IAES International Journal of Artificial Intelligence (IJ-AI)
Vol. 13, No. 4, December 2024, pp. 4062~4070
ISSN: 2252-8938, DOI: 10.11591/ijai.v13.i4.pp4062-4070

Implementation of fuzzy logic approach for thalassemia screening in children

Erliyan Redy Susanto[1,2], Admi Syarif[1], Warsito[1], Khairun Nisa Berawi[3], Putu Ristyaning Ayu Sangging[3], Agus Wantoro[2]
[1]Faculty of Mathematics and Natural Science, Lampung University, Bandar Lampung, Indonesia
[2]Department of Information System, Faculty of Engineering and Computer Science, Universitas Teknokrat Indonesia, Bandar Lampung, Indonesia
[3]Department of Biomolecular, Biochemistry and Physiology, Faculty of Medical, Lampung University, Bandar Lampung, Indonesia

Article Info

Article history:

Received May 22, 2023
Revised Nov 19, 2023
Accepted Dec 6, 2023

Keywords:

Artificial intelligence
Blood disorder
Fuzzy approach
Inherited disease
Thalassemia

ABSTRACT

Thalassemia is one of the most dangerous blood disorders that can lead to severe complications. It is an inherited disease, usually detected after a child is two to four years old. Identification of thalassemia is a complex task, involving many variables. Doctors generally diagnose thalassemia by using a complete blood count (CBC) and high-performance liquid chromatography (HPLC) test results. However, HPLC tests are expensive and time-consuming, hence the need for other methods to identify thalassemia. There are many studies on the application of artificial intelligence for medical applications. In this study, we developed a new fuzzy-based approach to identify thalassemia based on a patient's blood laboratory results. First, we analyzed the CBC data for blood disorder prediction. Secondly, we adopt the test results of peripheral blood smear (PBS) to identify whether the person has thalassemia. We conducted several experiments using 30 (thirty) hospital patient data and the results were compared with the results provided by experts. The experimental results show that the system can determine blood disorders with 93% accuracy and 100% precision in thalassemia prediction. This system is very effective to help doctors in diagnosing thalassemia patients.

Corresponding Author:

Admi Syarif
Department of Computer Science, Faculty of Mathematics and Natural Sciences, Lampung University
St. Prof. Dr. Sumantri Brojonegoro No.1, Bandar Lampung, Lampung 35145, Indonesia
Email: admi.syarif@fmipa.unila.ac.id

1. INTRODUCTION

Blood disorders are known to require very expensive medical expenses. Some blood disorders, such as thalassemia, hemophilia, blood clots, blood cancer, leukemia, lymphoma, and myeloma, require a lot of money. Diagnosing thalassemia is a challenging task. In addition to cancer, it is considered one of the most dangerous diseases in the world [1]. Thalassemia is one type of blood disorder due to genetic characteristics derived from both parents [2], [3]. Another possibility that it can cause is when a gene mutation occurs [4]. This disease is commonly known from infancy [5], [6]. In some cases, thalassemia is discovered after a person grows up [4]. When treatment is given late, the disease can cause growth delays in the child and other complications. Thalassemia is also divided into two categories: transfusion-dependent and nontransfusion-dependent [7]. The easiest way to perform a blood transfusion is by knowing the hemoglobin levels in the blood [7], [8]. If it is below the standard value, a blood transfusion should be initiated immediately. Thalassemia patients often experience anemia which can cause fatigue, weakness, and difficulty in

performing physical activity. They may also experience delayed growth and abnormal bone development. Most of these cases are found in children over the age of two years. Thalassemia detection can be done through a blood test in a laboratory, commonly called screening. Thalassemia screening has several components of blood tests, including complete blood count (CBC) and high-performance liquid chromatography (HPLC) [9], [10]. Doctors usually use CBC to predict a blood disorder [11], [12]. Some of the CBC components that have been used include hemoglobin (HGB), mean corpuscular volume (MCV), and mean corpuscular hemoglobin (MCH) [13]. We found the problem that HPLC inspection is expensive, and the consumption time is prolonged [10], [14], [15]. Thus, our study aims to use a new fuzzy-based approach to minimize costs and accelerate the screening time for thalassemia.

