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Research Article

Designing a robust blood supply chain model under conditions of uncertainty in demand

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Abstract

The blood supply chain is one of the most important challenges in health and medical networks. In this paper, a non-linear multi-objective robust model of the blood supply chain under the condition of blood demand uncertainty is presented. The proposed model is a three-level model including supply, processing, and distribution of blood. The decision variables determined after solving the model include, the amount of blood collected from donors in the collection centers and sent to the blood centers, the product sent from the blood centers to the hospital, the optimal number of blood collection centers, the amount of product inventory in each center and hospital, and the amount of product shortage in each center and hospital. The aim of the proposed model is to reduce the costs of blood transfusion, shortages, and waste of blood and increase the reliability of the blood supply chain. To validate the proposed model, sensitivity analyses were performed using real data with different dimensions in the Barron solver in GAMS software. Sensitivity analyses of the model were carried out on the costs of waste, shortage, and the objective function. The results confirmed the validity and efficiency of the proposed model.

***Keywords*:** Blood supply chain; Multi-objective; Robust model; Shortage; Uncertainty; Waste

1. Introduction

Blood products are essential items in the fields of health and medicine, and despite advances made in the medical field, a suitable alternative has not yet been found for it (Nahofti Kohneh et al., 2016). One of the most important issues in the blood supply chain is the provision of sufficient and healthy blood under normal and critical conditions. Due to the importance of blood products in saving human life, the perishable nature of blood products, and random behavior in supply and demand areas, the blood supply chain has received more attention from experts, scientists, and governments than the supply chain of other normal goods (Rezaei-Malek et al., 2016). Shortage of blood can increase mortality risks at hospitals; on the contrary, high inventory levels could generate wastage of this scare resource (Ramírez and Labadie, 2017).

In the design and modeling of the blood supply chain, researchers have paid less attention to blood collection centers by donors and timely blood and blood products transfusion to demand points (blood centers), while they have a significant impact on the reliability of the supply chain (Motamedi et al., 2019). To supply and respond to the blood demand needed by hospitals, shortages and wastages of blood should be considered as two factors of uncertainty because they have the greatest impact on the entire supply chain (Motamedi et al., 2020).

The aim of this research is to provide an optimal and robust model of the 3-level blood supply chain, including the supply, processing, and distribution of blood, considering the uncertainty in blood demand. A schematic of the research problem is presented in Figure 1. As can be seen, blood collected from donors is transported to blood centers for testing and preparing the blood products needed by patients. Then, blood centers meet the blood demand of hospitals and medical centers based on their need for blood and blood products. The decision variables determined after solving the model include, the amount of blood collected from donors in the collection centers and sent to the blood centers, the product sent from the blood centers to the hospital, the optimal number of blood collection centers, the amount of product inventory in each center and hospital, and the amount of product shortage in each center and hospital. Therefore, the decision variables of the model are determined in different scenarios with the objectives of maximizing the reliability of the supply chain and minimizing the costs of blood transfusion, waste and wastage, and blood shortage under conditions of uncertainty in the blood demand. Due to the non-deterministic parameters of the problem, the value of the objective functions and variables of the model under post-crisis conditions can be very different from those under pre-crisis conditions. To reduce the value of this difference, a robust model is first built based on non-deterministic parameters for all available scenarios. Then real data from a blood transfusion organization are applied to solve the model using exact methods.

The remainder of this paper is organized as follows: Section 2 reviews relevant literature, and at the end, the gap and research model are described. In section 3, the proposed approach of the research is presented. In section 4, sensitivity analyses are presented. Finally, section 5 presents the conclusions and future studies.

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2. Literature Review

In this section, the literature related to the blood supply chain is briefly reviewed. The results are summarized in Table 1.

Muriel et al. (2014) proposed an integer linear programming considering total cost minimization and the number of donors required. They considered distinct constraints such as capacity, proportionality, and demand fulfillment. Jokar and Hosseini-Motlagh (2015) presented an optimization model to decrease blood shortage, blood wastage, and blood supply costs in emergencies. The aim of this model was to determine the optimal number and service areas of blood facilities under different disaster scenarios using mixed integer linear programming. Fereiduni and Shahanaghi (2016) presented a multi-period model for a blood supply chain in an emergency situation to optimize decisions related to locating blood facilities and distributing blood products after natural disasters. They proposed a robust network to capture the uncertain nature of blood supply chain during and after disasters. Cheraghi et al. (2016) proposed a mixed integer linear programming model for blood supply chain network design with the need for making both strategic and tactical decisions throughout a multiple planning period. A robust programming approach was developed to handle the inherent randomness in the model parameters. Cheraghi and Hosseini-Motlagh (2017) presented a fuzzy-stochastic mixed integer linear programming model to design a blood supply chain network for disaster relief. To deal with the uncertainty in the model parameters, a fuzzy programming approach was considered, and a combination of the expected value and the chance constrained programming was applied to solve the proposed model. Ensafian et al. (2017) developed a stochastic multi-period mixed-integer model for collection, production, storage, and distribution of platelet in blood transfusion organizations, ranging from blood collection centers to clinical points. Patil et al. (2018) presented a model wherein the blood stocks are redistributed from one blood bank to another with the assurance of meeting the minimum demand during an emergency to avoid stockout.

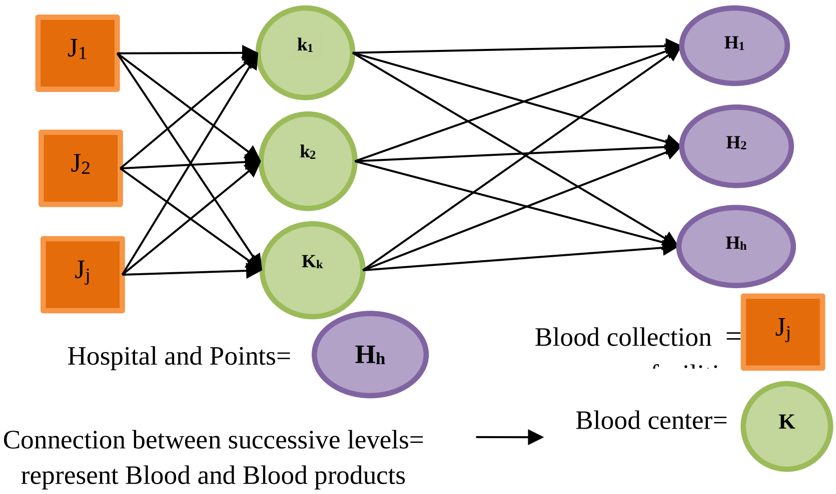

Fig. 1. Research problem schematic

Ekici et al. (2018) discussed the effect of processing time limit on collection operations. They believed that their discussions lead to interesting research areas worth future investigation from both practical and theoretical perspectives. The aim of the proposed model was to determine the quantity and location of facilities and the best strategy to allocate them under three different scenarios, while the goals are minimizing costs and shortages of blood. The proposed model was developed using a robust optimization approach. Baş et al (2018) considered the blood donation appointment scheduling problem, aiming at balancing the production of different blood types among days to provide a quite constant feeding of blood units to the blood donation system. They proposed a framework for appointment reservation that accounts for both booked donors and donors arriving without a reservation. Osorio et al. (2018) presented a multi-objective stochastic integer linear programming model to optimize two objectives: the total cost and the number of donors required. They developed an integrated approach that generates robust solutions that consider the stochastic nature of demand and guarantees that features such as proportionality and compatibility are met. Ghatreh Samani et al. (2018) proposed a multi-objective mixed integer linear programming model for designing an integrated blood supply chain network for disaster relief. The their model included all the special properties of blood supply chains involving uncertain demand of blood products and their irregular supply, perishability of blood products, and shortage avoidance.

