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Clinical decision support system to predict chronic kidney disease: A fuzzy expert system approach

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ABSTRACT

Background and objectives: Diagnosis and early intervention of chronic kidney disease are essential to prevent loss of kidney function and a large amount of financial resources. To this end, we developed a fuzzy logic-based expert system for diagnosis and prediction of chronic kidney disease and evaluate its robustness against noisy data.

Methods: At first, we identified the diagnostic parameters and risk factors through a literature review and a survey of 18 nephrologists. Depending on the features selected, a set of fuzzy rules for the prediction of chronic kidney disease was determined by reviewing the literature, guidelines and consulting with nephrologists. Fuzzy expert system was developed using MATLAB software and Mamdani Inference System. Finally, the fuzzy expert system was evaluated using data extracted from 216 randomly selected medical records of patients with and without chronic kidney disease. We added noisy data to our dataset and compare the performance of the system on original and noisy datasets.

Results: We selected 16 parameters for the prediction of chronic kidney disease. The accuracy, sensitivity, and specificity of the final system were 92.13 %, 95.37 %, and 88.88 %, respectively. The area under the curve was 0.92 and the Kappa coefficient was 0.84, indicating a very high correlation between the system diagnosis and the final diagnosis recorded in the medical records. The performance of the system on noisy input variables indicated that in the worse scenario, the accuracy, sensitivity, and specificity of the system decreased only by 4.43 %, 7.48 %, and 5.41 %, respectively.

Conclusion: Considering the desirable performance of the proposed expert system, the system can be useful in the prediction of chronic kidney disease.

1. Background and objectives

Chronic Kidney Disease (CKD) is defined as a persistent reduction in glomerular filtration rate (GFR) or evidence of structural or functional abnormalities in kidneys [1]. Until the progress of CKD, there are no severe signs of the disease, but the patient may have symptoms such as tiredness, and appetite loss [2]. In most cases, the causes of this disease are not stabilized and not fully recognized in many patients [3]. CKD imposes high medical costs [4] and is one of the common causes of mortality across the globe and its burden is increasing [5,6]. In 2012, it was estimated that around 500 million individuals would suffer from this disease [7]. The prevalence of this disease in developing countries is higher than that in developed countries [6]. In Iran, the incidence of CKD is increased by 2 % every year [8]. The prevalence of CKD in Iran is 12.6 % and its prevalence in each of the five stages is as follows: stage one: 2.2 %, stage two: 2.1 %, stage three: 7.8 %, stage four: 0.3 %, and stage five: 0.2 % [9].

The severity of CKD is determined conventionally using different

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate; ES, expert systems; FES, fuzzy expert systems; UCI, University of California Irvine; ROC, the receiver operating characteristic; AUC, the area under the curve; FRA, folate receptor alpha; MSLN, mesothelin; MPF, megakaryocyte potentiating factor; BMI, body mass index; ACR, urine albumin to creatinine ratio; HDL, high density lipoprotein; LDL, low density lipoprotein; TSH, thyroid-stimulating hormone; BUN, blood urea nitrogen; TG, triglyceride; MOM, the mean of maximum

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computational formulas based on different biomarkers. Currently, the glomerular filtration rate (GFR) is the most common indicator used in healthcare organizations to estimate the kidney function [4]. However, studies have shown that GFR is not sufficient to diagnose CKD [10]. GFR measurements using markers such as insulin or iothalamate are definitive measures, but none of them are practical and economical for routine applications [11]. On the other hand, general physicians are in the first line to identify and control CKD, but they mostly cannot diagnose this disease. Unlike most patients, some patients with cardiovascular diseases and diabetes have high GFR levels. Therefore, most general physicians are not able to diagnose CKD in these patients [10]. CKD in the early stages is silent and asymptomatic and completely remain without diagnosis [12]. Therefore, early diagnosis and quick interventions for CKD to prevent the waste of financial resources are necessary [13].

A variety of clinical decision support systems such as expert systems (ES) can be used to facilitate medical diagnosis [14]. Expert systems have the architecture, components, and functionalities that may improve overall decision-makers' ability to diagnose diseases. ES uses human knowledge to describe issues that require human intelligence. It also provides expert knowledge in the form of decision rules [15]. Many medical expert systems are developed in this field to help with the diagnosis or treatment of diseases [4,16,17]. On the other hand, fuzzy systems are used to describe uncertain phenomena, because real-world phenomena are so complicated [18,19]. The use of intelligent systems including fuzzy expert systems (FES) can transform information gathered by experts into knowledge, which can be used later for early diagnosis of diseases or develop treatment plans for patients [17,20]. A precise medical diagnosis requires the extraction of data and information to make a proper decision about health or guess the probability of a person's disease. The FES is focused on obtaining diagnostic knowledge from physicians and receiving uncertain and vague data from patients. An FES provides a framework for transferring medical knowledge to mathematical models to develop conclusions [21,22].

