A Two-Stage Expert System for Diagnosis of Leukemia Based on Type-2 Fuzzy Logic

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Abstract—Diagnosis and deciding about diseases in medical fields is facing innate uncertainty which can affect the whole process of treatment. This decision is made based on expert knowledge and the way in which an expert interprets the patient's condition, and the interpretation of the various experts from the patient's condition may be different. Fuzzy logic can provide mathematical modeling for many concepts, variables, and systems that are unclear and ambiguous and also it can provide a framework for reasoning, inference, control, and decision making in conditions of uncertainty. In systems with high uncertainty and high complexity, fuzzy logic is a suitable method for modeling. In this paper, we use type-2 fuzzy logic for uncertainty modeling that is in diagnosis of leukemia. The proposed system uses an indirect-direct approach and consists of two stages: In the first stage, the inference of blood test state is determined. In this step, we use an indirect approach where the rules are extracted automatically by implementing a clustering approach. In the second stage, signs of leukemia, duration of disease until its progress and the output of the first stage are combined and the final diagnosis of the system is obtained. In this stage, the system uses a direct approach and final diagnosis is determined by the expert. The obtained results show that the type-2 fuzzy expert system can diagnose leukemia with the average accuracy about 97%.

Keywords—Expert system, leukemia, medical diagnosis, type-2 fuzzy logic.

I. INTRODUCTION

A. Leukemia

IN people with leukemia, the bone marrow produces abnormal white blood cells. Over time, the accumulation of leukemia cells interferes with the production of normal cells. In each type of leukemia, the progress rate of leukemia is different [1]. The four main types of leukemia are [2]:
- Acute myeloid leukemia (AML)
- Chronic myeloid leukemia (CML)
- Acute lymphocytic leukemia (ALL)
- Chronic lymphocytic leukemia (CLL)

B. Expert Systems

Expert systems are programs to rehabilitate and provide the expertise, skills, and also they are the ability of the qualified experts for reasoning in a specific area.

Expert systems need detailed information about a specific area and strategies for using the information to solve problems.

In order to build a knowledge system, the knowledge should be formulated. In other words, it should be understood in formal formats, and should be provided to the computer; the knowledge must also be changed according to the problem-solving method [3].

Generally, a rule-based expert system consists of three main modules:
- Knowledge base: The rules and information that will be used in decision making are in this module.
- Inference engine: The inference process that is based on the adopted logic and infers inputs according to the rules of the knowledge base.
- Working memory: a space for temporary storage of input data, information and rules used in the inference module.

These modules are communicated by the user interface to the expert system user, the input information from the user and the final report of the final results are transmitted to the user by the user interface [4].

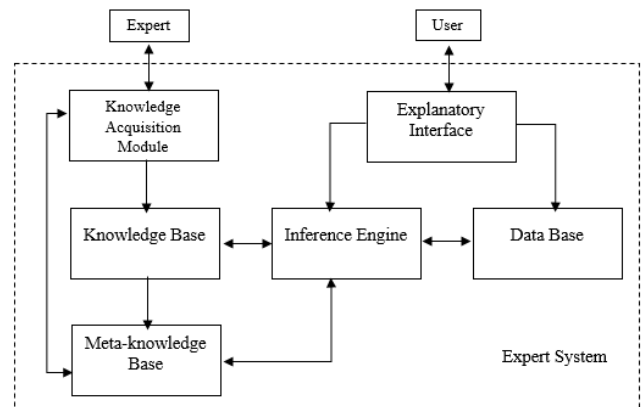Fig. 1 indicates the structure of an expert system.
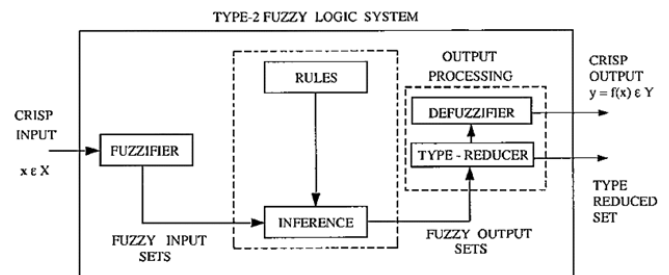