Khalilpourazari and Arshadi Khamseh (2019) proposed a new multi-objective mathematical model to design efficient and effective blood supply chain network in earthquakes. To solve the proposed multi-objective mixed integer linear programming model, five multi-objective decision-making methods as well as the lexicographic weighted Tchebycheff method were utilized to provide the decision maker with Pareto optimal solutions.

Hamdan and Diabat (2020) presented a bi-objective robust optimization model for the design of blood supply chains that are resilient against disaster. The two-stage stochastic optimization model was proposed with the aim of minimizing the time and cost of delivering blood to hospitals after the occurrence of a disaster while, considering possible disruptions in blood facilities and transportation routes. A Lagrangian relaxation-based algorithm was developed that was capable of solving large-scale instances of the model. Derikvand et al. (2020) presented a robust stochastic bi-objective programming model for an inventory-distribution problem in a blood supply chain. The first objective attempted to minimize the total number of shortages and wastages, and the second objective maximized the connection between two different types of hospitals. Mathematical approximations were employed to remove the nonlinear terms, and a hybrid solution approach, combining the ε-constraint and the Lagrangian relaxation method, was applied to solve the proposed bi-objective model.

Razavi et al. (2021) presented a multi-objective mathematical model with the objectives of minimizing costs, minimizing the maximum level of dissatisfaction with unfairness among affected areas in terms of blood distribution to field hospitals, and maximizing the greatest coverage of demand to allocate blood to field hospitals. A new hybrid algorithm based on improved multi-choice goal programming and genetic algorithm with real data was developed to solve the problem. Robust optimization was also used to deal with the uncertainty of the baseline scenario. Pouraliakbari‑Mamaghani et al. (2022) proposed a fuzzy-robust multi-objective optimization model for blood supply chain network design for disaster relief. The objective of this problem was to minimize (1) the expected total cost of the system, (2) the implicit cost associated with patients' waiting in hospitals, and (3) unsatisfied demands. Babazadeh Rafiei et al. (2023a) presented a mathematical model to reduce the risk of the blood supply chain under the conditions of the COVID-19 pandemic. They proposed a scenario-based multi-objective model with the aim of reducing the risk of the blood supply chain under the conditions of the COVID-19 pandemic. To avoid failures that may affect the entire supply chain, Babazadeh Rafiei et al. (2023b) identified and ranked the risks affecting the blood supply chain during the COVID-19 pandemic. Babazadeh Rafiei et al. (2024) provided a mathematical model to reduce the risk of the blood supply chain in pandemic conditions, based on which, a stable multi-objective scenario-based model was presented with the aim of reducing the risk of the blood supply chain in critical conditions.

As reviewed recently, most studies have ignored disruptions and uncertainties in the blood transfusion supply chain, and few studies have paid attention to the reliability of the blood supply chain. In addition, the blood transfusion supply chain has been seen to be less multi-level, and in most of the presented models, reliability in blood transfusion facilities is either not considered or addressed in the form of chains without levels. Therefore, in this research, reliability in blood transfusion centers will be considered at two levels: supply and production. On the other hand, most of the presented models have been in the form of integer linear programming, which has reduced the problem-solving space and rendered the results far from reality. In this paper, a mixed integer non-linear programming model is presented so that the results are closer to reality. In addition, in most previous studies, the blood supply chain model was considered with the aim of minimizing the shortage and waste of blood and blood products, and the maximization of effective factors was not addressed. In this research, in addition to minimizing the cost of shortages and waste of blood and blood products in the blood supply chain, maximizing the reliability of the supply chain is also considered.

Table 1
Summary of the reviewed papers

Reference	Supply chain network					Critical conditions	Target		Modeling approach	Uncertainty			Solution method			Period		Blood products		Case Study
	Supply and collection	Production	Demand and distribution	Inventory	Transportation		Single objective	Bi/Multi objective		Fuzzy / Possible	Accident	Robust	Heuristic	Accurate	Simulation	A course	Several courses	Single product	Several products	
Muriel (2014)	✓							Minimize donors needed to meet demand, minimize total production costs for planning horizons	Integer linear programming		✓			✓			✓		✓	

Jokar (2015)	✓					✓	Minimize shortage, waste and cost		Mixed integer linear programming			✓		✓		✓		✓		
Fereiduni (2016)	✓	✓	✓			✓	Minimize the total cost		Dynamic optimization model with robust optimization approach		✓	✓			✓		✓		✓	✓
Cheraghi (2016)	✓		✓				Minimize the cost of the entire network		Mixed integer linear programming model			✓		✓			✓	✓		
Ensafian (2017)	✓	✓	✓				Minimize the total cost		Stochastic multi-period mixed-integer model		✓				✓		✓	✓		✓
Cheraghi (2017)	✓	✓	✓		✓	✓	Minimize the total cost of the supply chain		Mixed integer linear programing	✓				✓			✓			✓
Patil (2018)			✓	✓		✓	Availability of blood bank inventory as well as waste reduction		Forecasting		✓			✓		✓		✓		
Ekici (2018)	✓		✓			✓	Cost minimization - maximizing blood collection and processing		Linear Programming & mixed integer programming	✓	✓						✓	✓		
Habibi-Kouchaksaraei (2018)	✓	✓	✓	✓		✓		Cost minimization & deficiency minimization	Bi-objective & multi-period			✓		✓			✓	✓		✓
Bas (2018)	✓						Maximum blood donation from donors		Mixed Integer Linear Programming		✓			✓			✓		✓	✓