Many studies have been conducted to make diagnosis or prediction of kidney-related diseases using machine learning techniques or expert systems [23–30]. Considering the CKD, various researchers have developed and implemented expert systems for the diagnosis of CKD [31–34], among them; the most accurate one (about 98 %) was developed by Muslim et al. with only six important factors. However, they did not consider other important factors and did not provide any information about the method for selection of these six factors and sensitivity and specificity of their system [31]. Additionally, some researchers have also developed machine learning-based classification models to diagnose this disease [32–37]. The majority of these studies have been based on the machine learning repository of California University (UCI) [38]. These studies have had a variety of results in terms of accuracy. Also, none of these systems or models has been tested against noisy data. Therefore, in this study, our purpose was twofold. From the clinical perspective, we aimed to develop an FES to early prediction of CKD for general physicians and from the technical perspective; we aimed to evaluate the robustness of our FES against any noisy data to show their applicability for real data that may have many noises.

2. Material and methods

This research was carried out in three phases. In the first phase, we identified the variables required to develop and determine FES rules. In the second phase, the FES prototype was developed and evaluated. In the third phase, we evaluated the robustness of the system against the generated noisy data.

2.1. Identification of the variables and rules for developing the FES

At first, a review of the literature was conducted in PubMed (Medline) using the following search strategy and studies that reported the diagnostic parameters of CKD were considered.

Chronic kidney disease [Title/Abstract] AND (diagnosis [Title/Abstract] OR parameter [Title/Abstract] OR clinical characteristic [Title/Abstract])

Our nephrologist consultant (H.S) confirmed 42 out of 49 parameters identified from the literature. For these 42 parameters, we developed a questionnaire and then invited all nephrologists of teaching hospitals affiliated with Iran University of Medical Sciences (18 physicians) to participate but only 13 of them finally participated. They were asked to rate parameters based on the degree of their importance (five-point Likert scale) for each parameter (The highest importance: 5 to the least importance: 1). The reliability of the questionnaire was assessed using Cronbach's alpha coefficient (a = 0.89). The mean of the scores given to each parameter was calculated. Since selecting many variables may result in numerous rules, we only selected the most important ones and considered the most agreed upon variables. To this end, we included those variables that their mean score was in the first quartile (75 % of the possible points) which is equal to 3.75 out of 5 [39].

After identifying important parameters, reviewing the literature and guidelines [20,40,41] and consulting with a nephrologist, a set of rules for the prediction of CKD was defined in the form of if-then rules (36 rules). All rules were independent and there were no nested rules. According to these rules, a questionnaire was developed and the same nephrologists (18 doctors) were asked to determine their agreement or disagreement for each rule, the reasons for their disagreement and their suggestions. Seven physicians participated in this step. Since the questionnaire had two options (agree or disagree) for a response, those rules that were approved by more than 50 % of the respondents were selected. The reliability of the second questionnaire was assessed using Kuder-Richardson (r = 0.61).

2.2. Development and evaluation of the system

Based on the results of the previous phase, the CKD diagnostic fuzzy expert system was coded and implemented using the MATLAB software. The Mamdani Inference System was developed. We developed several systems based on different membership functions for different parameters and selected the best one based on their performance.

The system was evaluated using data extracted from medical records of patients in two teaching hospitals in Tehran, Iran. The sample size was calculated using the formula 1 given P0 = 0.126 [9]. Therefore, medical records of 108 patients with CKD and 108 patients with other kidney diseases were reviewed. All 216 medical records were randomly selected from the medical records of patients discharged in one year from September 2017 to September 2018.

$$N = [Z1 - (\alpha/2) \times \sqrt{(P0(1 - P0))} + Z1 - \beta \times \sqrt{(P1(1 - P1))}]\hat{}2/d\hat{}2 \quad (1)$$

(α = first type error / β = second type error / P0 = probability of existence the disease in population/ P1 = probability of occurrence of disease in healthy group)

We developed a data extraction form included the identified variables. A trained researcher (F.H) reviewed the paper-based medical record of patients and extracted the data about these variables and filled the extraction formfor each patient. Then, data were entered into an Excel spreadsheet.

To evaluate the system, all data was exported to the developed system and the system output was compared with the diagnosis recorded in the medical records. The Kappa test, the receiver operating characteristic (ROC) Curve, the area under the curve (AUC), as well as the accuracy, sensitivity, and specificity were used to evaluate the FES performance to predict the CKD. Formulas 2–4 were used to calculate these indices [42,43].

$$\text{Sensitivity} = TP/(TP + FN) \quad (2)$$

$$\text{Specificity} = TN/(TN + FP) \quad (3)$$

$$\text{Accuracy} = (TP + TN)/(TP + FP + TN + FN) \quad (4)$$

2.3. Evaluation of the system with noisy data

To evaluate the robustness of the fuzzy system against noisy data, we generated noisy data and added it to our dataset using R software. In the first experiment, we added noisy data to the class data (CKD or no-CKD) and in the second experiment; we added noisy data to all input variables. In each experiment, we added 5%, 10 %, 15 %, 20 % and 25 % of noisy data, respectively. To this end, in the first experiment, we randomly selected 5%–25% of records and changed the class values (changing the CKD to non-CKD and inverse). In the second experiment, we selected the 5%–25% of values of all of the input variables (not class variable) and inverted the values for binary data (for example, Yes to No, or No to Yes) or changed the values based on the mean and standard deviation using Uniform Distribution Function. Finally, we imported these 10 noisy datasets to our system and evaluated it using the formulas 2–4.

