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ARTICLE

A MATHEMATICAL PROGRAMMING APPROACH TO PAIRED KIDNEY EXCHANGE: THE CASE OF TURKEY

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ABSTRACT

Background: *Kidney exchange has become a very common and important treatment alternative for patients suffering from serious kidney diseases with incompatible donors. Factors such as blood type, HLA matches and PRA existence are considered to determine compatibility. In a paired exchange, two incompatible patient-donor pairs switch their donors who are compatible with the other recipient. Currently, each hospital in Turkey operates individually in a decentralized manner using its own list. This list may contain patients having more than one incompatible donor, which differentiates the current work from those existing in literature.* ***Methods:*** *In this study, mathematical models are developed to propose an easy and practical approach for the paired kidney exchange problem in Turkey. Data are generated by employing a real data set provided by a hospital specialized in kidney transplantation.* ***Results:*** *The optimal solutions are obtained by using GAMS/CPLEX, and different scenario analyses are performed to measure the impact of "gender differences" and "age" on the solution. Furthermore, the original patient-donor list provided by the hospital is used to compare the model's solution with the planned transplantations. The study also evaluates a centralized approach which integrates all hospitals performing paired kidney exchange in Istanbul.* ***Conclusions:*** *As the optimal solution of the model is obtained in a basis of seconds, the developed approach offers an easy and applicable procedure for paired kidney exchange. Comparison of decentralized and centralized approaches reveals that the centralized approach is more favorable in terms of HLA compatibility and number of transplantations.*

KEY WORDS
OR in health services, paired kidney exchange, living donor, mathematical modelling

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INTRODUCTION

Organ transplantation is the process of replacing a failing organ with a healthy one from another person or from a different part of the patient's body. Nowadays, most of the organs, such as; kidney, liver, heart, pancreas, lung and small intestine can be transplanted from donors to patients who are suffering from organ failure throughout the world.

Healthy organs can be obtained from either deceased or living donors. According to relevant literature [1], the insufficient number of cadaveric organ donations is leading to an increase in organ transplants from living donors. In 1933, the first successful kidney transplant was performed from cadaver by the Ukrainian Professor Yurii Woronoy, MD, whose patient died 48 hours after the operation due to shortages in technical equipment and limited knowledge on transplantation. The first successful kidney transplantation from a living donor was carried out in 1954 in Boston, USA, and was more successful than the previous one. After 1950s, kidney transplantation has become a more popular treatment for the patients around the world. In Turkey, the first successful kidney transplant was performed from a mother to her son on October 3, 1975 by Professor Mehmet Haberal, MD, and his team. In 1978, the same team accomplished the first cadaver transplantation in Turkey using a cadaver that was brought from abroad via "Eurotransplant".

In paired kidney exchange, two incompatible patient-donor pairs exchange their donors who are compatible with the other recipient. During this process, important factors such as blood type, HLA (Human Leukocyte Antigens) matches, gender, age, and PRA (Panel Reactive Antibody) existence are considered to determine the compatibility, and these factors may cause some difficulties in finding compatible kidneys especially if two-way swaps is used. HLA is a parameter used to measure the tissue compatibility of pairs whereas PRA shows the immunological status of a patient awaiting organ transplantation. The main goal of paired kidney exchange is to determine the optimal coupling between volunteering living donors and potential recipients who are on the transplant waiting list. Optimal coupling refers to the high HLA compatibility between patients and donors.

In this study, a mathematical model is developed for the paired kidney exchange problem in Turkey. Moreover, the effects of gender and age on transplantation results are discussed. Some donor-patient matches are considered as undesirable by receivers, due to gender and age differences. For example; a patient-donor pair having a young donor may not accept the kidney from a pair with an older donor, as the younger donor's kidney is more preferable. Another unwanted situation may arise from gender differences, and consequently, a male donor's patient may not want to receive the organ of the other pair's female donor.

There are 22,436 patients suffering from kidney failure in Turkey who are registered in the central waiting list of cadaver kidney transplantation, and unfortunately this number is increasing each year. The total number of kidney transplantations between years 2011-2017 in terms of living and deceased donors are displayed in [Table 1]. The motivation of the current study is based on this fact, and aims to propose an improvement in the kidney transplantation system.