Osorio (2018)	✓	✓						Minimize the total cost of collecting blood and minimize the number of blood donors	Integer linear programming model & multiple objective programming		✓			✓		✓			✓	✓
Ghatreh Samani (2018)	✓	✓	✓			✓		Minimization: total supply chain cost, maximum indirect demand, time interval between blood production in regional blood centers and consumption in hospitals	Multi-objective mixed integer linear programming model	✓	✓			✓			✓		✓	✓
Khalilpourazari (2019)	✓			✓	✓	✓		Minimize total blood supply chain costs & total shipping time	Multi-objective mixed integer linear programming model,					✓			✓	✓		✓
Derikvand (2020)			✓	✓				Minimize the total number of deficiencies and wastes	Robust stochastic bi-objective model			✓	✓				✓	✓		✓
Hamdan (2020)	✓		✓		✓	✓		Minimize the time and cost of blood transfusions to hospitals	Two-stage robust optimization model			✓	✓				✓		✓	✓
Razavi (2021)	✓		✓		✓	✓		Cost minimization, maximizing coverage of demand points and balanced distribution of blood between demand points	Multi-objective mathematical model			✓	✓				✓			✓
Pouraliakbari-Mamaghani (2022)	✓		✓	✓		✓		Minimize the cost of the entire system, the cost of waiting for patients in the hospital and unforeseen demand	Robust possibility programming			✓					✓	✓		✓
Babazadeh Rafiei (2023a)	✓	✓	✓	✓		✓		Multi-objective model with the aim of reducing the risk and uncertainty in supply	Robust stochastic bi-objective model			✓					✓		✓	✓

Babazadeh Rafiei (2023b)	✓		✓			✓	Identified and ranked the risks affecting the blood supply chain during the COVID-19 pandemic		Risk matrix								✓	✓		✓
Babazadeh Rafiei (2024)	✓	✓	✓	✓		✓			Scenario-based multi-level and multi-objective mathematical model					✓			✓		✓	✓
This Research	✓	✓	✓	✓		✓		Minimize total cost and maximize reliability	Multi-objective mixed nonlinear programming model			✓		✓			✓		✓	✓

3. Proposed Approach

3.1. Model formulation

In this section, a scenario-based supply chain model is presented to describe the discussed problem. Thus, scenarios must be specified in the first stage. The scenarios considered in this study are defined as follows. According to the amount of supply and demand of blood and its products in different periods of time and especially in critical situations, there will always be three states of shortage, surplus, and balance in the amount of blood storage. In the blood supply chain, shortages or wastes occur if supply and demand changes are not at the same level. In other words, if the change in supply is more than the demand, it causes waste, and if it is less than the demand, it causes a shortage (and vice versa in connection with the changes in demand). Table 2 presents all possible situations related to changes in supply and demand. In this research, two scenarios are considered, one based on increasing demand and the other based on decreasing demand. In the first scenario, the demand for blood decreases (row 3 of Table 2), and in the second scenario, the demand for blood increases (row 5 of Table 2). According to experts from the blood transfusion organization, the probabilities of the first and second scenarios are 0.6 and 0.4, respectively. In the following, a scenario-based model is presented to describe the problem in more detail. A mixed non-linear two-objective mathematical model is presented to describe the problem. The indicators, parameters, and decision variables of the model are introduced in Table 3.

Table 2
Scenarios related to changes in supply and demand

Row	Supply	Demand	Result
1	Increase supply by amount X	Increase demand by amount X	Balance in the blood supply chain
2	Increase supply by amount X	Consider demand as a constant	The wastage of blood
3	Increase supply by amount X	Reduce demand by amount Y	The wastage of blood
4	Reduce supply by amount Y	Consider demand as a constant	The shortage of blood
5	Reduce supply by amount Y	Increase demand by amount X	The shortage of blood
6	Reduce supply by amount X	Reduce demand by amount X	Balance in the blood supply chain
7	Consider supply as a constant	Consider demand as a constant	Balance in the blood supply chain

Table 3
Indices, parameters, and decision variables in the mode

Indicas and Parameters	
$j \in J$	Collection of Blood Collection Facilities
$k \in K$	Collection of Blood Centers
$h \in H$	Hospital Complex
$t \in T$	Period
$p \in P$	Collection of Blood Products
$s \in S$	Possible Scenario
Parameters	
$\bar{\beta}_1$	Average confidence in the condition and safety of blood transfusion in terms of temperature and other items from the collection site ***j*** to the blood center ***k***
$\bar{\beta}_2$	Average confidence in the operation of laboratory equipment in collection centers
$\bar{\beta}3^s_{jkt}$	Average confidence in meeting the blood demand in the blood center ***k*** from the collection center ***j*** in period ***t***.
$\bar{\delta}^1_j$	Average percentage of non-standard blood packaging at the collection site ***j***
$\bar{\delta}^2_k$	Blood and blood products in the blood center ***k.***
CC_{jt}	The cost of collecting each unit of blood from donors by the j collection facility in period t.
CV_{pkht}	The cost of transporting each unit of product ***p*** from the blood center ***k*** to hospital ***h*** in period ***t***.
CP_{pkt}	Production cost per unit of product ***p*** in the blood center ***k*** in period ***t***.
CV'_{jk}	The cost of transporting each unit of blood from the collection point ***j*** blood center ***k*** in period ***t***.
CH'_{pht}	Average cost of maintaining each unit of product type ***p*** in hospital ***h*** in period ***t***.
CH''_{pkt}	Average cost of maintaining each unit of product type ***p*** in the blood center ***k*** in period ***t***.

Equations 1 and 2 describe the objective functions. The first objective function (1) maximizes the reliability value of the blood supply chain in different scenarios, which include: confidence in the conditions and safety of blood transportation in terms of temperature fluctuations, confidence in the operation of laboratory equipment in the blood collection center, and confidence in meeting the blood demand in the blood center. The second objective function (2) minimizes the total cost of the supply chain in different scenarios, which includes the costs of non-standard blood packaging, storage, transportation, production, shortage, and waste. Constraint (3) guarantees that the blood produced does not exceed the blood sent from the collection centers in scenario (*s*). Constraint (4) shows the maximum storage capacity of product (*p*) in the hospital for scenario (*s*). Constraint (5) shows the maximum capacity of blood centers to store product (*p*) in scenario (*s*). Constraint (6) shows the maximum blood collection facility capacity in scenario (*s*). Constraint (7) shows the inventory balance in the hospital for scenario (*s*). Constraint (8) shows the inventory balance in the blood center for scenario (*s*). Constraint (9) determines the amount of blood wastage in the blood centers for scenario (*s*). Constraints (10 and 11) indicate the shortage in hospital and blood center, respectively, in scenario (*s*). Constraint (12) guarantees that the product produced exceeds the product sent to the hospital in scenario (*s*). Constraint (13) indicates to the amount of product sent to demand point in scenario (*s*). Constraint (14) guarantees that blood is not collected more than the blood centers require in scenario (*s*). Constraints (15, 16 and 17) ensure that blood centers have either an inventory or shortage in a given period. Constraint (18) ensures flow balance in the collection facilities and transfers all the blood received by the collection facilities to the blood centers. Constraint (19) shows the amount of product (*p*) produced from the amount of blood sent to the blood centers in scenario (*s*). Constraint (20) shows the control constraint for the uncertainty in the demand of product (*p*) in scenario (*s*) in the hospital. If the value of ξ^s_{pht} is equal to zero, we will not have unsatisfied demand, and otherwise we have unsatisfied demand. Constraints (21, 22, and 23) express the types of decision variables.

