision-making, technology integration, etc. These theoretical contributions enrich the broader academic discourse on supply chain theory and its application in complex and critical healthcare logistics systems.

6.8 Chapter Summary

Multi-objective interactive fuzzy programming was used to solve the numerical example of plasma supply chain of the twin-cities of Islamabad and Rawalpindi as defined in Chapter 5. A Payoff table was developed for the objective functions, in order to obtain the lower and upper bound of the optimal objective Value. The values of the payoff table are then used to compute the satisfaction levels of the Optimal Objective Function value. The Optimal

Objective Function value of each objective along with the satisfaction level shown in Table 6.2 and Table 6.3, presents the final solution of the methodology and the mathematical model applied for studying the case of the twin cities of Pakistan. Based on the mathematical model developed for plasma supply chain, the methodologies adopted, and the results generated, practical and theoretical implications of the study along with the managerial insights are provided in this section, as well.

CHAPTER 6: CONCLUSION

In the dynamic landscape of healthcare logistics, the management of centralized plasma supply chains with the context of uncertain demand and supply has been a topic of critical importance. This research considers the complexities in this field, aiming to address key objectives of operational cost minimization, enhanced traceability through RFID technology, and the optimization of plasma transfusions with a focus on blood type compatibility prioritization. Through the development of a multi-objective linear programming mathematical model for the designed centralized plasma supply chain and the application of advanced methodologies along with validation through a real-time case study, this study has provided valuable insights and recommendations for practitioners and stakeholders in the healthcare sector.

This research, being the first of its kind, aims to optimize the multi-objective linear programming model developed. The supply chain network developed for this research is based on four echelon centralized plasma supply chains: consisting of donor blood groups, blood collection facilities, blood centers and. The multi-tier supply chain model includes various blood types donated by voluntary donors, which are collected at the mobile collection facilities and collection facilities. The collected blood units of various blood types are then transported to the central or the regional blood bank. Where the blood units are screened for diseases and infections and then plasma is separated from screened blood through the process of centrifugation; and RFID Tags are implemented. Plasma units are then transported from the blood bank to the demand point or hospitals. To satisfy the demand of patients at the hospital plasma substituted-transfusion along with standard

plasma transfusion are opted. Outsourcing of plasma units of various blood types is also made by hospitals in case of emergencies, from the other hospitals and the blood bank of the centralized system. This process of substituted-transfusion is prioritized and the whole plasma transfusion process optimized as the third objective of the study. Where the top three most compatible blood type plasma is used for substituted-transfusion, in case same blood type plasma is not available.

Moving on, the multi-objective mathematical model is developed such that the first objective function minimizes the total operational cost of the plasma supply chain network designed. The second objective function of the model focuses on maximizing the plasma supply chain traceability through RFID implementation. Here traceability employed is in terms of undamaged product received by the demand point, or to be more specific, the healthy plasma units received and transfused only at the hospitals. The third objective function maximizes the Compatibility-Prioritized Plasma Transfusions using the Compatibility Prioritization Substitution Index. Where Priority is defined in three levels i.e., “s=1” has the highest substitution priority, “s=2” has intermediate substitution priority and “s=3” has the lowest substitution priority; in order to satisfy demand.

Furthermore, the integration of RFID-enabled traceability systems enhances the quality and safety of plasma units by providing real-time monitoring and tracking, reducing the likelihood of transfusion errors. While Blood type compatibility prioritization in plasma transfusions, as emphasized in this research, contributes to improved patient and transfusion outcomes. As it significantly reduces the usage of bad or expired blood and mitigates the chances of adverse reaction to the transfused plasma type due to prioritization of top three blood types. Hence, by aligning plasma units with compatible blood types and

introducing RFID-enabled traceability, healthcare facilities can mitigate the risk of adverse transfusion reactions and optimize the use of this precious resource.

Moreover, Two-fold methodology has been employed for this study. Firstly, the chance constraint programming is implemented through the mean-variance approach. Which offers a robust solution to mitigate uncertainties in the supply chain by converting the uncertain parameters of demand and supply into deterministic parameters by incorporating their respective mean and variance. This method equips decision-makers with the tools to ensure the stability and reliability of plasma supply networks in the face of changing demand and supply conditions. Secondly, the core methodology of interactive multi-objective fuzzy programming is applied to solve the developed mathematical model. Providing a flexible framework for organizations to navigate trade-offs among cost reduction, traceability enhancement, and blood type compatibility prioritization. This approach empowers decision-makers to make informed choices tailored to their specific goals and constraints.