Fig. 1 Architecture of an expert system [5]

Fig. 2 Components of type-2 fuzzy logic system [8]

C. Type 2 Fuzzy

Uncertainty is an inherent part of the intelligent systems that are used in the real world. It is no secret that the use of the new methods is crucial to control the effects of inappropriate

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information. Fuzzy logic can provide mathematical modeling for many concepts, variables, and systems that are unclear and ambiguous and also can provide a framework for reasoning, inference, control, and decision making in conditions of uncertainty. In systems with high uncertainty and high complexity, fuzzy logic is a suitable method for modeling [6]. Type-1 fuzzy sets that are used in conventional fuzzy systems do not completely cover the uncertainty of problems and

ambiguity that occurs in intelligent systems. In other words, type 2 fuzzy sets can better control these uncerainties owing to the fact that these sets have more parameters [7]. In type 2 fuzzy sets, unlike type 1 which have a numerical definite membership degree, the membership degree of each element is itself a fuzzy set. Fig. 2 demonstrates the components of type 2 fuzzy systems.

TABLE I
THE MOST IMPORTANT STUDIES OF FUZZY MEDICAL EXPERT SYSTEMS

No.	Authors	Year	Application	Ref.
1	Adeli and Neshat	2010	Diagnosis of heart disease	[9]
2	Kumar and Kaur	2013	Diagnosis of heart disease	[10]
3	Allahverdi et al.	2007	Determination of coronary heart disease risk	[11]
4	Kumar	2013	Diagnosis the heart disease by advanced fuzzy resolution mechanism	[12]
5	Oad et al.	2014	Predict risk level of heart disease	[13]
6	Lavanya et al.	2011	Diagnosis of lung cancer	[14]
7	Malathi and Santra	2013	Diagnosis of lung Cancer disease using neuro-fuzzy logic	[15]
8	Farahani et al.	2015	Diagnosis of lung cancer	[16]
9	Saritas et al.	2003	Diagnosis of prostate cancer	[17]
10	Balanica et al.	2011	Evaluation of breast cancer risk	[18]
11	Latha et al.	2013	Assessment of breast cancer risk prognosis	[19]
12	Patel et al.	2012	Diagnosis of asthma severity	[20]
13	Anand et al.	2013	Detection and estimate of the level of asthma and chronic obstructive pulmonary disease	[21]
14	Zarandi et al.	2010	Diagnosis of asthma	[22]
15	Mayilvaganan and Rajeswari	2014	Human blood pressure classification	[23]
16	Chandra and Singh	2014	High blood pressure diagnosis	[24]
17	Kaur and Kaur	2014	Diagnosis of hypertension	[25]
18	Djam et al.	2011	Management of Malaria	[26]
19	Onuwa	2014	Diagnosis of Malaria	[27]
20	Sharma et al.	2013	Diagnosis of Malaria and Dengue disease	[28]
21	Kadhim et al.	2011	Diagnosis of back pain	[29]
22	Zarei et al.	2012	A fuzzy mathematical model of HIV infection	[30]
23	Imianvan et al.	2011	Diagnosis of HIV	[31]
24	Khanale and Ambilwade	2011	Diagnosis of hypothyroidism	[32]
25	Biyouki et al.	2015	Diagnosis of thyroid disease	[33]
26	Hasan and Chowdhury	2010	Human disease diagnosis	[34]
27	Govinda et al.	2013	Fever diagnosis	[35]
28	Hole and Gulhane	2014	Diagnosis of memory low diseases	[36]
29	Singh et al.	2012	Diagnosis of arthritis	[37]
30	Baig et al.	2012	Detection of critical events during anaesthesia and diagnosis of a hypovolaemia event in anaesthetized patients	[38]
31	Chandra	2014	Analysis and diagnosis of migraine	[39]
32	Ghahazi et al.	2014	Diagnosis of multiple sclerosis	[40]
33	Maftouni et al.	2015	Ankylosing spondylitis diagnosis	[41]
34	Zarandi et al.	2009	Diagnosis of brain tumors	[42]
35	Talukdar et al.	2014	Blood cancer detection	[43]
36	Nosrat Abadi and Mohsen Taheri	2010	Diagnosis of Blood Cancer	[44]
37	Obi and Imianvan	2011	Diagnosis of leukemia	[45]
38	Noorizadeh and Hosseini	2014	Acute leukaemia diagnosis	[46]
39	Harun et al.	2015	Unsupervised pixel segmentation for segmenting the blast in ALL and AML images	[47]
40	Bhattacharjee	2015	Detection of acute lymphoblastic leukemia	[48]
41	Priya et al.	2015	Detection of leukemia in blood microscopic images	[49]
42	Purushotham and Tripathy	2015	Processing the leukaemia images	[50]
43	Amin et al.	2015	Recognition of acute lymphoblastic leukemia cells in microscopic images	[51]
44	Latifi et al.	2015	Acute lymphocytic leukemia in children	[52]
45	Sadat Asl and Zarandi	2017	Diagnosis of types of leukemia	[53]