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Table 1: The total number of kidney transplants performed (retrieved from T.R. Ministry of Health, 8 December 2017) [2]

Year	Number of Transplantations		The Total Number of Transplantations Performed
	Living Donor	Deceased Donor	
2017	2476	659	3135
2016	2639	784	3423
2015	2534	670	3204
2014	2299	626	2925
2013	2361	585	2946
2012	2384	525	2909
2011	2435	517	2952
Total	17,128	4366	21,494

Literature review

Roth, Sönmez and Ünver [3, 4] contributed the related literature with two significant articles. They recommended mechanisms to organize kidney transplantation in a Pareto-efficient and dominant strategy encouragement-compatible manner under several restrictions on swap sizes and preferences of the receivers for a static receiver population. Same scholars showed that the increasing number of non-directed donors would lead to a relaxation in synchronicity restriction [5, 6]. Particularly, since a chain is initiated by an altruistic donor, a patient-donor pair does not have to donate a kidney before they receive one. Hence, longer chains can be organized non-simultaneously without the need for integration of high number of operating rooms and surgical teams. After the publication of the work by Rees et al. [7] in which leading ten exchanges have been submitted from the initial non-simultaneous chains, an expanding number of long non-simultaneous chains have been performed. Gentry and Segev [8] and Ashlagi et al. [9] have argued whether long chains enhance effectiveness beyond simultaneous small cycles or not. One of the significant causes is that, long chains could not raise performance if they simply acquired exchanges that could otherwise have been obtained in various shorter loops [1, 8, 10, 11, 12].

Another article by Ünver [13] demonstrated how swap exchanges should be managed through a centralized mechanism in a dynamically developing agent pool with time and compliance based preferences. They proposed dynamically efficient two-way and multi-way swap procedures that maximize total discounted swap. In recent years, various living donor kidney exchange programs have been developed to help incompatible donors of end-stage kidney disease patients. Since kidney swap models can be considered as a special case of the general assignment problem, the progress in this area can be applied to the kidney exchange model as well.

Roth et al. [3] recommended mathematical models for two-way and multi-way kidney exchange problems. By performing simulation methodology, they analyzed the effect of different exchange strategies on the number of assignments for various population sizes. The researchers concluded that the four-way exchange displays the most effective strategy. A similar conclusion is obtained both in the work by Ünver [13] who uses dynamic programming, and in the studies conducted by Ashlagi et al. [9].

Saidman et al. [14] also studied the multi-way kidney transplantation problem. The purpose of their work was to develop living donor kidney transplantation by finding compatible donor and patient pairs. A simulation based on the *Organ Procurement and Transplantation Network and Scientific Registry of Transplant Recipients (OPTN/SRTR)* data was used to appreciate the practical significance of multiple exchange combination. The results of this study demonstrated that, if three-way swaps are allowed, number of potential exchanges will increase independent of the current patient list.

The paper by Standford et al. [15] tested the policies on a simulator. This study first shows that ABO identical transplantation cannot achieve equity between different blood groups. Then, it presents a model for restricted cross-transplantation which indicates how comparable waiting times for all blood types could be achieved.

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Constantino et al. [16] evaluated kidney allocation problem by proposing distinct integer-programming formulations and showing the differences between existing models in literature. They concluded that, the developed compact formulations are computationally more preferable for large problem sizes.

More recently, Anderson et al. [17] described a long-term optimization approach that supports the *Alliance for Paired Donation (APD)* works. They also explained how a team of physicians and operations researchers worked to overcome the scepticism and resistance of the medical community to the non-simultaneous extended altruistic donor innovation.

In all of the studies mentioned above, the authors designed solutions to the living donor kidney transplantation problem. These papers emphasized the significance of kidney exchange by the help of some simulation and optimization based approaches.

As the living donor kidney allocation regulations are varying for each country, problems having different characteristics and restrictions are observed in distinct countries. So far, to the best of our knowledge, Turkey's living donor kidney allocation problem with its special factors such as; HLA score, age effect, gender differences, and existence multiple donors for a patient, has not been previously addressed through optimization models. Due to Turkey's different customs, the application of altruistic donors to hospitals is not common behavior. With all these characteristics, it is worthwhile to note that, living donor kidney exchange problem existing in Turkey has many differences from the current problems studied in literature. The next subsection explains these differences in detail.