2.4. Ethical considerations

Clinical and laboratory data were used without the patients' identification data. The ethical approval was granted by Iran University of Medical Sciences (IR.IUMS.REC 1395.9311553002).

3. Findings

3.1. The variables and rules for developing the FES

Initially, a list of diagnostic variables and risk factors for the diagnosis of CKD were identified based on the literature review. Next, according to a nephrologist consultation, seven out of the 49 identified parameters, including cysteine C, hematuria, exosomal ncRNAs, folate receptor alpha (FRA), mesothelin (MSLN), megakaryocyte potentiating factor (MPF) and genetic biomarker were not confirmed. Finally, 42 remaining parameters were used to prepare the questionnaire. Considering the mean score above 3.75, age, systolic blood pressure, diastolic blood pressure, proteinuria, albuminuria, creatinine serum, GFR, BUN, history of hypertension, history of diabetes, and family history of CKD were selected as the final parameters.

We consulted the nephrologist about the parameters with a mean score of 3.0–3.75 (uric acid, blood glucose, polar height to pole in ultrasound, phosphorus, calcium, potassium, hemoglobin, albumin to creatinine ratio), therefore, polar height to pole in ultrasound, phosphorus, calcium, and hemoglobin were added to the final list of parameters. Finally, 16 parameters were selected as the final parameters (Table 1).

3.2. Development of FES

3.2.1. Developing fuzzy sets and variables

The first component of the fuzzy inference system is the input fuzzification. The expert system had 16 input variables and one output variable. To define the membership functions, the numerical ranges of each of the parameters were firstly extracted from the literature and guidelines [20,40,41,71]. Next, the membership functions of the input variables were determined during consultation sessions with a nephrologist. The linguistic variables and range of values related to the input and output variables of the CKD diagnostic system are shown in Table 2.

To achieve the best combination of membership functions for input variables and the best performance, we used a trial and error approach. Firstly, we developed the system with each of the Gaussian, Trapezoidal, and Triangular functions for each parameter, except for "family history of CKD" which is a binary variable and the singleton function was used. Secondly, we used a combination of membership functions for various input variables and evaluated the performance of each system. Finally, the system with the best results was selected. Table 2 shows the membership functions for the final selected system. Some believe that GFR is deterministic and should not be fuzzified. Therefore, we also developed the system with non-fuzzified GFR and compared the results. Supplementary Fig. 1 shows some examples of membership functions associated with the input and output variables of the final system.

To develop the rules, we first defined the rules based on the literature review and then asked the nephrologists to state their agreement or disagreement for each rule. All of 36 rules were approved by 100 % of the respondents. Mamdani fuzzy model was used to develop the inference engine of this system based on the 36 if-then rules. In our system, all rules are fired independently. Fig. 1 shows some of the fuzzy rules for the system.

3.2.2. The expert system user interface for the prediction the CKD

The graphical user interface of the expert system was implemented using the MATLAB software (Fig. 2).

3.3. Evaluation of the system

We evaluated different systems using various triangular, trapezoidal and Gaussian functions as well as the combination of all membership functions. The membership functions for variables in the best performing system are shown in Table 2. According to Table 3, the accuracy, sensitivity, and specificity of the best system reported as 90.74 %, 95.37 %, and 86.11 %, respectively. The Kappa and AUC were 0.81 and 0.90, respectively. We re-tested this system with non-fuzzified GFR (system 2). The accuracy, specificity, Kappa, and AUC increased. We found that removing GFR from the system resulted in reduced performance (system 3). According to the results (Table 3 and Fig. 3), we selected the system 2 as our final system. Besides, we performed the surface analysis in Matlab. The surface plot shows a 3D surface from two input variables and the output of the system to display the dependency of the output on the inputs (Supplementary Fig. 2). Besides, some part of rule viewer is presented in Supplementary Fig. 3.

3.4. Evaluation of the system with noisy data

Medical data is often noisy in the real world. To evaluate the resistance of our system against noisy data, we added 5%–25% noise to the dataset. In the first experiment, we added noise to the class data. As expected (Table 4), the accuracy, sensitivity, and specificity were decreased with increasing the amount of noise. However, in the worse scenario (25 % noise), the accuracy, sensitivity, and specificity are 73.76 %, 72.03 %, and 68.72 %, respectively. In the second experiment, we added the noise to all of the input variables. As seen in Table 4, in the worse scenario, the accuracy, sensitivity, and specificity are 87.69 %, 87.89 %, and 83.47 %, respectively.