The process of diagnosing and deciding about the disease is uncertain and complicated. This decision is made based on the

expert knowledge and its type of interpretation of the patient's condition. Besides, the interpretation of different experts from

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the patient's condition can be various. Thus, we present an expert system for diagnosis of leukemia by using type 2 fuzzy logic.

II. Literature Review

Medical problems, including diagnosis of disease, are always associated with uncertainty, and the use of expert systems by using different logic has always been to assist experts. CREAM system in the field of cardiology, DIAS in the area of diagnosis and consultation of diabetes, MYCIN for diagnosis of bacterial infections, and many other cases are examples of medical expert systems.

Among the reviewed cases, we investigated the researches about creation of medical expert systems for the diagnosis of various diseases that use the fuzzy method for inference. Table I summarizes the fuzzy expert systems for diagnosis of different types of disease. In above studies, no one has considered indirect approach in the field of leukemia. We propose an intelligent system that, in the first stage, uses fuzzy modeling with an indirect approach, where the rules are extracted automatically by implementing a clustering approach.

In order to increase the accuracy of the proposed system, in the diagnosis of leukemia, type 2 fuzzy logic that is more capable than the type 1 fuzzy in uncertainty modeling is used. Using the output of the first phase, according to the doctor's

opinion, the inference of the second phase of the system is performed, which led the proposed system to act based on a hybrid indirect-direct approach. The high accuracy of the proposed system demonstrates the proper performance of the proposed system for the diagnosis of leukemia.

III. Proposed System

The proposed system consists of two stages. In the first stage, the inference of the blood test state is determined. In this step, we follow an indirect approach fuzzy modeling where the rules are extracted automatically by implementing a clustering approach. In the second stage, signs of leukemia, duration of disease until its progress and the output of the first phase are combined and the final diagnosis of the system are obtained. In other words, our system uses a hybrid indirect-direct approach for inference.

TABLE II
NORMAL RANGE OF THE BLOOD TEST ITEMS [54]

Blood test item	Women	Men	Children
Hemoglobin	12-16	14-18	9.5-15.5
RBC	4.2-5.4	4.7-6.1	4-5.5
WBC	4500-11000	5000-10000	5000-10000
HCT (%)	37-47	42-52	32-44
PLT	150000-400000	150000-400000	150000-400000

TABLE III
NON-CANCEROUS CONDITIONS [54]