Paired kidney exchange in Turkey

In Turkey, organ transplantation assignments are performed by the *National Organ and Tissue Transplantation Coordination System* which is called "Ulusal Organ ve Doku Nakli Koordinasyon Sistemi (UKS)". This system collects all data from the database established by the Ministry of Health, and contains data regarding all organ and tissue donations, transplantations records, receiver and donor information in the country. Hospitals registered in the system, and the Regional Coordination Centers have to input the donor and patient data to this database. Currently, there are 9 Regional Coordination Centers and 69 kidney transplantation centers in Turkey. It should be noted that, UKS manages deceased donor kidney transplantations in a centralized manner. On the other hand, living donor kidney transplantations are performed individually by hospitals in a decentralized way, that is, paired exchanges are planned by only considering the hospital's own list.

Turkey holds a good position in terms of transplants from living donors as a result of close family relations. However unlike USA and some European countries, these exchanges are managed through a decentralized system. Additionally, it is possible to observe multi-donor situations for a patient in Turkey. There are even cases where a patient joins the exchange with five donors which increases her/his transplantation possibility. Florence Nightingale Hospital and Memorial Hospital, both located in Istanbul, are two of the centers which perform living donor kidney exchange operations. However, this process is managed manually without using any software. Kidney transplant operation is a highly successful method resulting in a longer and healthier life for a patient with kidney failure. In Turkey, the number of patients whose treatment is only possible through a kidney transplant is increasing every year which emphasizes the importance of living donor kidney transplantation.

This study aims to solve the living donor kidney transplantation problem by considering case specific parameters and restrictions. These are, number of HLA matches between patient and donor, total HLA score of patient and donor pair, PRA existence of patient against a donor, blood group of exchange pairs, age and gender of patient and donor.

In the current problem, HLA parameter is composed of three main groups; A, B and DR. For each HLA type, three cases can happen: case with two matches, case with one match and case with zero matches (which indicate a "mismatch" case). Moreover, while calculating the HLA score of a patient and donor pair; 5 points, 50 points and 150 points are used for each A, B and DR antigen match, respectively.

PRA parameter is another important factor in the problem. A patient having a PRA against a donor's antigen causes incompatibility. Hence, PRA is defined as a binary parameter; if a patient has a PRA against a donor, this parameter takes the value 0 (zero), otherwise, it is 1.

The other parameter, which is blood group compatibility, is incorporated via general blood transfusion rules. In order to perform a kidney exchange, these rules should be satisfied between the patient-donor pairs.

Additionally, some patient-donor matches may not be accepted by the experts of the field or the patients because of gender and age differences. For example; the patient who has a younger donor may not accept an exchange with a pair having an older donor, since a younger donor's kidney is more preferable. Generally, when using the age as a parameter, certain age ranges between the donors of two pairs are taken into consideration. Gender differences also have an important role in this problem. Male donors' kidneys are more preferable than female donors' due to their powerful filtering capability. For this reason, effect of gender differences should also be integrated as a parameter into the model.

As described above, each parameter has to be calculated for each patient-donor pair in the problem, and the most suitable donors for each patient should be determined. However, as the number of pairs in an exchange list increases, an efficient method which automatically evaluates the optimal assignments is required. The lack of such a method in Turkey is the motivation of this study.

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MATERIALS AND METHODS

For the paired kidney exchange problem, an integer linear programming (ILP) based mathematical model which is presented in the following subsections is developed.

Mathematical model for paired kidney exchange

The notation used in the formulation of the mathematical model (PKE_O) is provided below:

Indices

i, j, k : patient – donor pair index

Parameters

$page_i$: age of patient of pair *i*
$dage_i$: age of donor of pair *i*
$pgender_i$: gender of patient of pair *i* (0, female; 1, male)
$dgender_i$: gender of donor of pair *i* (0, female; 1, male)
pbg_i : blood group of patient of pair *i*
dbg_i : blood group of donor of pair *i*
nd_i : number of donors for patient *i*
HLA_A_{ij} : number of HLA "A" match between patient of pair *i* and donor of pair *j*
HLA_B_{ij} : number of HLA "B" match between patient of pair *i* and donor of pair *j*
HLA_DR_{ij} : number of HLA "DR" match between patient of pair *i* and donor of pair *j*
PRA_{ij} : 0, if patient of pair *i* has a PRA against donor of pair *j*; 1, otherwise
$bgABOmatch_{ij}$: 1, if patient of pair *i* and donor of pair *j* have compatible blood groups in terms of transfusion rules; 0, otherwise
$exfeas_{ij}$: 1, if patient of pair *i* can receive a kidney from donor of pair *j*; 0, otherwise
$HLAscore_{ij}$: total HLA score for patient of pair *i* and donor of pair *j*