4. Discussion

In this study, we developed and evaluated a fuzzy expert system for predicting CKD and also, we evaluated our system with noisy data. In the first phase, after reviewing the literature and considering the nephrologists' knowledge, we found the main parameters for the diagnosis of CKD as age, systolic blood pressure, diastolic blood pressure, proteinuria, albuminuria, creatinine, GFR, BUN, parathyroid hormone, hemoglobin, calcium, phosphorus, polar height to pole in ultrasound, history of hypertension, history of diabetes, and family history of CKD. In the study of Tahmasebian et al. the important parameters for CKD

Table 1
CKD diagnostic variables based on literature review and the nephrologists' perspectives.

Variables	References	Nephrologists' responses Mean ± (Standard Deviation)
Age	[44,45,46,47,48,49,50,51]	4.17 ± (0.835)
Sex	[46,47,50,52]	2.11 ± (1.537)
Height	[47,53]	1.00 ± (0.0)
Weight	[53,54]	1.17 ± (0.408)
Body mass index (BMI)	[47,50,51,53,55,56]	2.00 ± (1.414)
Systolic blood pressure	[44,45,47,48,50,57]	4.08 ± (0.760)
Diastolic blood pressure	[44,45,47,48,50,57]	4.08 ± (0.760)
Proteinuria	[12,45,47,50,52,54,56,58,59,60]	4.77 ± (0.599)
Albuminuria	[2,12,44,45,46,48,50,53,57,59]	4.62 ± (0.650)
Serum creatinine	[44,46,47,50,51,53,55,56,58]	4.77 ± (0.832)
Urine albumin to creatinine ratio (ACR)	[12,44,45,50,51]	3.15 ± (0.899)
Glomerular filtration rate (GFR)	[2,12,44,46,47,48,49,50,51,52,53,55,58,59]	4.62 ± (0.650)
Hemoglobin	[44,47,48,51,56]	3.50 ± (1.179)
Total cholesterol	[47,50,61]	2.00 ± (1.414)
High density lipoprotein (HDL)	[44,62]	2.00 ± (1.225)
Low density lipoprotein (LDL)	[44,62]	2.00 ± (1.225)
Sodium	[50,57,63]	2.86 ± (1.069)
Calcium	[47,48,50,55,57,63]	3.25 ± (0.965)
Phosphorus	[47,48,50,57,63]	3.25 ± (0.965)
Potassium	[48,50,56,63]	3.30 ± (0.949)
Polar height to pole in ultrasound	[12,45,46,47,57,64]	3.00 ± (1.773)
Polar width to pole in ultrasound	[12,45,46,47,57,64]	3.00 ± (1.915)
Renal parenchyma thickness in ultrasound	[12,45,46,47,57,64]	2.91 ± (1.514)
Blood glucose	[52,54]	3.60 ± (1.174)
Parathyroid hormone	[48,55,65]	2.67 ± (1.435)
Thyroid-stimulating hormone (TSH)	[51,66]	1.67 ± (0.577)
Blood urea nitrogen (BUN)	[2,44,48,53,55,59]	3.75 ± (0.965)
Triglyceride (TG)	[65,66]	2.00 ± (0.500)
Uricacid	[44,48,55]	3.55 ± (1.293)
Hypertension	[44,46,49,50,51,52,53]	4.00 ± (0.853)
Obesity	[45,52]	2.27 ± (1.009)
Diabetes mellitus	[44,45,46,48,50,51,52,53,55,56,59,67]	4.31 ± (0.855)
Cardiovascular disease	[45,46,48,49,50]	2.42 ± (1.165)
Stroke	[49,62]	2.30 ± (1.059)
Hydronephrosis	[65]	2.67 ± (1.155)
Acute kidney damage	[54,65]	2.54 ± (1.266)
Anemia	[54,62]	2.25 ± (1.055)
Smoking	[62,65]	2.00 ± (0.739)
Alcohol consumption	[62,65]	2.09 ± (0.944)
Family history of CKD	[45,46,49,54,62,68]	3.77 ± (1.092)
History of kidney stone	[62,65]	2.25 ± (1.138)
Income level	[46,49,50]	1.57 ± (1.138)
Cysteine C *	[12,56,59]	–
Hematuria*	[46]	–
Exosomal ncRNAs*	[66]	–
Folate receptor alpha (FRA) *	[51,69]	–
Mesothelin (MSLN) *	[58]	–
Megakaryocyte potentiating factor*	[58]	–
Genetic biomarker*	[60,70]	–

* These variables were excluded according to the opinion of the clinical advisor of this study.