$$\textbf{Max Z1} = \sum_s pro_s \left(\left(\bar{\beta}_1 \times \sum_k \sum_t \sum_j cb'^s_{jkt} \div Db^s_{jkt}\right)\right) \times \left(\bar{\beta}_2 \times \sum_j \sum_t N''^s_{jt} \times u2_{jt} \div \sum_k Db^s_{jkt}\right)\right) \times (\bar{\beta}3^s_{jkt} \times \sum_k \sum_t (Cb'^s_{jkt} \div Db^s_{kjt}) \tag{1}$$

$$\textbf{Min Z2} = \sum_s pro_s \Big(\left(\sum_p \sum_k \sum_t IN'^s_{pkt} \times CH''_{pkt}\right) + \Big(\sum_j \sum_t (N''^s_{jt} \times ccn\Big) + \left(\sum_p \sum_h \sum_t IN''^s_{pht} \times CH'_{pht}\right) + \left(\sum_p \sum_k \sum_h \sum_t Q^s_{pkht} \times CV_{pkht}\right) + \left(\sum_p \sum_h \sum_t De'^s_{pht} \times CS'_{pht}\right) + \left(\sum_p \sum_k \sum_t De''^s_{pkt} \times CS''_{pkt}\right) + \left(\sum_j \sum_k \sum_t Cb'^s_{jkt} \times CV'_{jkt}\right) + \left(\sum_p \sum_k \sum_t PR^s_{pkt} \times CP_{pkt}\right) - \left(\sum_j \sum_t Cb^s_{jt} \times CC_{jt}\right) + \tag{2}$$

$$\sum_j \left(\bar{\delta}_j^1 \times \left(\sum_t Cb_{jt}^s \times CC_{jt}\right)\right) + \sum_k \left(\bar{\delta}_k^2 \times \left(\sum_p \sum_t PR_{pkt}^s \times CP_{pkt}\right)\right) + \left(\sum_p \sum_k \sum_t {WB'_{pkt}}^s \times CW'_{pkt}\right)\right)$$

Subject to:

$\sum_j Cb'^s_{jkt} \geq \sum_p PR_{pkt}^s$	$\forall\ k \in K, t \in T, s \in S$	(3)
${IN''_{pht}}^s \leq u4_{pht}$	$\forall\ p \in P, h \in H, t \in T, s \in S$	(4)
${IN'_{pkt}}^s \leq u1_{pkt}$	$\forall\ p \in P, k \in K, t \in T, s \in S$	(5)
${N''_{jt}}^s \times u2_{jt} \geq Cb'^s_{jkt}$	$\forall\ j \in J, t \in T, s \in S$	(6)
${IN''_{ph(t-1)}}^s + \sum_k Q_{pkht}^s - \sum_k D_{pkht}^s + De'^s_{pht} = {IN''_{pht}}^s$	$\forall\ p \in P, h \in H, t \in T, s \in S$	(7)
$\sum_j Cb'^s_{jkt} \geq \sum_p PR_{pkt}^s$	$\forall\ k \in K, t \in T, s \in S$	(8)
${IN''_{pht}}^s \leq u4_{pht}$	$\forall\ p \in P, h \in H, t \in T, s \in S$	(9)
${IN'_{pkt}}^s \leq u1_{pkt}$	$\forall\ p \in P, k \in K, t \in T, s \in S$	(10)
${N''_{jt}}^s \times u2_{jt} \geq Cb'^s_{jkt}$	$\forall\ j \in J, t \in T, s \in S$	(11)
${IN''_{ph(t-1)}}^s + \sum_k Q_{pkht}^s - \sum_k D_{pkht}^s + De'^s_{pht} = {IN''_{pht}}^s$	$\forall\ p \in P, h \in H, t \in T, s \in S$	(12)
$\sum_p {IN'_{pkt-1}}^s + \sum_j Cb'^s_{jkt} - Db_{kt}^s - \sum_p {WB'_{pkt}}^s = \sum_p {IN'_{pkt}}^s$	$\forall\ k \in K, t \in T, s \in S$	(13)
$\sum_p {WB'_{pkt}}^s = \sum_j Cb'^s_{jkt} \times \varphi$	$\forall\ k \in K, t \in T, s \in S$	(14)
$De'^s_{pht} \leq \sum_k D_{pkht}^s - {IN''_{pht}}^s$	$\forall\ p \in P, h \in H, t \in T, s \in S$	(15)
$De''^s_{pkt} \leq Db_{kt}^s - \sum_p {IN'_{pkt}}^s$	$\forall\ k \in K, t \in T, s \in S$	(16)
$PR_{pkt}^s \geq \sum_h Q_{pkht}^s$	$\forall\ p \in P, k \in K, t \in T, s \in S$	(17)
$\sum_h Q_{pkht}^s = \sum_h D_{pkht}^s - De'^s_{pht}$	$\forall\ p \in P, k \in K, t \in T, s \in S$	(18)
$\sum_j Cb'^s_{jkt} \leq Db_{kt}^s$	$\forall\ j \in J, k \in K, t \in T, s \in S$	(19)
${IN''_{pht-1}}^s - {IN''_{pht}}^s + \xi_{pht}^s + \sum_k Q_{pkht}^s = \sum_k D_{pkht}^s$	$\forall\ p \in P, h \in H, t \in T, s \in S$	(20)
$Q_{pkht}^s, PR_{pkt}^s, N''_{jt}, {WB'_{pkt}}^s \in Z^+$		(21)
${De'_{pht}}^s, {De''_{pkt}}^s, PR_{pkt}, Cb_{jt}^s, Cb'^s_{jkt}, {IN'_{pkt}}^s, {IN''_{pht}}^s$ and $\xi_{pht}^s \geq 0$		(22)
$z_1, z_2, y_1, y_2\ \epsilon\{0.1\}$		(23)

3.2. Robust optimization model

Due to fluctuations and uncertainty in demand, the values of objective functions and optimal variables of the investigated problem can be different from the values of objective functions and variables obtained from the presented model. To reduce the value of this difference, a robust model is first built based on non-deterministic parameters for all available scenarios. In a robust optimization model, there are two types of variables: design variables and control variables. The design variables are decision variables whose optimal value is not conditioned on the realization of uncertain parameters. The variables in this set cannot be adjusted once a specific realization of the data is observed. Control variables are decision variables that are subject to adjustment once uncertain parameters are observed. Their optimal value depends both on the realization of uncertain parameters and on the optimal value of the design variables. The constraints of the robust model include: structural and control constraints. Structural constraints do not have parameters and non-deterministic variables, whereas control constraints have parameters or non-deterministic variables. In this paper, a robust formulation based on Mulvey et al. (1995) is used to stabilize the research model in the face of fluctuations and uncertainty in demand.