The real-time case study conducted in the twin cities of Islamabad and Rawalpindi, of the developing country of Pakistan; serves as a practical benchmark for organizations facing resource limitations and unique healthcare challenges. It underscores the adaptability and applicability of the methodologies discussed in this research, showcasing how they can be customized to meet the specific needs of diverse healthcare systems.

However, it is important to recognize the limitations inherent in this research, such as model complexity, data availability, technological barriers, and regional variations, as they may impact the generalizability and implementation of these findings. The success of

the proposed methodologies depends on the availability and quality of data. In developing countries as Pakistan, data collection and storage infrastructure are not adequate enough to ensure data accuracy and completeness. The issue is further aided by the lack of cooperation by the medical facilities. Who, due to their fear of allegations malpractice and in order to ensure confidentiality, are unwilling to address data quires. Also, implementing some of the proposed strategies, such as blood type compatibility prioritization, may require additional resources that the Healthcare sector may struggle to allocate. Similarly, implementing RFID-enabled traceability systems might also possess as a challenging for the healthcare industry that lacks the necessary technological infrastructure, expertise and the Initial set-up costs can be significant limitations.

Moreover, models assume that uncertainties in the mathematical model follow a specific probability distribution, which may not always hold in all the real-world scenarios. Deviations from these assumptions can impact the accuracy of the model's predictions. Healthcare systems, especially in the developing countries, face severe resource constraints. Also, the real-time case study focuses on a specific region in a developing country, and the findings may not be universally applicable. Plasma supply chains can vary significantly from one location to another, and the findings might not be generalizable to all contexts.

Furthermore, the research does not account for all external factors that can affect plasma supply chains, such as natural disasters, political instability, and economic fluctuations. These factors can have a significant impact on supply chain operations. The research also doesn’t account for the dynamic nature of healthcare regulations. Ethical considerations, such as consent and privacy, regarding the use of RFID and patient data,

might pose a significant limitation in model implementation; hence must be carefully managed. These limitations should be considered when applying the research findings and methodologies in practice. Organizations and researchers should adapt the approaches to their specific contexts and address these limitations as they strive to improve centralized plasma supply chain management.

In conclusion, the research offers a comprehensive framework for addressing the uncertainties and complexities within centralized plasma supply chains. By embracing these methodologies and adapting them to their contexts, organizations can achieve more cost-effective, traceable, and patient-focused plasma supply chain management. This not only strengthens the resilience of healthcare systems but ultimately enhances the quality of care provided to patients, making a significant contribution to the advancement of healthcare logistics in both developing and developed regions.

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APPENDIX A: RESEARCH DATA

The following are the names and the location of the facilities opted for the development of a centralized plasma supply chain model, of the Twin-cities case study along with their notations.

Blood Type

1. AB+ (b1)
2. AB- (b2)
3. A+ (b3)
4. A- (b4)
5. B+ (b5)
6. B- (b6)
7. O+ (b7)
8. O- (b8)

Collection Centers

1. AIFT Blood Donation Center, RWP (c1)
2. Blood Donation Society Pakistan Center, ISB (c2)

Mobile Collection Centers

1. Pakistan Red Crecent Society (m1)
2. Blood Donation Society Twin Cities (m2)
3. Pakistan Thalassemia Center (m3)

4. BDSP NUST Drive (m4)

Blood Bank

1. Regional Blood Center, Islamabad (k)

Hospitals

1. Ali Medical Center (h1)
2. Quaid-e-Azam International Hospital (h2)
3. PAF Hospital (h3)

The following tables contain the data set used for numerical problem solving, obtained through market research and literature of the same problem size.

Table A.1: Distance between collection centers and blood bank

Collection Center	**Distance to the Blood Bank (km)**
AIFT Blood Donation Center, RWP (c1)	18.3 km
Blood Donation Society Pakistan Center, ISB (c2)	36.3 km

Table A.2: Distance between mobile collection centers and blood bank

Mobile Collection Center	**Distance to the Blood Bank (km)**
Pakistan Red Crecent Society (m1)	13.4 km
Blood Donation Society Twin Cities (m2)	36.3 km
Pakistan Thalassemia Center (m3)	14.6 km
BDSP NUST Drive (m4)	21.7 km

Table A.3: Distance between the blood bank and hospitals

Blood Bank	**Ali Medical Center**	**Quaid-e-Azam International Hospital**	**PAF Hospital**
Regional Blood Center, Islamabad	15.1 km	24.3 km	18.4 km

Table A.4: Capacity of collection centers

Collection Center	**Capacity (units)***
AIFT Blood Donation Center, RWP (c1)	50000
Blood Donation Society Pakistan Center, ISB (c2)	60000