were GFR, diastolic blood pressure, triglyceride, MAP, weight, LDL, hematocrit, systolic blood pressure, FBS and HDL [72]. In another study, age, blood glucose, blood urea, serum creatinine, sodium, potassium, hemoglobin, red blood cells, and white blood cells were used for diagnosing CKD [73]. Muslim also used variables such as age, hemoglobin, serum creatinine, urine plasma levels, and GFR for CKD diagnosis [31]. In many studies, the UCI data are used to train the model for diagnosing CKD. UCI data include following variables: age, blood pressure, specific gravity, albumin, sugar, pus cell, pus cell clumps, bacteria, blood glucose random, blood urea, serum creatinine, sodium, potassium, hemoglobin, packed cell volume, white blood cell count, red blood cell count, hypertension, diabetes mellitus, coronary artery disease, appetite, pedal edema, and anemia. We also included these variables in our survey on nephrologists; however, only six of them including age, blood pressure, serum creatinine, hemoglobin, high blood pressure, and diabetes were validated in our study. Additionally, we used additional eight factors including proteinuria, albuminuria, calcium, phosphorus, BUN, parathyroid hormone, polar height to pole in ultrasound, and family history of CKD which have not been used in previous studies.

The accuracy, sensitivity and specificity and AUC of our system were 92.13 %, 95.37 %, and 88.88 %, and 0.92, respectively. The value of $K = 0.84$, according to Landis and Koch [74], indicated a very high correlation between the output of the final system and the final diagnosis recorded by physicians in the patients' medical records. Comparing with our system (Table 5), there are some other expert systems for CKD. In the Zarandi's study, the accuracy of the FES was created using a type I fuzzy inference system, and its improvement using the adaptive neuro-fuzzy inference system (ANFIS) model was estimated as 80 % [73]. In another study by Abdolkarimzadeh, type-II fuzzy diagnosed CKD with an average accuracy of 90 %; however, the accuracy of our system was better [75]. Moslem developed another CKD fuzzy inference system using the MOM and the bisector defuzzification methods, and the accuracy of these two methods was 97.14 % and 98.86 %, respectively [31]. The reported accuracies by Moslem et al. are higher (5–6 %) than that achieved in our study; however, they did

Table 2
Input variables and the value range for the diagnosis of chronic kidney disease.

Variables	Linguistic terms	Range of values	Fuzzy membership functions of the selected system
Age	Young	1 – 18	[0.11 0.33 19.5 20]
	Middle-aged	18 – 60	[16 39.5 65]
	Old	60 <	[55 57 130 130]
Systolic blood pressure	Normal	100 – 140	[90 95 123 160]
	Abnormal	140 <	[120 154.5 260 260]
Diastolic blood pressure	Normal	0 – 90	[0 0 73.5 120]
	Abnormal	90 <	[75 109 260 260]
Proteinuria	Normal	0 – 150	[0 0 160 252]
	Abnormal	150 <	[130 279 8120 8120]
Albuminuria	Normal	30 – 150	[20 25 156.5 226]
	Abnormal	150 <	[130 190 8120 8120]
Serum creatinine	Normal	0.6 – 1.4	[0.4 0.5 1.1 1.9]
	Abnormal	1.4 <	[1 1.6 32 32]
GFR *	Normal	100 – 120	[90 95 125 135]
	Before the disease	60 – 90	[50 75 100]
	During the disease	60 >	[-114 – 99.5 65 70]
BUN	Normal	0 – 21	[0 0 17.5 30]
	Abnormal	21 <	[18 23.5 236 236]
Parathyroid hormone	Normal	0 – 65	[0 0 58.5 75]
	Abnormal	65 <	[60 69 751 751]
Hemoglobin	Normal	13.3 – 16.2	[10 13.5 17 20]
	Abnormal	13.3 >	[0 0 11 14.5]
Calcium	Normal	8.6 – 10.3	[8 8.7 10.5 11]
	Abnormal	8.6 >	[0 0 8 8.8]
Phosphorus	Normal	2 – 5	[1 1.5 4.2 6]
	Abnormal	5 <	[3 5.3 11 11]
Polar height to pole in ultrasound	Normal	100 – 120	[85 108.5 131 151]
	Before the disease	80 – 100	[70 85 95 110]
	During the disease	60 – 80	[50 55 72.3 85]
History of hypertension (years)	Low	5 >	[0 0 4 7]
	High	5 <	[3.5 6.3 100 100]
History of diabetes mellitus (years)	Low	5 >	[0 0 4 7]
	high	5 <	[3.5 6.3 100 100]
Family history of CKD	No	0	[0]
	Yes	1	[1]

* We developed three different systems, one with fuzzified GFR, one with Non-fuzzified GFR and one without GFR.

not include many features that our experts considered important.