The total score of paired exchange between pair *i* - pair *j* pair is calculated as follows;

$$HLAscore_{ij} = 5 \cdot HLA\_A_{ij} + 50 \cdot HLA\_B_{ij} + 150 \cdot HLA\_DR_{ij} \qquad \forall i, \forall j \qquad (1)$$

Decision variables

X_{ij} : 1, if a paired kidney exchange occurs between patient of pair *i* and donor of pair *j*; 0, otherwise

Model PKE_O is given below:

max z =

$$\sum_i \sum_j bgABOmatch_{ij} \cdot bgABOmatch_{ji} \cdot PRA_{ij} \cdot PRA_{ji} \cdot HLAscore_{ij} \cdot exfeas_{ij} \cdot X_{ij} \qquad (2)$$

Subject to:

$$\sum_{\substack{i \\ i \neq j}} bgABOmatch_{ij} \cdot bgABOmatch_{ji} . exfeas_{ij} \cdot X_{ij} \leq 1 \qquad \forall j \qquad (3)$$

$$\sum_{\substack{j \\ j \neq i}} bgABOmatch_{ij} \cdot bgABOmatch_{ji} \cdot exfeas_{ij} \cdot X_{ij} \leq 1 \qquad \forall i \qquad (4)$$

$$X_{ij} = X_{ji} \qquad \forall i,\ \forall j,\ i \neq j \qquad (5)$$

$$\sum_j \sum_{\substack{i \\ i \neq j \\ k \leq i \leq k + nd_k - 1 \\ nd_k > 1}} X_{ij} \leq 1 \qquad \forall k \qquad (6)$$

$$X_{ij} \in \{0,1\} \qquad \forall i, \forall j \qquad (7)$$

The objective function (2) aims to maximize the total score of the paired kidney exchange swaps by considering blood group matches and PRA compatibilities. Constraint sets (3) and (4) ensure that a patient-donor pair can receive and can give at most one kidney from/to another pair in terms of blood group compatibility. Constraint set (5) assures that the exchange occurs between the same patient *i* - donor *j* and patient *j* - donor *i* pairs. Finally, constraint (6) ensures that each patient has to attend the barter with just one donor. For instance, if patient 1 has three donors (nd_1 = 3), pairs 1, 2 and 3 are all pairs of patient 1. Hence, among the first three pairs, only one of them can attend the exchange. The integrality of the decision variables are given in constraint set (7).

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Integration of the age effect

Age parameter is a significant factor on the exchange problem. To incorporate the age effect in the model, certain age ranges between donors of pair *i* and pair *j* are defined. Moreover, Equation (8) which has two new parameters, *at* and *M,* are added to PKE_O. This model is named as PKE_A.

Additional parameters

at : age threshold

M_1 : a very big number

$$\left|dage_i - dage_j\right| \le at + M_1(1-X_{ij}) \qquad \forall i, \forall j \qquad (8)$$

Integration of the gender effect

Gender differences poses another considerable role in this problem. It is preferable to have an exchange as follows: if a patient's donor is female (male), then the patient can receive a kidney from a pair with a female (male) donor. After adding Equation (9) to PKE_O, gender restriction can be controlled. This model is referred to as PKE_G. M_2 is a very big number.

$$dgender_i - dgender_j \le M_2(1-X_{ij}) \qquad \forall i, \forall j \qquad (9)$$

RESULTS

In order to test the validity of the proposed models, data representing real life cases are generated. The results obtained are discussed in the subsequent sections.

Data generation

The data generation phase is conducted together with the experts working in the area of kidney transplantation. A sample data of donors and patients are obtained from a hospital which is one of the leading kidney transplantation centers in Istanbul, and the characteristics of the data are analyzed. Based on this analysis, data employed in the models are generated and discussed with the specialists, so as to design realistic situations.