The linear optimization models have the following structure (24 to 27). In this model, X and Y denote the vectors of the design and control variables, respectively. In addition, S and P_s represent the set of available scenarios and the probability of each scenario, respectively ($\sum_{s=1}^{S} P_s = 1$). Constraints (25) and (26) denote the structural and control constraints of the problem, respectively.

$$\boldsymbol{min\ Z} = C^T X + d^T Y \tag{24}$$

Subject To:

$$AX = b \tag{25}$$

$$B_s X + C_s Y = e_s \qquad \forall\ s \tag{26}$$

$$X \text{ and } Y \geq 0 \qquad \forall\ s \tag{27}$$

Now, we define δ_s as a set of error vectors that measure the infeasibility of the control constraints under scenario s. Therefore, the robust mathematical model for the above mathematical model (24 to 27) can be expressed as follows.

$$\boldsymbol{min}\ \sigma(x, y_1, y_2, \dots, y_s) + \omega\, p(\delta_1, \delta_2, \dots, \delta_s) \tag{28}$$

Subject To:

$$AX = b \tag{29}$$

$$B_s X + C_s Y_S + \delta_s = e_s \qquad \forall s \tag{30}$$

$$X \text{ and } Y_s \geq 0 \qquad \forall s \tag{31}$$

In the above model, $\sigma(x, y_1, y_2, \dots, y_s)$ and $p(\delta_1, \delta_2, \dots, \delta_s)$ measure the stability of the solution, and the stability of the model, respectively. It should be noted that different functions can be defined for each statement; for example $p(\delta_1, \delta_2, \dots, \delta_s)$ is usually considered equal to$\sum_{s\epsilon S} P_s \delta_s$. In multiple scenarios, the objective function $Z = C^T X + d^T Y$ becomes a random variable taking the value $Z_s = C^T X + {d_s}^T Y_s$, with probability P_s. The term $\sigma(x, y_1, y_2, \dots, y_s)$ was defined by Malloy et al. (1995) as the sum of the expected value (32), and λ was considered as the coefficient of variance of the objective function.

$$\sigma(x, y_1, y_2, \dots, y_s) = \sum_{s \in S} P_s \; Z_s + \lambda \sum_{s \in S} P_s \, (Z_s - \sum_{s' \in S} P_{s'} \, Z_{s'} \,)^2 \tag{32}$$

A quadratic linear programming model will be obtained by replacing $\sigma(x, y_1, y_2, \dots, y_s)$ in the objective function (28). Yu and Lie (2000) suggested that the expression $\sum_{s \in S} P_s \, (Z_s - \sum_{s' \in S} P_{s'} \, Z_{s'} \,)^2$, which increases the time required to solve the problem, can be replaced by an expression containing the absolute term. Therefore, the stability of the solution changes as Eq. (33):

$$\sigma(x, y_1, y_2, \dots, y_s) = \sum_{s \in S} P_s \; Z_s + \lambda \sum_{s \in S} P_s \; \left| Z_s - \min \sum_{s' \in S} P_{s'} \; Z_{s'} \right| \tag{33}$$

The objective function (33) is a non-linear equation. Yu and Lie (2000) proved that the minimization of $\sigma(x, y_1, y_2, \dots, y_s)$ is equivalent to the linear programming model with additional equations (34) to (36) as follows.

$$\mathbf{min} \sum_{s \in S} P_s \; Z_s + \lambda \sum_{s \in S} P_s \; \left(Z_s - \min \sum_{s' \in S} P_{s'} \; Z_{s'} + 2\theta_s \right) \tag{34}$$

Subject To:

$$Z_s - \min \sum_{s' \in S} P_{s'} \; Z_{s'} + \theta_s \geq 0 \qquad \forall s \tag{35}$$

$$\theta_s \geq 0 \qquad \forall s \tag{36}$$

Finally, the linear optimization model with structures (24 to 27) transformed into the model with the following structure.

$$\min \sum_{s \in S} P_s \; Z_s + \lambda \sum_{s \in S} P_s \; \left(Z_s - \sum_{s' \in S} P_{s'} \, Z_{s'} \; + 2\theta_s \right) + \sum_{s \in S} P_s \; \delta_s \tag{37}$$

Subject To:

(29), (30), (31), (35), and (36)

To stabilize the scenario-based mathematical model with the model proposed by Mulvey et al. (1995), objective functions (1) and (2) are replaced by objective functions (38), and (39) respectively, and constraints (40), (41), and (42) are added to the model.

$$\begin{aligned} \mathbf{Max}\ \mathrm{Z1} = {} & \textstyle\sum_{s \in S} \; pro_s \, ((\bar{\beta}_1 \times \sum_k \sum_t \; \sum_j \; Cb'^{\,s}_{jkt} \div Db^s_{jkt})) \times \left(\bar{\beta}_2 \times \sum_j \; \sum_t \; (N''^{\,s}_{jt} \; \times u2_{jt} \div \sum_k \; Db^s_{jkt}) \right) \times (\bar{\beta}3^s_{jkt} \times \\ & \textstyle\sum_k \; \sum_t \; (Cb'^{\,s}_{jkt} \div Db^s_{kjt}))) + \lambda \sum_{s \in S} pro_s \left[\left((\bar{\beta}_1 \times \sum_k \sum_t \; \sum_j \; Cb'^{\,s}_{jkt} \div Db^s_{jkt}) \right) \times \left(\bar{\beta}_2 \times \sum_j \; \sum_t \; (N''^{\,s}_{jt} \; \times u2_{jt} \div \right. \right. \\ & \textstyle\left. \sum_k \; Db^s_{jkt}) \right) \times (\bar{\beta}3^s_{jkt} \times \sum_k \; \sum_t \; (Cb'^{\,s}_{jkt} \div Db^s_{kjt})) \Big) - \sum_{\acute{s} \in S} pro_{\acute{s}} \; \left((\bar{\beta}_1 \sum_k \sum_t \; \sum_j \; Cb'^{\,\acute{s}}_{jkt} \div Db^{\acute{s}}_{jkt})) \times \left(\bar{\beta}_2 \times \right. \right. \\ & \textstyle\left. \left. \left. \sum_j \; \sum_t \; (N''^{\,\acute{s}}_{jt} \; \times u2_{jt} \div \sum_k \; Db^{\acute{s}}_{jkt}) \right) \times (\bar{\beta}3^{\acute{s}}_{jkt} \times \sum_k \; \sum_t \; (Cb'^{\,\acute{s}}_{jkt} \div Db^{\acute{s}}_{kjt})) \right) + 2\theta^s_1 \right] \end{aligned} \tag{38}$$