Many researchers have also developed machine learning models to diagnose CKD. In these studies, different models were developed and different results were reported (Table 5). Our system showed a higher better performance than that of some machine learning models (support vector machine and K-nearest neighborhood reported by Sinah [76], artificial neural network reported by Gharibdousti [34] as well as ant colony based optimization (ACO), particle swarm optimization (PSO), and Olex-genetic algorithm (OlexGA) reported by Elhoseny [77]. However, most machine learning models had a better performance than fuzzy expert systems [32–37,77]. These machine learning studies were based on the UCI machine learning data repository and their diagnostic variables were parts of the parameters of this educational data set. However, nephrologists who participated in our study did not consider many of these variables important for diagnosing CKD and these variables were not included in our system. This is one of the reasons for the different results of machine learning systems with those of the present study. Although machine learning algorithms may outperform, we should consider that these algorithms are mainly trained by data and this process has complex mathematical and statistical computations that may not be understandable by physicians. However, one of the most important advantages of fuzzy expert systems is that the rules and variables are defined and understandable by domain experts. This involvement and understanding may influence the acceptance of the system in real practice. Furthermore, many previous studies did not consider GFR in their systems or models, however, we found that this variable is important based on nephrologists' perspectives and also it improved the diagnostic performance of the system.

We evaluated the noise tolerance of our system. Noise tolerance generally refers to the sensitivity of models to a small noise in input data. As we expected, the accuracy of the system has been declined with increasing noisy data. Although in the first experiment, the accuracy, sensitivity, and specificity of the system decreased by 18.37 %, 23.34 %, and 20.06 %, respectively, in the real world, such systems are used to diagnose patients' conditions; in fact, we do not face with noisy data in the class variables. Our experiment related to the noisy input variables indicated that in the worse scenario, the accuracy, sensitivity, and specificity of the system decreased by 4.43 %, 7.48 %, and 5.41 %, respectively and therefore, the performance of the system on noisy data is close to the original data.

This study had some limitations such as carrying out a survey to identify the necessary parameters only by specialists from four hospitals affiliated with Iran University of Medical Sciences (18 specialists), that might reduce the generalizability of findings of the first phase of the study. Also, the evaluation of this system was performed using data from only two hospitals. Lastly, this system was not evaluated in a real clinical environment. In addition to diagnosis and prediction, the treatment of patients is also important and our system can not recommend treatments or control methods for patients.

5. Conclusion and future studies

The result of this research can be used for the creation of a fuzzy expert system for the diagnosis of CKD to prevent and accurately inform the presence of CKD. The accuracy, sensitivity, and specificity of the system were 92.12 %, 95.37 %, and 88.88 %, respectively. Besides, the robustness of our system against any noisy input data indicates great applicability for real data. In the future, to determine the rules and

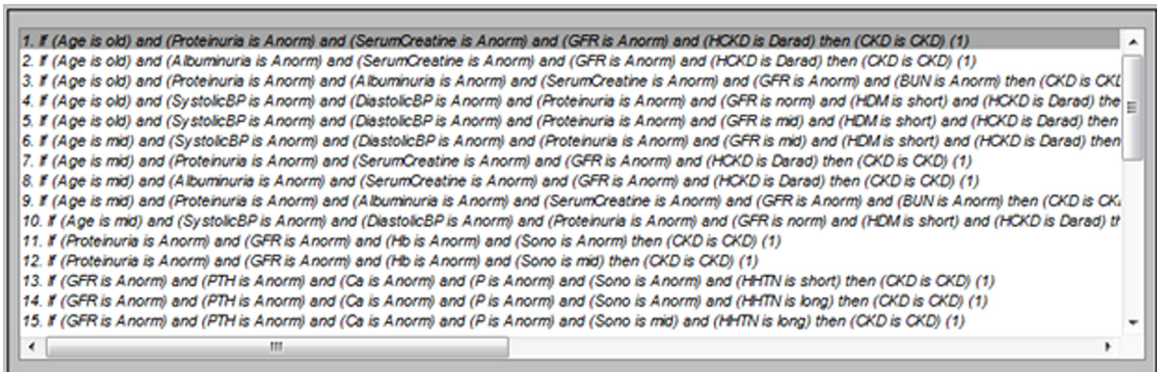

Fig. 1. Some of the rules used to develop the system.