	Red Cells	White Cells	Platelets
High Counts	▪ Smoking ▪ Carbon monoxide exposure ▪ Chronic lung disease ▪ Kidney disease ▪ Certain forms of heart disease ▪ Alcoholism ▪ Liver disease ▪ Conditions that affect the body's fluid level	▪ Infection ▪ Inflammation ▪ Severe physical or emotional stress (such as fever, injury or surgery) ▪ Burns ▪ Kidney failure ▪ Lupus ▪ Rheumatoid arthritis ▪ Malnutrition, thyroid problems ▪ Certain medicines	▪ Bleeding ▪ Mild to moderate iron deficiency ▪ Problems with bone marrow function
Low Counts	▪ Anemia from too little iron, folic acid or vitamin B12 ▪ Bleeding ▪ Inflammatory bowel disease ▪ Other diseases that might cause malnutrition ▪ Certain drugs	▪ Infection ▪ Chemotherapy and other medicines ▪ Malaria ▪ Alcoholism ▪ AIDS ▪ Lupus ▪ Enlarged spleen	▪ Pregnancy ▪ Idiopathic thrombocytopenic purpura ▪ Thrombotic thrombocytopenic purpura ▪ Hemolytic uremic syndrome ▪ Autoimmune diseases

A. The First Stage of the Proposed System

The first phase of the proposed system is designed to determine whether the blood test is healthy or sick with regard to the factors introduced for the disease by expert. In type 2 fuzzy modeling, Platelet (PLT), Hematocrit (HCT), White Blood Cell (WBC), Red Blood Cell (RBC) and hemoglobin are considered as system inputs, and the blood test state i.e. sickness or healthy blood test is determined. The normal values of the blood test items are given in Table II. However, the violation of the normal range of each item cannot definitely indicate that the blood test is healthy or sick. In other words, if one or more of blood test items are higher or lower than normal range, it cannot definitely indicate the

cancerous condition of the blood test for a person.

Many non-cancerous cases and conditions may be associated with high or low blood cell counts. Table III indicates the non-cancerous conditions that contribute to low or high red and white cells and platelets counts. Thus, according to the aforementioned analysis, in the first phase, the proposed system is based on type 2 fuzzy logic according to the individual's gender, viz., adults (women and men) and children. A dataset containing 345 blood tests (113 women, 193 men and 39 children) of a governmental hospital was used for construction and evaluation of the system in the first stage. We should construct the system for women, men and children separately owing to the fact that the difference in normal range of the blood test items for them may create different cancerous

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models. For each category, the system is made by almost 80% of the dataset and is appraised by the rest of the dataset. The data of each part are modeled using the MISO system (multiple inputs - single outputs).

Among the various items of blood test, the items PLT, HCT, WBC, RBC, and hemoglobin have been used to determine the inference of the blood test state in diagnosis of leukemia according to the expert. After that, the system is constructed using fuzzy c-means clustering algorithm for clustering of the blood test data. Then, for determining the number of rules, the proposed index by Zarandi et al. is used. This validity index V_{ECAS} can find the number of clusters as the maximum of its function with respect to c as [55]:

$$V_{ECAS} = ECAS\,(c) = \frac{EC_{comp}(c)}{max_c(EC_{comp}(c))} - \frac{ES_{sep}(c)}{max_c(ES_{sep}(c))}, \qquad (1)$$

$EC_{comp}(c)$ and $ES_{sep}(c)$ are exponential compactness and separation measures, respectively.

$$EC_{comp}(c) = \sum_{i=1}^{c}\sum_{j=1}^{n} u_{ij}^{m} \exp\left[-\left(\frac{\|x_i - v_j\|^2}{\beta_{comp}} + \frac{1}{c+1}\right)\right], \qquad (2)$$

$$ES_{sep}(c) = \sum_{i=1}^{c} \exp\left[-min_{i \neq k}\left(\frac{(c-1)\|v_i - v_k\|^2}{\beta_{sep}}\right)\right]. \qquad (3)$$

$\beta_{comp} = \frac{\sum_{k=1}^{n}\|x_k - \overline{v}\|^2}{n(i)}$ and $\beta_{sep} = \frac{\sum_{l=1}^{n}\|v_l - \overline{v}\|^2}{c}$, respectively. Furthermore, $n(i)$ is the number of data in cluster i and $\overline{v} = \frac{\sum_{j=1}^{n} x_j}{n}$.

In this study, we obtained the appropriate number of clusters or rules by the validity index. The best number of clusters was obtained 3 clusters for adults and children.