$$\textbf{Min } Z2 = \sum_s pro_s \Big(\big(\sum_p \sum_k \sum_t IN'^{\,s}_{pkt} \times CH''_{pkt}\big) + \big((\sum_s \sum_j \sum_t N''^{\,s}_{jt} \times ccn)\big) + \big(\sum_p \sum_h \sum_t IN''^{\,s}_{pht} \times CH'_{pht}\big) + \big(\sum_p \sum_k \sum_h \sum_t Q^s_{pkht} \times CV_{pkht}\big) + \big(\sum_p \sum_h \sum_t De'^{\,s}_{pht} \times CS'_{pht}\big) + \big(\sum_p \sum_k \sum_t De''^{\,s}_{pkt} \times CS''_{pkt}\big) + \big(\sum_j \sum_k \sum_t Cb'^{s}_{jkt} \times CV'_{jkt}\big) + \big(\sum_p \sum_k \sum_t PR^s_{pkt} \times CP_{pkt}\big) + \big(\sum_j \sum_t Cb^s_{jt} \times CC_{jt}\big) + \sum_j \big(\bar{\delta}^1_j \times (\sum_t Cb^s_{jt} \times CC_{jt})\big) + \sum_k \big(\bar{\delta}^2_k \times (\sum_p \sum_t PR^s_{pkt} \times CP_{pkt})\big) + \big(\sum_p \sum_k \sum_t WB'^{\,s}_{pkt} \times CW'_{pkt}\big)\Big) + \lambda \sum_{s\in S} pro_s \Big[\Big(\big((\sum_p \sum_k \sum_t IN'^{\,s}_{pkt} \times CH''_{pkt}\big) + \big((\sum_s \sum_j \sum_t N''^{\,s}_{jt} \times ccn)\big) + \big(\sum_p \sum_h \sum_t IN''^{\,s}_{pht} \times CH'_{pht}\big) + \big(\sum_p \sum_k \sum_h \sum_t Q^s_{pkht} \times CV_{pkht}\big) + \big(\sum_p \sum_h \sum_t De'^{\,s}_{pht} \times CS'_{pht}\big) + \big(\sum_p \sum_k \sum_t De''^{\,s}_{pkt} \times CS''_{pkt}\big) + \big(\sum_j \sum_k \sum_t Cb'^{s}_{jkt} \times CV'_{jkt}\big) + \big(\sum_p \sum_k \sum_t PR^s_{pkt} \times CP_{pkt}\big) - \big(\sum_j \sum_t Cb^s_{jt} \times CC_{jt}\big) + \sum_j \big(\bar{\delta}^1_j \times (\sum_t Cb^s_{jt} \times CC_{jt})\big) + \sum_k \big(\bar{\delta}^2_k \times (\sum_p \sum_t PR^s_{pkt} \times CP_{pkt})\big) + \big(\sum_p \sum_k \sum_t WB'^{\,s}_{pkt} \times CW'_{pkt}\big)\big)\Big) - \sum_{\acute{s}\in S} pro_{\acute{s}} \Big(\big((\sum_p \sum_k \sum_t IN'^{\,\acute{s}}_{pkt} \times CH''_{pkt}\big) + \big((\sum_{\acute{s}} \sum_j \sum_t N''^{\,\acute{s}}_{jt} \times ccn)\big) + \big(\sum_p \sum_h \sum_t IN''^{\,\acute{s}}_{pht} \times CH'_{pht}\big) + \big(\sum_p \sum_k \sum_h \sum_t Q^{\acute{s}}_{pkht} \times CV_{pkht}\big) + \big(\sum_p \sum_h \sum_t De'^{\,\acute{s}}_{pht} \times CS'_{pht}\big) + \big(\sum_p \sum_k \sum_t De''^{\,\acute{s}}_{pkt} \times CS''_{pkt}\big) + \big(\sum_j \sum_k \sum_t Cb'^{\acute{s}}_{jkt} \times CV'_{jkt}\big) + \big(\sum_p \sum_k \sum_t PR^{\acute{s}}_{pkt} \times CP_{pkt}\big) - \big(\sum_j \sum_t Cb^{\acute{s}}_{jt} \times CC_{jt}\big) + \sum_j \big(\bar{\delta}^1_j \times (\sum_t Cb^{\acute{s}}_{jt} \times CC_{jt})\big) + \sum_k \big(\bar{\delta}^2_k \times (\sum_p \sum_t PR^{\acute{s}}_{pkt} \times CP_{pkt})\big) + \big(\sum_p \sum_k \sum_t WB'^{\,\acute{s}}_{pkt} \times CW'_{pkt}\big)\big)\Big) + 2\theta^s_2\Big] \tag{39}$$

Subject To:

$$(\bar{\beta}_1 \times \sum_k \sum_t \sum_j Cb'^{s}_{jkt} \div Db^s_{jkt}) \times (\bar{\beta}_2 \times \sum_j \sum_t (N''^{\,s}_{jt} \times u2_{jt} \div \sum_k Db^s_{jkt})) \times (\bar{\beta}3^s_{jkt} \times \sum_k \sum_t (Cb'^{s}_{jkt} \div Db^s_{kjt})) - \sum_{\acute{s}\in S} pro_{\acute{s}} ((\bar{\beta}_1 \times \sum_k \sum_t \sum_j Cb'^{\acute{s}}_{jkt} \div Db^{\acute{s}}_{jkt})) \times (\bar{\beta}_2 \times \sum_j \sum_t (N''^{\,\acute{s}}_{jt} \times u2_{jt} \div \sum_k Db^{\acute{s}}_{jkt})) \times (\bar{\beta}3^{\acute{s}}_{jkt} \times \sum_k \sum_t (Cb'^{\acute{s}}_{jkt} \div Db^{\acute{s}}_{kjt})) + \theta^s_1 \geq 0 \qquad \forall s \tag{40}$$