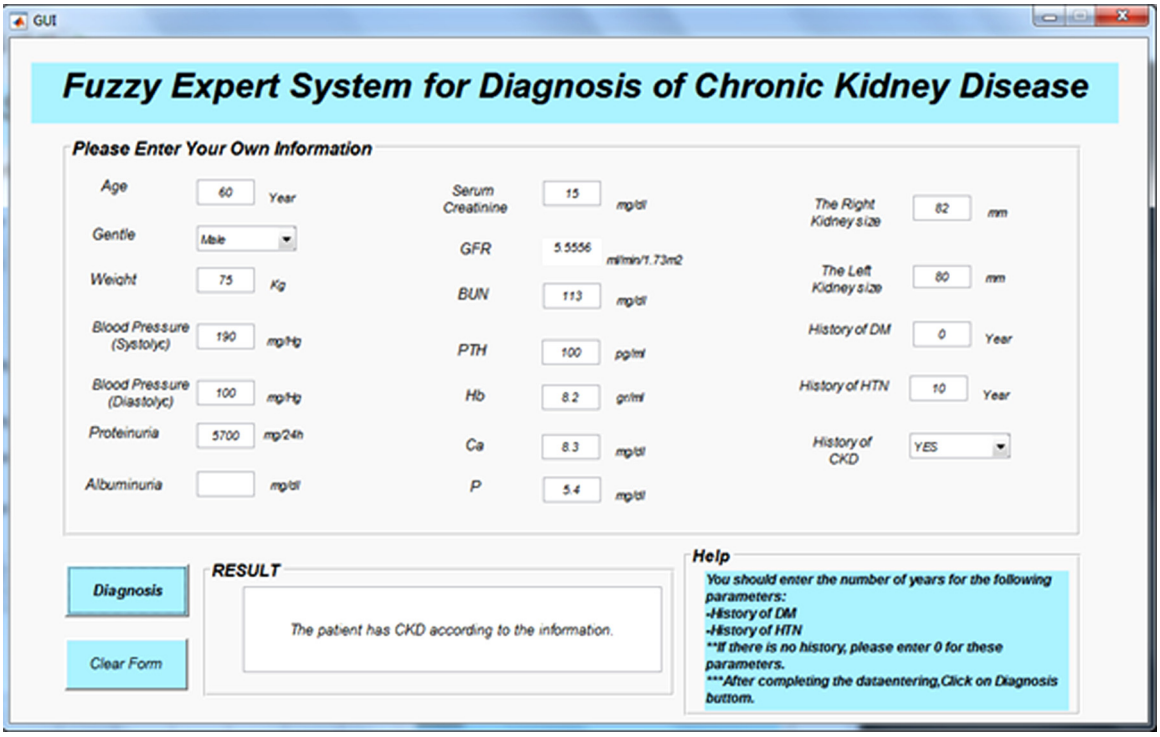

Fig. 2. The user interface of the FES system for prediction of chronic kidney disease.

Table 3
Performance of the systems for chronic kidney disease.

	System 1 (Fuzzified GFR)	System 2 (Non-fuzzified GFR)	System 2 (Without GFR)
Accuracy	90.74	92.13	84.25
Sensitivity	95.37	95.37	96.14
Specificity	86.11	88.88	70.37
Kappa	0.81	0.84	0.68
AUC	0.90	0.92	0.84

values of the parameters, a type II fuzzy system may be used. Additionally, this system cannot detect the different stages of the CKD, the degree of disease progression, and recommend treatment, that should be studied in future research.

Table 4
Comparison of the performance of the developed system with original and noisy data.

		Accuracy	Sensitivity	Specificity
The selected system		92.13	95.37	88.88
Noisy class data	5 % noise	87.01	95.20	75.84
	10 % noise	87.45	96.32	75.87
	15 % noise	78.42	79.09	72.50
	20 % noise	76.18	78.87	71.41
	25 % noise	73.76	72.03	68.72
	Mean ± SD	80.56 ± 6.31	84.30 ± 10.85	72.87 ± 3.05
Noisy input data	5 % noise	91.32	93.02	86.22
	10 % noise	90.03	90.53	86.22
	15 % noise	88.84	88.71	85.13
	20 % noise	87.30	87.65	83.47
	25 % noise	87.69	87.89	83.47
	Mean ± SD	89.04 ± 1.66	89.56 ± 2.24	84.9 ± 1.38

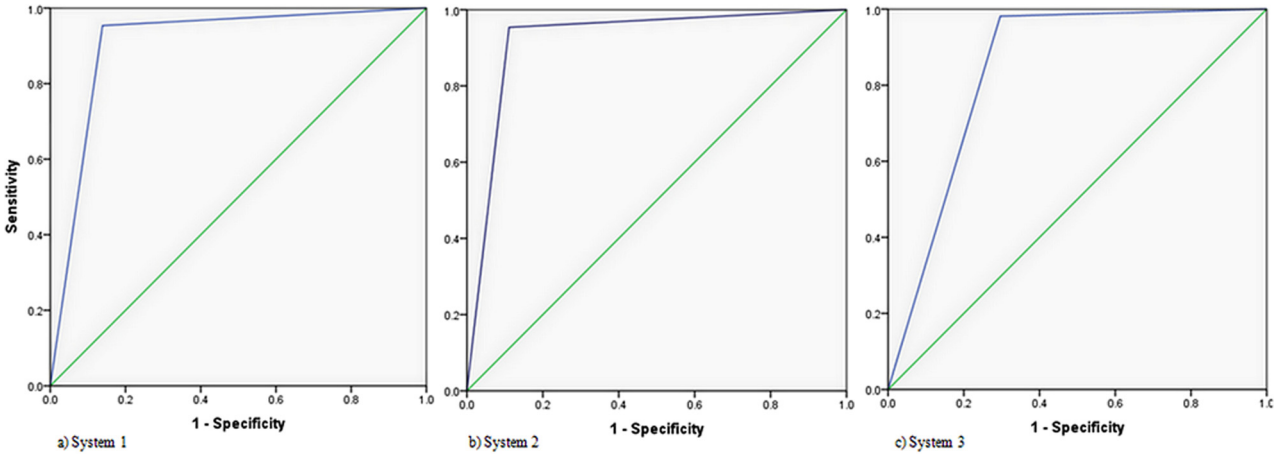

Fig. 3. Receiver Operating Characteristic (ROC) of the developed systems. (a) System 1, (b) System 2, (c) System 3.