[Table 2] displays the data generated for the parameters of the paired kidney exchange model. As it can be seen from the table, uniform distribution is commonly used in determining the value of the parameters. For example, *HLA* is a discrete uniform random variable that takes values 0, 1, and 2; representing zero matches (mismatch), one match, and two matches, respectively. The age of patient *i*, $page_i$, is also a discrete uniform random variable which has different probabilities for different age intervals. Note that, for each patient *i*, the number of donors generated are denoted by nd_i, and found by using the probabilities given in [Table 2].

Using the data of [Table 2], a list of 40 patient-donor pairs given in [Table 3] is generated. Due to space limitation, only a sample part of [Table 3] is provided here. As it can be seen from this table, P8 and P9 are exactly the same patients having two donors, D8 and D9, whereas P11-P14 denote the same patient with four donors, D11-D14.

Table 2: Data generation for paired kidney exchange

Parameter	Explanation
HLA_A_{ij}, HLA_B_{ij}, HLA_DR_{ij}	U(0,2)
nd_i	"1" with probability 0.85 "2" with probability 0.05 "3" with probability 0.05 "4" with probability 0.05
pbg_i, dbg_j	U(0,3) 0 represents "0" blood group, 1 represents "A" blood group, 2 represents "B" blood group, 3 represents "AB" blood group
PRA	"0" with probability 0.60 "1" with probability 0.40
$page_i$	U(0,19) with probability 0.068,

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	U(20,44) with probability 0.609, U(45,64) with probability 0.272, U(65,74) with probability 0.049, U(75,80) with probability 0.002,
$dage_j$	U(20,75)
$pgender_i$, $dgender_j$	"Male(1)" with probability 0.60 "Female(0)" with probability 0.40
$bgmatch_{ij}$	"1", if $pbg_i = dbg_j$ "0", otherwise

Table 3: Patient-donor characteristics of generated data

Patient Data				Donor Data			
Patient ID	Gender	Age	Blood Group	Donor ID	Gender	Age	Blood Group
P1	Female	8	AB	D1	Male	31	AB
P2	Female	3	A	D2	Male	20	B
P3	Female	27	0	D3	Male	34	0
P4	Female	21	AB	D4	Female	47	A
P5	Female	28	B	D5	Female	28	0
P6	Male	24	A	D6	Female	29	B
P7	Male	36	AB	D7	Female	38	0
P8	Female	34	AB	D8	Female	37	0
P9	Female	34	AB	D9	Male	37	AB
P10	Male	27	AB	D10	Female	73	AB
P11	Male	36	B	D11	Female	74	AB
P12	Male	36	B	D12	Male	40	B
P13	Male	36	B	D13	Female	40	0
P14	Male	36	B	D14	Female	62	A
P38	Female	66	B	D38	Female	36	0
P39	Female	72	B	D39	Female	24	AB
P40	Male	75	B	D40	Female	42	0

Results of paired kidney exchange

By using the generated data described above, the proposed mathematical models are solved using GAMS optimization software [18] and CPLEX solver [19]. The characteristics of model PKE_O are listed in [Table 4]. The solution of the proposed model with the default settings of CPLEX version 12.0 indicates that the optimal solution is found at the root node in 0.484 CPU seconds.

Table 4: Characteristics of the constructed model

Item	Value
Number of binary variables	1560
Number of constraints	1681
Number of nodes	0
Number of iterations	39
Solver memory (MB)	4
CPU time (seconds)[a]	0.484

[a]Desktop computer with Intel Core i5 processor and 4 GB of RAM.

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32 transplantation assignments are obtained as the optimal solution of model PKE_O for 40 patient-donor pairs. Due to space limitation, only three of the paired exchanges are presented in [Table 5]. As an example it is observed that, P11-P14 who is the same patient with four donors has attended the exchange with his donor D12, and has received the kidney from the donor of pair P5-D5.