In the next step, the output space is projected onto the input space and the membership functions of the input and output variables are estimated. Eventually, the type 1 fuzzy rule base is transformed into interval type-2 fuzzy rule base with uncertain standard deviation and fixed mean by Liang and Mendel [56] method (for more detail refer to [56]). Fig. 3 demonstrates the interval type 2 fuzzy rule based on blood test for adults and children. After determining the rules, Mamdani inference system is used by multiple inputs-single output modeling with standard operators. Then, the type 2 fuzzy output set needs to be type-reduced and defuzzified to obtain final result.

B. The Second Stage of the Proposed System

After determining the blood test result for each person, in the second stage, symptoms, duration of illness until its progress and the output of the first stage are combined and final diagnosis of the leukemia is obtained. This stage is based on the expert knowledge and follows a direct approach for inference. For this purpose, according to the result of the first stage, the expert analyzes the patient symptoms and duration of them. Based on the physician knowledge, the marked symptoms usually occur in each type of leukemia. Also, if the symptoms suddenly occur, the risk of ALL and AML will increase. In the other hand, if the symptoms occur in a long time, the risk of CLL and CML will increase owing to the fact that in acute myeloid and lymphocytic leukemia the cancer progression rate is high. Thus, their symptoms suddenly occur. Also, in chronic myeloid and lymphocytic leukemia the cancer progression rate is low and their symptoms occur in a long time.

After the inference of symptoms state and duration of disease until its progress, the proposed system combines the output of stage 1 and finally diagnoses leukemia. The system predicts the presence or suspicion of presence or absence of leukemia. If a patient suffers from leukemia, the proposed system determines type of leukemia by the knowledge base acquired by the expert. If the system predicts suspicion of presence of leukemia, the patient should refer to a physician to investigate the presence or absence of cancer cells using biopsy. Below is a part of the inferential general rules that lead to the diagnosis of leukemia:

➤ Rule 1: If Blood Test is *sick* and Sick Time is *sudden start* and Sick Sign is *ALL*. Then Assessment is *ALL*
➤ Rule 2: If Blood Test is *sick* and Sick Time is *sudden start* and Sick Sign is *AML*. Then Assessment is *AML*
➤ Rule 3: If Blood Test is *sick* and Sick Time is *long time* and Sick Sign is *CLL*. Then Assessment is *CLL*
➤ Rule 4: If Blood Test is *sick* and Sick Time is *long time* and Sick Sign is *CML*. Then Assessment is *CML*

TABLE IV
ANALYSIS OF THE LEUKEMIA SYMPTOM

Symptoms	CML	CLL	AML	ALL
Vomit			✓	✓
Headache	✓			
Anorexia			✓	✓
Enlarged lymph nodes		✓		
Infection		✓	✓	
Enlarged liver or spleen			✓	✓
Anemia	✓	✓	✓	✓
Asthenia	✓		✓	
Sweating		✓		
Bleeding			✓	
Fatigue			✓	
Weight Loss	✓	✓		
Fever		✓	✓	
Confusion	✓			
Shortness of breath	✓			

C. Evaluation of the Proposed System

After logging into the expert system environment, the user is entered into blood test inference screen that must submit the requested items in order to infer blood test state. After entering the information by the user, the system infers the blood test and reports its state to the user. Fig. 4 shows the inference of the blood test of a patient. After the blood test inference stage, the user clicks on the next and then new screen is opened. In the new screen the user should mark the symptoms. This window is shown in Fig. 5. Then, by clicking on the final diagnosis button, the expert system gives the final result to the user. The proposed expert system has the ability to diagnose leukemia with the average accuracy of about 97%.