$$\Big(\big(\sum_p \sum_k \sum_t IN'^{\,s}_{pkt} \times CH''_{pkt}\big) + \big((\sum_s \sum_j \sum_t N''^{\,s}_{jt} \times ccn)\big) + \big(\sum_p \sum_h \sum_t IN''^{\,s}_{pht} \times CH'_{pht}\big) + \big(\sum_p \sum_k \sum_h \sum_t Q^s_{pkht} \times CV_{pkht}\big) + \big(\sum_p \sum_h \sum_t De'^{\,s}_{pht} \times CS'_{pht}\big) + \big(\sum_p \sum_k \sum_t De''^{\,s}_{pkt} \times CS''_{pkt}\big) + \big(\sum_j \sum_k \sum_t Cb'^{s}_{jkt} \times CV'_{jkt}\big) + \big(\sum_p \sum_k \sum_t PR^s_{pkt} \times CP_{pkt}\big) - \big(\sum_j \sum_t Cb^s_{jt} \times CC_{jt}\big) + \sum_j \big(\bar{\delta}^1_j \times (\sum_t Cb^s_{jt} \times CC_{jt})\big) + \sum_k \big(\bar{\delta}^2_k \times (\sum_p \sum_t PR^s_{pkt} \times CP_{pkt})\big) + \big(\sum_p \sum_k \sum_t WB'^{\,s}_{pkt} \times CW'_{pkt}\big)\Big) - \sum_{\acute{s}\in S} pro_{\acute{s}} \Big(\Big(\big(\sum_p \sum_k \sum_t IN'^{\,\acute{s}}_{pkt} \times CH''_{pkt}\big) + \big((\sum_{\acute{s}} \sum_j \sum_t N''^{\,\acute{s}}_{jt} \times ccn)\big) + \big(\sum_p \sum_h \sum_t IN''^{\,\acute{s}}_{pht} \times CH'_{pht}\big) + \big(\sum_p \sum_k \sum_h \sum_t Q^{\acute{s}}_{pkht} \times CV_{pkht}\big) + \big(\sum_p \sum_h \sum_t De'^{\,\acute{s}}_{pht} \times CS'_{pht}\big) + \big(\sum_p \sum_k \sum_t De''^{\,\acute{s}}_{pkt} \times CS''_{pkt}\big) + \big(\sum_j \sum_k \sum_t Cb'^{\acute{s}}_{jkt} \times CV'_{jkt}\big) + \big(\sum_p \sum_k \sum_t PR^{\acute{s}}_{pkt} \times CP_{pkt}\big) - \big(\sum_j \sum_t Cb^{\acute{s}}_{jt} \times CC_{jt}\big) + \sum_j \big(\bar{\delta}^1_j \times (\sum_t Cb^{\acute{s}}_{jt} \times CC_{jt})\big) + \sum_k \big(\bar{\delta}^2_k \times (\sum_p \sum_t PR^{\acute{s}}_{pkt} \times CP_{pkt})\big) + \big(\sum_p \sum_k \sum_t WB'^{\,\acute{s}}_{pkt} \times CW'_{pkt}\big)\Big)\Big) + \theta^s_2 \geq 0 \quad \forall s \tag{41}$$

$$\theta^s_1, \theta^s_2 \geq 0 \qquad \forall s \tag{42}$$

In order to combine the first and second robust objective functions and the degree of model stability, an appropriate weight is assigned to each objective according to the opinion of the decision-maker. The final objective function is obtained by minimizing the weighted sum of objectives as Eq. (43).

$$Min\ Z = w_1 z_1 - w_2 z_2 + w_3 \sum_p \sum_t \sum_{s\in S} P_s\, \xi_{phts} \tag{43}$$

4. Computational Results and Sensitivity Analysis

4.1. Computational results of the robust scenario-based model

In order to evaluate the ability to solve the robust model based on the scenario for different dimensions, 6 samples in different sizes were produced. Baron solver in GAMS software on a home computer was used to solve the proposed mathematical model. The values of the model parameters were taken from the real data of Davoudi Kia Kalate et al. (2012) and Nehfti Kohneh et al. (2016). The model was solved using the above data after normalizing the parameters. The related results are shown in Table 4. The second column of this table lists the number of members of each sample. The members are (*j*, *k*, *h*, *t*, *p* and *s*), where *j* is the number of blood collection facilities, *k* is the number of blood centers, *h* is the number of hospitals, *t* is the number of periods, *p* is the number of products, and *s* is a possible scenario. The results presented in Table 4 indicate that the model could to solve the samples in a reasonable time. To confirm the performance of the model, a sensitivity analysis was performed on the change in parameters of wastage cost, shortage cost, and performance of the objective functions, the results of which are shown in the next sections.

Table 4
The ability to solve examples using the proposed model

Number of samples	Sample size	The optimal value of the first objective function	The optimal value of the second objective function	The optimal value of the objective function of the problem (×10^9)	Solve time (the watch)
1	(2, 2, 7, 2, 2, 2)	3.795	868.130	2.678798	02:36:30
2	(3, 2, 7, 2, 2, 2)	4.174	814.901	2.656398	02:34:32
3	(6, 2, 7, 2, 2, 2)	4.854	657.238	2.670948	02:24:54
4	(6, 2, 10, 2, 3, 2)	6.086	720.655	5.767847	02:26:59
5	(6, 2, 20, 2, 3, 2)	6.439	849.465	11.56960	01:40:14
6	(6, 2, 30, 3, 3, 2)	5.235	700.675	11.57080	02:50:06

4.2. Sensitivity analysis of wastage and shortage cost

In this section, the sensitivity analysis of the model is carried out on two important parameters influencing decision-making to more precisely examine the validity of the proposed model: wastage and shortage costs. Sensitivity analysis was performed on the samples with dimensions (5, 2, 15, 2, 2 and 2). Tables 5 and 6 show the output results of the model for waste and shortage costs, respectively.

As can be seen in Table 5, with the increase in the cost of waste, the amount of waste decreased, but it led to an increase in the cost of the supply chain in the relevant objective function (the second objective function). However, despite these changes and the increase in the second objective function, the total objective function remained constant and robust. As can be seen in Table 6, with the increase in the cost of shortage, the amount of shortages remained constant and did not increase the corresponding cost function (second objective function). The results presented in Tables 5 and 6 confirm the validity of the proposed model. Therefore, the results obtained from the sensitivity analysis were consistent with reasonable and logical expectations.

Table 5
Sensitivity analysis of cost of waste products in the blood center

Experiment	Cost of waste product in the blood center	Product type	Blood Center	The amount of product lost in the blood center				Objective function values	
				Period 1		Period 2		Second objective function	Total objective function (×10^9)
				S_1	S_2	S_1	S_2		
1	0.00000	P1	1 K			210	290	610.702	5.759197
			2 K	203		203			
		P2	1 K	203	290	22			
			2 K		290		290		
2	0.00262	P1	1 K			210	290	615.671	5.759197
			2 K	203		203			
		P2	1 K	203	290	22			
			2 K		290		290		
3	0.00530	P1	1 K			203	290	621.115	5.759197
			2 K		290				
		P2	1 K	203	290				
			2 K	203		203	290		
4	0.02120	P1	1 K			203	261	652.508	5.759197
			2 K	106		173			
		P2	1 K	203		319			
			2 K	126	290	1	290		
5	0.04240	P1	1 K	179			290	696.007	5.759197
			2 K	124	319	203			