Table 5: Results of the paired kidney exchange

Patient ID	Gender	Age	Blood Group	Donor ID	Gender	Age	Blood Group
P12	Male	36	B	D5	Female	28	0
P5	Female	28	B	D12	Male	40	B

Patient ID	Gender	Age	Blood Group	Donor ID	Gender	Age	Blood Group
P24	Male	38	B	D2	Male	20	B
P2	Female	3	A	D24	Female	48	0

Patient ID	Gender	Age	Blood Group	Donor ID	Gender	Age	Blood Group
P21	Male	21	0	D8	Female	37	0
P8	Female	34	AB	D21	Female	22	A

Results of Age Effect

As shown in [Table 6], a number of experiments are performed by changing the value of age threshold, *at*, in model PKE_A. The number of *at* is studied for 5, 10, 15, 20 and 25 in a population of 40 patient-donor pairs. For example, when the age difference between donors of pair *i* and *j* pair is less than or equal to 10, the paired kidney exchange model results in 24 transplantations with an objective function value of 5790. However, when the results of models PKE_O and PKE_A are compared, model PKE_O has a higher objective function value and total exchange score. As expected, this result points out the fact that, the addition of age constraint will limit both the number of transplants and the total HLA score of assignments.

Table 6: Age effect on paired kidney exchange with different age threshold values for 40 patient and donor pairs

at	Pair Kidney Exchange	
	*z**	*TT*
5	4435	16
10	5790	24
15	6520	26
20	7025	28
25	7070	28
None	8350	32

z: Objective Function Value, *TT*: Total Number of Transplantations, *at*: Age Threshold

Results of gender effect

The comparative results of models PKE_O and PKE_G for the given 40 patient-donor pairs are displayed in [Table 7]. It is observed that, PKE_O has better results in terms of objective function value and number of

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transplantations. This indicates that adding a gender constraint restricts the number of transplantations, as expected.

Table 7: Gender effect for 40 patient-donor pairs

Gender Restriction	Pair Kidney Exchange	
	z^*	*TT*
None	8350	32
M-M **F-F**	6360	22

z: Objective Function Value, *TT*: Total Number of Transplantations, M-M: Male to Male, F-F: Female to Female

Implementation at a hospital in Turkey

In order to compare the model's solution with the planned transplantations at one of the leading kidney transplantation centers located in Istanbul, the original patient-donor list provided by the hospital is input to the model. [Table 8] displays the real waiting list of patients and their donors. For example, P9-P12 is a female patient who is 64 years old and has an A blood group type. She has four donors, D9-D12, whose characteristics are shown in [Table 8]. On the other hand, the male patient P13 has a single donor D13 who is a female.

By using the real data given in [Table 8], model PKE_O is solved using GAMS optimization software [4] and CPLEX solver [18]. For this data set, 4 transplantation assignments are obtained in the optimal solution. As it can be seen from Table 9, pairs P7-D7 and P14-D14 have exchanged their kidneys. The female donor D7 with B blood group type has given her kidney to P14 who is a female patient with the same blood group. In this exchange, the male patient P7 with A blood group has received a kidney from the 0 blood group male donor D14. In the second swap, P9-P12 who is the same patient with four donors has participated the exchange with her donor D11, and has received the kidney from the donor of pair P13-D13.

For this real data set, the hospital could not find any assignments manually. Hence, they shared the data to apply the suggested optimization approach. By the help of the developed model, two swaps are obtained, which is a considerable contribution to both the hospital and the patients. The proposed method automatically evaluates the optimal assignments and eliminates personal mistakes.

Table 8: Real list of patients and donors

Patient Data				Donor Data			
Patient ID	**Gender**	**Age**	**Blood Group**	**Donor ID**	**Gender**	**Age**	**Blood Group**
P1	Female	62	A	D1	Female	34	A
P2				D2	Female	40	A
P3				D3	Female	56	A
P4				D4	Female	54	A
P5	Female	53	A	D5	Male	52	A
P6	Female	55	A	D6	Female	40	A
P7	Male	42	A	D7	Female	39	B
P8	Male	63	A	D8	Female	55	AB
P9	Female	64	A	D9	Male	41	A
P10				D10	Male	44	B
P11				D11	Male	39	B
P12				D12	Female	42	A
P13	Male	42	B	D13	Female	35	A
P14	Female	60	B	D14	Male	54	0

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P15	Female	50	0	D15	Female	40	A
P16	Male	62	0	D16	Male	36	A
P17				D17	Female	33	A
P18	Female	54	0	D18	Male	20	0
P19	Female	50	0	D19	Male	54	0
P20	Female	54	0	D20	Male	69	A
P21	Female	34	0	D21	Male	33	A

Table 9: Assignments of paired kidney exchange model for real data

Patient ID	Gender	Age	Blood Group	Donor ID	Gender	Age	Blood Group
P7	Male	42	A	D14	Male	54	0
P14	Female	60	B	D7	Female	39	B
Patient ID	**Gender**	**Age**	**Blood Group**	**Donor ID**	**Gender**	**Age**	**Blood Group**
P11	Female	64	A	D13	Female	35	A
P13	Male	42	B	D11	Male	39	B

Comparison of decentralized and centralized approaches

In order to compare the results of decentralized and centralized approaches, a random data set for each of the five hospitals in Istanbul that are capable of performing kidney exchanges is generated by considering their location and size. [Table 10] displays the number of patients in the waiting list of each hospital.