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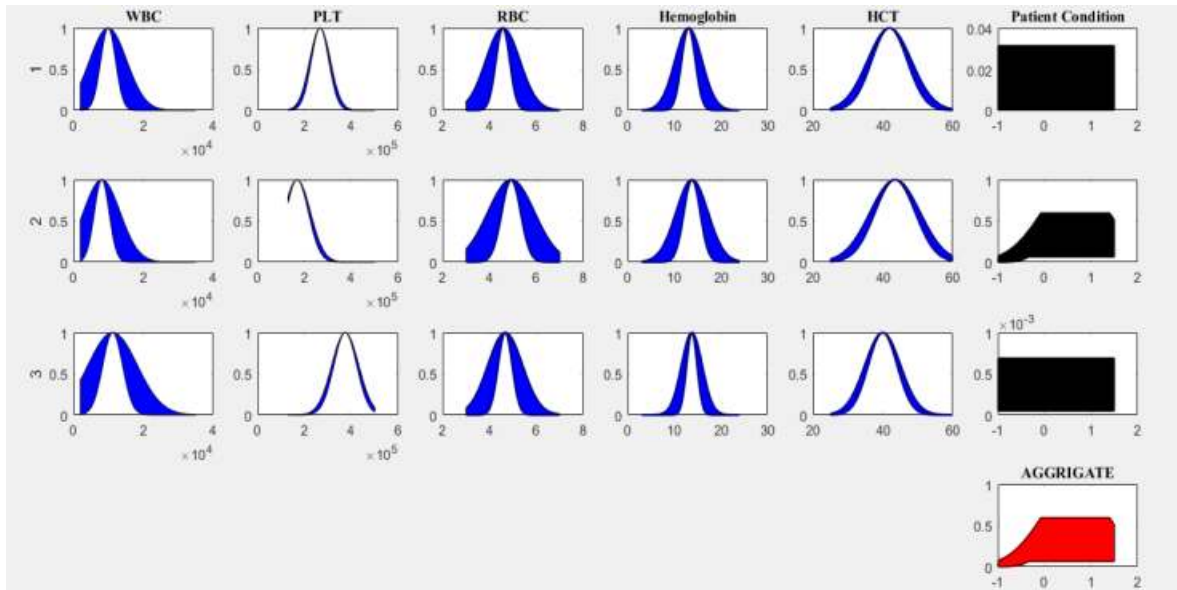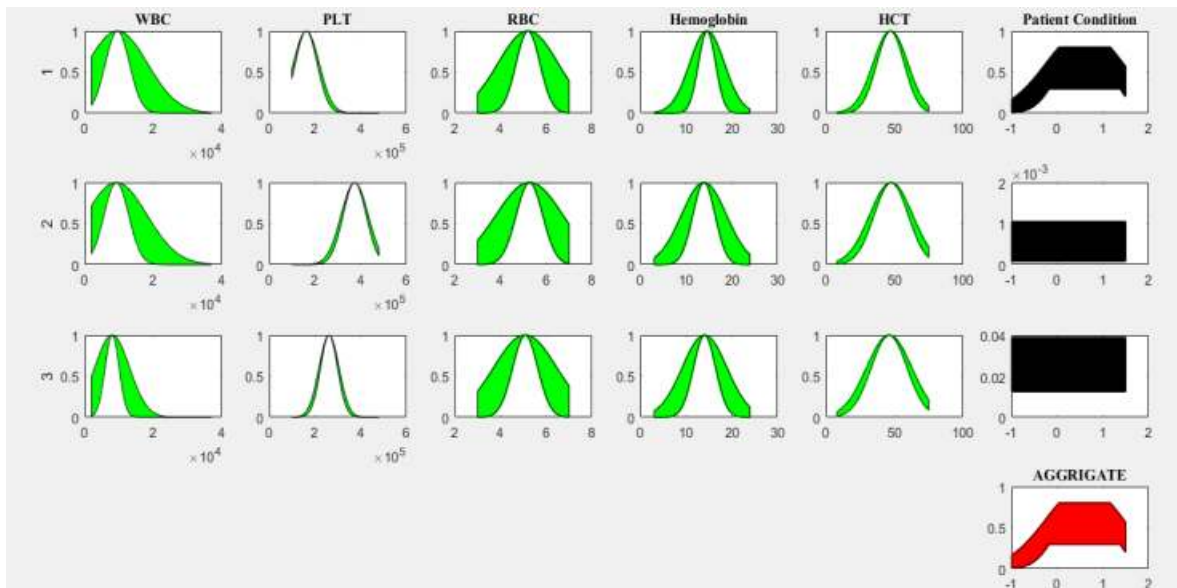Vol:13, No:2, 2019