Table A.5: Capacity of mobile collection centers

Mobile Collection Center	**Capacity (units)***
Pakistan Red Crecent Society (m1)	1500
Blood Donation Society Twin Cities (m2)	500
Pakistan Thalassemia Center (m3)	2000
BDSP NUST Drive (m4)	1000

Table A.6: Capacity of the blood bank

Blood Bank	**Capacity (units)***
Regional Blood Center, Islamabad (k)	200000

**Note: 1 unit of blood is equivalent to 500 ml of blood*

Table A.7: Capacity of the hospitals

Hospitals	**Ali Medical Center (h1)**	**Quaid-e-Azam International Hospital (h2)**	**PAF Hospital (h3)**
Capacity (units)*	20000	30000	70000

Table A.8: Blood testing capacity of blood bank

Blood Bank	**Capacity (units)***
Regional Blood Center, Islamabad (k)	150000

Table A.9: Blood to plasma conversion capacity of blood bank

Blood Bank	**Capacity (units)***
Regional Blood Center, Islamabad (k)	100000

**Note: 1 unit of blood is equivalent to 500 ml of blood*

Table A.10: Rate of disposing plasma units at hospitals.

Hospitals	**Ali Medical Center (h1)**	**Quaid-e-Azam International Hospital (h2)**	**PAF Hospital (h3)**
Outdated Plasma Discarded (%)	0.04%	0.048%	0.05%

Table A.11: Weekly demand of plasma units at the hospitals

Plasma Type Demand (units)	**Ali Medical Center (h1)**	**Quaid-e-Azam International Hospital (h2)**	**PAF Hospital (h3)**
AB+ (b1)	4000	8000	16000
AB- (b2)	1000	5000	10000
A+ (b3)	16000	22000	48000
A- (b4)	7000	12000	25000
B+ (b5)	5000	10000	20000
B- (b6)	7000	12000	25000
O+ (b7)	18000	25000	50000
O- (b8)	10000	18000	40000

Table A.12: Cost of collecting blood units at the collection centers.

Time period 1 (2022)		**Time period 2 (2023)**	
Collection Center	**Cost ($)**	**Collection Center**	**Cost ($)**
AIFT Blood Donation Center, RWP (c1)	$ 8.0	AIFT Blood Donation Center, RWP (c1)	$ 9.0
Blood Donation Society Pakistan Center, ISB (c2)	$ 8.0	Blood Donation Society Pakistan Center, ISB (c2)	$ 9.0

Table A.13: Cost of collecting blood units at the mobile collection centers.

Time period 1 (2022)		**Time period 2 (2023)**	
Mobile Collection Center	**Cost ($)**	**Mobile Collection Center**	**Cost ($)**
Pakistan Red Crecent Society (m1)	$ 8.7	Pakistan Red Crecent Society (m1)	$ 10.0
Blood Donation Society Twin Cities (m2)	$ 9.0	Blood Donation Society Twin Cities (m2)	$ 10.3
Pakistan Thalassemia Center (m3)	$ 8.7	Pakistan Thalassemia Center (m3)	$ 10.0
BDSP NUST Drive (m4)	$ 9.4	BDSP NUST Drive (m4)	$ 11.0

Table A.14: Cost of collecting blood units at blood bank.

Time period 1 (2022)		**Time period 2 (2023)**	
Blood Bank (k)	**Cost ($)**	**Blood Bank (k)**	**Cost ($)**
Regional Blood Center, Islamabad	$ 6.5	Regional Blood Center, Islamabad	$ 7.2

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Table A.15: Cost of transportation from collection centers to blood bank

Time period 1 (2022)		**Time period 2 (2023)**	
Collection Center	**Transportation Cost ($)**	**Collection Center**	**Transportation Cost ($)**
AIFT Blood Donation Center, RWP (c1)	$ 2.2	AIFT Blood Donation Center, RWP (c1)	$ 2.4
Blood Donation Society Pakistan Center, ISB (c2)	$ 2.4	Blood Donation Society Pakistan Center, ISB (c2)	$ 2.5

Table A.16: Cost of transportation from mobile collection center to blood bank

Time period 1 (2022)		**Time period 2 (2023)**	
Mobile Collection Center	**Transportation Cost ($)**	**Mobile Collection Center**	**Transportation Cost ($)**
Pakistan Red Crecent Society (m1)	$ 2.7	Pakistan Red Crecent Society (m1)	$ 2.9
Blood Donation Society Twin Cities (m2)	$ 2.9	Blood Donation Society Twin Cities (m2)	$ 3.0
Pakistan Thalassemia Center (m3)	$ 2.7	Pakistan Thalassemia Center (m3)	$ 2.9
BDSP NUST Drive (m4)	$ 3.0	BDSP NUST Drive (m4)	$ 3.3