Table 5
Comparing our results with other related work.

Author (Reference)	Model	Data set	Input variables	Results
Moslem [31]	Fuzzy expert system (Mam and bisector methods)	Data taken from patients' medical records	6	Accuracy of Mam: 97.14 Accuracy of bisector: 98.86 Sensitivity: NR Specificity: NR
Zarandi [73]	Fuzzy type 1 improved by ANFIS model	Data taken from patients'medical records	9	Accuracy: 80 Sensitivity: 77.27 Specificity: 83.33
Abdolkarimzadeh [75]	Type II fuzzy rough set rule-based expert system	Data taken from patients'medical records	15	Accuracy: 90 Sensitivity: 91.17 Specificity: 90.38
Polat [32]	Machine learning: support vector machine (SVM)	CKD dataset from UCI	24	Accuracy: 98.5 Sensitivity: 98.5 Precision: 98.6
Subasi [33]	Machine learning: random forest, artificial neural network (ANN), C4.5, K-nearest neighborhood (KNN), SVM	CKD dataset from UCI	24	ANN, SVM, KNN, C4.5, Random forest, respectively: Accuracy: 98, 98.5, 95.7, 99, 100 Precision: 98, 98.5, 96.2, 99, 100 Random forest: Sensitivity: 100 Specificity: 100
Chen [35]	Machine learning: Fuzzy rule-building expert system (FuRES), Fuzzy optimal associative memory (FOAM), Partial least squares discriminant analysis (PLS-DA)	CKD dataset from UCI	24	FuRES, FOAM, PLS-DA, respectively: Accuracy: 99.6, 98, 95.5 Sensitivity: 99.3, 99.9, 100 Specificity: 95.5, 100, 89.5
Almansour [37]	Machine learning: support vector machine and ANN	CKD dataset from UCI	24	ANN, SVM, respectively: Accuracy: 99.75, 97.75 Sensitivity: 99.6, 96.4 Precision: 1, 1
Sinha [76]	Machine leraning: SVM and K-nearest neighborhood (KNN)	CKD dataset from UCI	24	KNN, SVM, respectively: Accuracy: 78.75, 73.75 Recall/Sensitivity: 76.6, 100 Precision: 85.7, 50.0
Gharibdousti [34]	Machine learning: SVM, ANN, logistic regression (LR), decision tree (DT), naïve Bayesian (NB)	CKD dataset from UCI	24	NB, DT, LR, SVM, ANN, respectively: Accuracy: 96.7, 99.2, 98.3, 98.3, 63.3 Sensitivity: 94.7, 98.7, 98.7, 98.7, 100 Specificity: 100, 100, 97.7, 97.7, 0.0
Abdelaziz [36]	Machine learning: Hybrid LR and NN	CKD dataset from UCI	24	Accuracy: 97.8 Recall /sensitivity: 100 Precision: 96.2
Elhoseny [77]	Machine learning: Density based feature selection (DFS) with ant colony based optimization (D-ACO), particle swarm optimization (PSO), Olex-genetic algorithm (OlexGA)	CKD dataset from UCI	24	D-ACO, ACO, PSO, OlexGA, respectively: Accuracy :95.0, 87.5, 85.0, 75.0 Sensitivity: 96.0, 88.8, 88.0, 80.0 Specificity:93.3, 84.6, 80.0, 66.6

Authors' contribution

Farahnaz Hamedan: She involved in conceptualization, data gathering and analysis, software development and drafting the manuscript.

Azam Orooji: She involved in conceptualization, data analysis, software development, technical supervision and revising the manuscript.

Houshang Sanadgol: He involved in conceptualization, data analysis, clinical supervision, and revising the manuscript.

Abbas Sheikhtaheri: He involved in conceptualization, analysis, funding acquisition, project administration, resources, supervision of the project and revising the manuscript.

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Summary table

What was already known on the topic

- Chronic Kidney Disease (CKD) in the early stages is asymptomatic.
- Early prediction and quick interventions for CKD are necessary.
- There are many machine-learning-based studies to diagnose this disease.

What this study added to our knowledge

- We developed a fuzzy expert system to early predict the CKD using literature review and consultation with nephrology experts.
- The accuracy, sensitivity and specificity and area under the curve (AUC) of our system were 92.13 %, 95.37 %, 88.88 %,

and 0.92, respectively.
- The performance of the system on noisy data shows that this system is robust against noises.

Declaration of Competing Interest

The authors have no conflicts of interest relevant to this article to disclose.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.ijmedinf.2020.104134.

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