Table 10: Number of patients at each hospital

Hospital	Number of Patients
H1	25
H2	20
H3	15
H4	20
H5	13
Total	93

The “decentralized approach” represents the current situation at which the hospitals perform the swaps within their individual waiting lists. On the other hand, in the proposed “centralized approach”, hospitals are working in a coordinated manner and sharing their waiting list information with each other. The resultant single common list can lead to the realization of exchanges between two different hospitals. By using the data given in [Table 10], model PKE_O is run for both approaches. Comparison of the results of two approaches is displayed in [Table 11].

In the decentralized system, while approximately 45% of the patients undergo transplantation, this ratio becomes approximately 60% in a centralized system. Since the exchange and compatibility probability increases with an expansion in the waiting list size, the total HLA score as an indicator of exchange compatibility improves by 53% in the centralized case. Moreover, the number of swaps is increased through coordination. Consequently, it will be possible to minimize both waiting time of emergency patients and post-transplantation complications.

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Table 11: Comparison of the decentralized and centralized approaches

Hospital	Decentralized Approach		Centralized Approach	
	Total HLA Score	Number of Transplantations	Total HLA Score	Number of Transplantations
H1	3010	10	4115	13
H2	2045	8	3315	10
H3	1645	8	2180	9
H4	2795	10	4415	14
H5	1830	6	3295	10
Total	11,325	42	17,320	56

[Table 12] gives the distribution of patients and donors matched in the centralized approach. In the centralized approach, appropriate patient-donor pair matching takes place between different hospitals, whereas, in the decentralized approach, transplantations are performed within the pairs belonging to the same hospital. For example, the individual waiting list of H4 results in 10 swaps in the decentralized system. This number increases to 14 in the proposed approach. Among those exchanges, 2 are from its own waiting list, while 3, 1, 3, and 5 exchanges result from the coordination with hospitals H1, H2, H3 and H5, respectively.

Table 12: The distribution of patients and donors matched in centralized approach

Patient's Hospital	Donor's Hospital				
	H1	H2	H3	H4	H5
H1	6	3	1	3	0
H2	3	2	2	1	2
H3	1	2	2	3	1
H4	3	1	3	2	5
H5	0	2	1	5	2

These results are promising and indicate that a centralized approach will be more advantageous in terms of number of swaps, probability of exchange and compatibility.

CONCLUSION

Kidneys are among the vital organs of the human body, and for patients suffering from kidney failure or serious kidney diseases, transplantation is the most desirable treatment alternative. Statistics show that, the number of patients suffering from kidney diseases in Turkey is increasing each year. This study introduces an easy and practical approach to the paired kidney allocation problem. Currently, each hospital in Turkey operates in a decentralized manner. A patient in this list may have more than one incompatible donor, which constitutes the main difference of this work from others in literature.

To solve the paired kidney exchange problem considering all important factors, integer linear programming models are proposed to maximize the total allocation score between compatible patient and donor pairs under some system constraints. GAMS software and CPLEX solver is used to obtain the optimal solutions of the developed models. Different scenarios are generated to measure the impact of "gender differences" and "age" on the solution. Moreover, the real patient-donor list provided by a hospital located in Istanbul is employed in the model for comparison of the model's solution with the planned transplantations. The study also incorporates and evaluates a centralized approach which integrates all the hospitals performing paired kidney exchange in Istanbul. In terms of HLA compatibility and number of transplantations performed, the centralized approach seems to be more favourable in comparison to decentralized approach. During the course of this study, feedbacks have been taken continuously from specialists working in this area.

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As an extension, three-way and multi-way kidney exchange models can also be developed. We hope that this study will be of assistance to the paired kidney allocation problem of the Ministry of Health, and the National Coordination Center in Turkey.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

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FINANCIAL DISCLOSURE

None

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