Fig. 3 (a) Interval type 2 fuzzy rule based of the proposed system for women's blood tests

Fig. 3 (b) Interval type 2 fuzzy rule based of the proposed system for men's blood tests
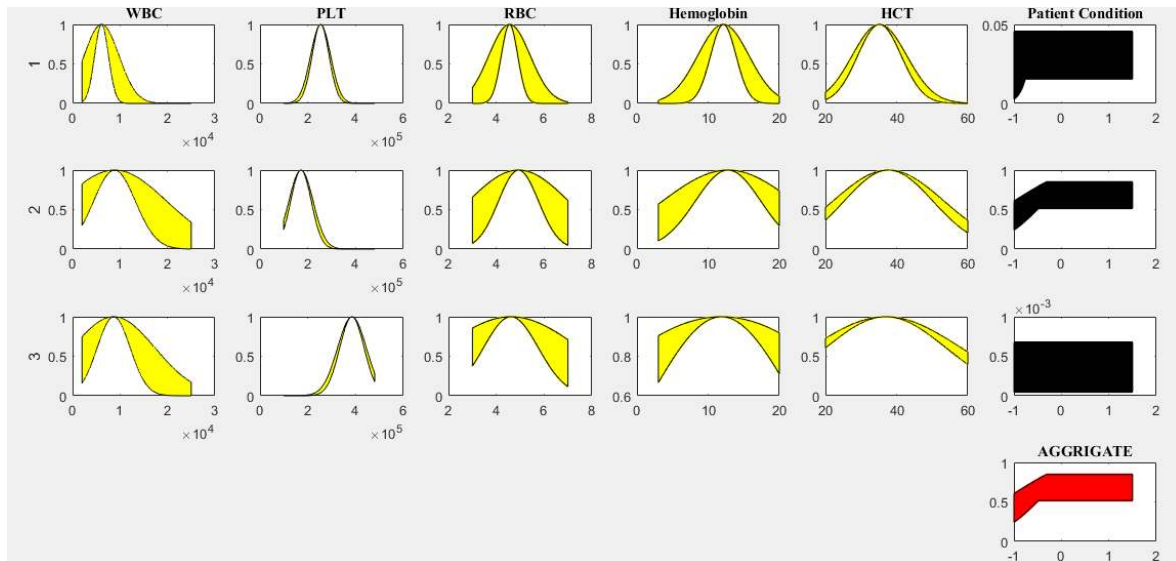
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Fig. 3 (c) Interval type 2 fuzzy rule based of the proposed system for children's blood test

Fig. 4 The inference screen of the blood test of a patient

IV. CONCLUSION

The prevalence of leukemia is increasing day by day and it is becoming a global epidemic. Increasing cancer cells in the bone marrow produces leukemia. Leukemia is a progressive and malignant disease of the blood-forming organs of the body.

Since a timely and accurate diagnosis of leukemia has a major impact on the way and cost of treatment, and the amount of lesions resulting from it, it is very important to provide an intelligent system for the diagnosis of this disease. In addition, fuzzy logic can provide a framework for reasoning, inference, control, and decision making in conditions of uncertainty.

In systems with high uncertainty and high complexity,

fuzzy logic is a suitable method for modeling. Due to the greater ability of type 2 fuzzy logic in uncertainty modeling, in this paper, we presented a type 2 fuzzy expert system for diagnosis of leukemia. The proposed system includes two stages. In the first stage, the inference of the blood test state is determined. In this step, we use Mamdani inference system with standard operators. In the second stage, leukemia symptoms, duration of disease until its progress and the output of the first stage are integrated and the final diagnosis of the system is obtained. By relying on the results, the type-2 fuzzy expert system can diagnose leukemia with the average accuracy about 97%.

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Fig. 5 The inference screen of the blood test of a patient

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