Table A.17: Cost of transportation from blood bank to hospitals

Time period 1 (2022)				**Time period 2 (2023)**			
	Transportation Cost ($)				**Transportation Cost ($)**		
Blood Bank (k)	**Ali Medical Center (h1)**	**Quaid-e-Azam International Hospital (h2)**	**PAF Hospital (h3)**	**Blood Bank (k)**	**Ali Medical Center (h1)**	**Quaid-e-Azam International Hospital (h2)**	**PAF Hospital (h3)**
Regional Blood Center, Islamabad	$ 2.5	$ 2.5	$ 2.5	Regional Blood Center, Islamabad	$ 2.7	$ 2.7	$ 2.7

Table A.18: Cost of processing blood units at blood bank

Time period 1 (2022)		**Time period 2 (2023)**	
Processes at Blood Bank (k)	**Cost ($)**	**Processes at Blood Bank (k)**	**Cost ($)**
Screening & Testing	$ 4.7	Screening & Testing	$ 6.5
Conversion of Blood into Plasma	$ 12.6	Conversion of Blood into Plasma	$ 14.5

Table A.19: Cost of plasma units transfusion at hospitals

Time period 1 (2022)				**Time period 2 (2023)**			
	Ali Medical Center (h1)	**Quaid-e-Azam International Hospital (h2)**	**PAF Hospital (h3)**		**Ali Medical Center (h1)**	**Quaid-e-Azam International Hospital (h2)**	**PAF Hospital (h3)**
Plasma Transfusion Cost ($)	$ 21.7	$ 20.0	$ 16.3	**Plasma Transfusion Cost ($)**	$ 27.0	$ 25.3	$ 21.7

Table A.20: Cost of outsourcing plasma units from blood bank for hospitals

Time period 1 (2022)				**Time period 2 (2023)**			
	Plasma Outsourcing Cost ($)				**Plasma Outsourcing Cost ($)**		
Blood Bank (k)	**Ali Medical Center (h1)**	**Quaid-e-Azam International Hospital (h2)**	**PAF Hospital (h3)**	**Blood Bank (k)**	**Ali Medical Center (h1)**	**Quaid-e-Azam International Hospital (h2)**	**PAF Hospital (h3)**
Regional Blood Center, Islamabad	$ 32.5	$ 29.0	$ 28	Regional Blood Center, Islamabad	$ 36.2	$ 32.5	$ 30.7

Table A.21: Cost of discarding blood and plasma units at blood bank

Time period 1 (2022)		**Time period 2 (2023)**	
Discarded at Blood Bank	**Cost ($)**	**Discarded at Blood Bank**	**Cost ($)**
Blood after Screening	$ 14.5	Blood after Screening	$18.1
Outdated Plasma	$ 21.7	Outdated Plasma	$ 25.3

Table A.22: Cost of discarding plasma units at hospitals

Time period 1 (2022)				**Time period 2 (2023)**			
	Ali Medical Center (h1)	**Quaid-e-Azam International Hospital (h2)**	**PAF Hospital (h3)**		**Ali Medical Center (h1)**	**Quaid-e-Azam International Hospital (h2)**	**PAF Hospital (h3)**
Outdated Plasma Discarding Cost ($)	$ 23.5	$ 23.5	$ 23.5	Outdated Plasma Discarding Cost ($)	$ 27	$ 27	$ 27

Table A.23: Cost of holding plasma units at blood bank.

Time period 1 (2022)		**Time period 2 (2023)**	
Plasma at Blood Bank	**Cost ($)**	**Plasma at Blood Bank**	**Cost ($)**
Holding Cost	$ 6.5	Holding Cost	$ 7.2

Table A.24: Cost of holding plasma units at hospitals.

Time period 1 (2022)				**Time period 2 (2023)**			
Plasma at the Hospitals	**Ali Medical Center (h1)**	**Quaid-e-Azam International Hospital (h2)**	**PAF Hospital (h3)**	**Plasma at the Hospitals**	**Ali Medical Center (h1)**	**Quaid-e-Azam International Hospital (h2)**	**PAF Hospital (h3)**
Holding Cost ($)	$ 7.6	$ 6.9	$ 6.7	Holding Cost ($)	$ 9.0	$ 8.3	$ 8.0

Table A.25: Cost of RFID tag implementation

Time period 1 (2022)		**Time period 2 (2023)**	
Discarded at Blood Bank	**Cost ($)**	**Discarded at Blood Bank**	**Cost ($)**
Blood after Screening	$ 1.6	Blood after Screening	$ 2.2