Table 6
Sensitivity analysis of cost of product shortages in the hospitals

Experiment	Cost of product shortages in the hospital	Product type	The rate of product shortage in the hospital				Objective function values
			Period 1		Period 2		Second Objective Function
			S_1	S_2	S_1	S_2	
1	0.00000	P1	1938.0	943.25	1854	958.0	621.153
			1934.0	990.50	1958	957.5	621.153

		P2	1938.5	942.75	1853	958.0	
			1934.0	990.50	1958	957.5	
		P1	1938.5	943.75	1854	958.0	
2	0.15625		1934.0	990.50	1958	957.5	621.153
		P2	1938.5	943.75	1854	958.0	621.153
			1934.0	990.50	1958	957.5	
		P1	1938.0	942.25	1853	958.0	
3	0.31250		1934.0	990.50	1958	957.5	621.153
		P2	1938.0	943.25	1854	958.0	621.153
			1934.0	990.50	1958	957.5	
		P1	1938.5	942.75	1853	958.0	621.153
			1934.0	990.50	1958	957.5	
4	0.62500	P2	1938.5	943.75	1854	958.0	621.153
			1934.0	990.50	1958	957.5	
5	1.87500	P1	1938.5	943.75	1854	958.0	621.153
			1934.0	990.50	1958	957.5	

4.3. Sensitivity analysis of the objective function

The proposed model is a non-linear multi-objective robust model of the blood supply chain with two objective functions of maximizing reliability and minimizing the total cost of the blood supply chain (transfusion, wastage, and shortage). The weight method is used to solve the model. To analyze the sensitivity of the objective function, different weights with a value between 0 and 1 were considered for the objective functions of a problem with dimensions (2, 2, 2, 7, 2 and 4). The results obtained from this sensitivity analysis are shown in Figures 2 and 3. The changes of the first objective function, i.e., maximization of reliability, compared with the changes of the second objective function, i.e., minimization of the total cost of the blood supply chain, according to different weight coefficients for the objectives, are shown in Figure 2. The changes in reliability according to the number of blood collection facilities are shown in Figure 3.

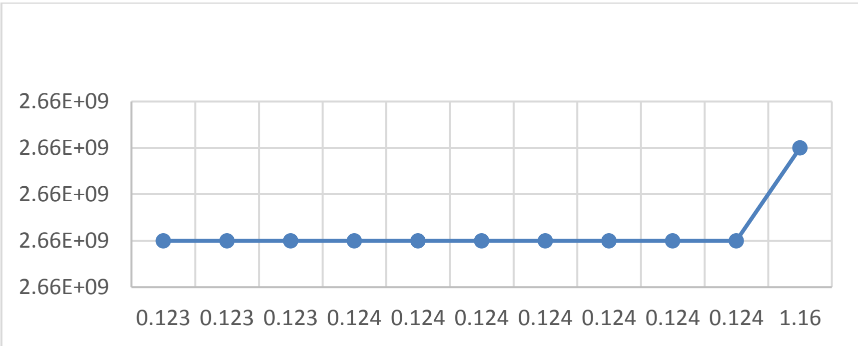

Fig. 2. Objective value of reliability (x-axis) relative to total cost of blood supply chain (y-axis)

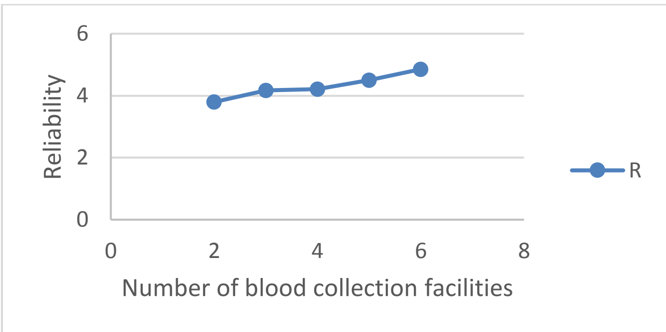

Fig. 3. Objective value of reliability relative to number of blood collection facilities

4.4. Discussion

Reliability modeling in the supply chain has been less investigated in the literature. Aghiani et al. (2015) proposed a robust optimization model for the reliable design of a blood supply chain network by considering possible disruptions in blood collection facilities, blood transfusion routes, and blood centers during crisis. Their goals included minimizing the lack of coverage of demand points and increasing the reliability of the blood supply chain in crisis situations. The results of this research are in accordance with those of Aghiani et al. (2015), and both studies demonstrated a direct relationship between the number of blood collection facilities and the reliability of the supply chain. Zandedel, et al. (2014) also considered only the disturbance at a particular location, and their results showed the importance of reliability in a location discussion. Clay et al. (2018) concluded that only a small disturbance in the transportation of blood products causes instability and fluctuations in the model. They showed that modifications can be made to the structure of blood inventories to reduce these fluctuations. A reduction in the volatility of blood inventories has a concomitant effect on the supply of blood from donors. Therefore, the reduction in fluctuations leads to less shortages and waste. The results of this research indicate that by managing blood inventories in blood centers, the shortage can be reduced to zero, and waste can be minimized.

5. Conclusion and Future Research

Supply chain network design is one important and fundamental strategic decision. This research designed a three-level supply chain for blood and blood products, including: supply, processing, and distribution of blood. The aim of the supply chain is to reduce the costs of blood transfusion, shortages, and waste of blood and increase the reliability of the blood supply chain. For this purpose, a multi-objective non-linear mathematical model of the blood supply chain is presented under the condition of uncertainty in blood demand. The robust formulation based on Mulvey et al. (1995) was used to stabilize the research model in the face of fluctuations and uncertainty in demand. To validate the proposed model, sensitivity analyses were performed using real data with different dimensions in the Barron solver in GAMS software. Sensitivity analyses of the model were carried out on the costs of waste, shortages, and the objective function. The results showed that it is possible to increase the reliability of the supply chain by increasing the number of collection centers and the amount of blood sent from these centers and managing the blood inventory in these centers. In addition, the time required to solve the model increases significantly when the dimensions of the problem increase, especially if more products are considered. In future research, the proposed mathematical model can be developed from different perspectives. As a suggestion for future research, product life, delivery time, and reliability at other levels of the supply chain can be considered, although the problem would be very difficult to solve. Furthermore, due to the increasing dimension of the problem, the problem-solving time increases; thus, heuristic and meta-heuristic methods are suggested for future research.

Declarations

- Ethics approval and consent to participate: This paper does not contain any studies with human or animal subjects. There are no human subjects in this paper and informed consent is not applicable.
- Consent for publication: This paper does not contain data from any individual person and informed consent is not applicable.
- Data availability statement: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.
- Competing interests: All co-authors have seen and agree with the contents of the manuscript and there is a financial and no financial interest to report. The authors declare that they have no competing interests.
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