Artificial intelligence (AI) is one of the fields of computer science that is constantly developing and widely applied in various fields [16]. In multiple studies, AI has been widely used to solve problems related to medicine, agriculture, and business [17], [18]. It is also used to predict the presence of blood disorders [18], [19]. A significant problem in AI applications is dealing with non-deterministic data or information. One popular approach to this issue is to adopt a fuzzy approach. Since Zadeh [20] introduced it, fuzzy has been widely used for various applications to solve various problems of disease in humans [21], animals [22], and also plants [23]. A fuzzy approach to predicting thalassemia in children can overcome several challenges [24]. Fuzzy logic can help analyze interpretations that are incomplete, ambiguous, or subject to interpretation. This problem makes them suitable for dealing with thalassemia's complex and diverse clinical picture. The proposed method uses a fuzzy approach to provide a more accurate and efficient method for predicting thalassemia in children.

Thalassemia is very important to study and many studies on the use of AI for thalassemia problems have been conducted. The use of AI has addressed a number of challenges associated with thalassemia. We have summarized some AI approaches to solve some problems in thalassemia presented in Table 1.

Table 1. AI research on thalassemia

Year	Methods	Topics	Authors
2010	Multi-layer perceptron, k-nearest neighbors, bayesian networks, naïve-Bayes, and multinomial logistic regression	The effeciency of data types for classification performance of machine learning techniques for screening β-Thalassemia	Paokanta *et al.* [25]
2016	Fuzzy logic	Design of a fuzzy model for thalassemia disease diagnosis: using mamdani type fuzzy inference system (FIS)	Thakur *et al.* [11]
2017	Fuzzy logic	Thalassemia risk prediction model using fuzzy inference systems: an application of fuzzy logic	Thakur and Raw [12]
2017	Fuzzy logic	Using fuzzy logic for improving daily clinical care of β-Thalassemia patients	Santini *et al.* [23]
2018	Support vector machine	Detection of β thalassemia carriers by red cell parameters obtained from automatic counters using mathematical formulas	Roth *et al*. [13]
2019	K-nearest neighbor and naïve Bayes	Classification of thalassemia data using k-nearest neighbor and naïve Bayes	Siswantining *et al.* [24]
2020	Random forest	Classification of thalassemia data using random forest algorithm	Aszhari *et al.* [17]
2020	Machine learning and deep learning	Artificial intelligence in hematology: current challenges and opportunities	Radakovich *et al.* [18]
2021	Ensemble classifiers	Classification of β-thalassemia carriers from red blood cell indices using ensemble classifier	Sadiq *et al.* [16]
2022	Machine learning and deep learning	A review of artificial intelligence applications in hematology management: current practices and future prospects	Alaoui *et al.* [19]

Table 1 shows that various thalassemia problems worked a lot with AI. Some studies on AI with fuzzy logical approaches have excellent prediction accuracy [23], [26], [27]. Therefore, we use this approach to solve problems in thalassemia. This article aims to predict blood disorder in a child, focusing on thalassemia with a fuzzy approach. Our systems require data from laboratory tests such as CBC and peripheral blood smear (PBS). Thalassemia, referred to in this article, is a beta (β) type. This type of Thalassemia is most common in Indonesia and other Asian countries. This article perfected previous research on classifying Thalassemia [11], [28] by adding PBS as a new parameter.

This article consists of two stages. First, the system detects blood disorders by analyzing CBC laboratory results containing HGB, MCV, and MCH. Second, the CBC analysis results that detect blood abnormalities are then matched with expert knowledge of thalassemia symptoms on PBS. Our system will provide a prediction of the patient's condition based on the analysis performed using CBC and PBS data.

Thus, the system can recommend the patient's diagnosis result to the doctor. In this case, we use fuzzy method to make thalassemia prediction using CBC and PBS data as an alternative to CBC and HPLC data. We propose a new approach of using CBC and PBS to predict thalassemia as an alternative to CBC and HPLC which are commonly used by doctors today. We evaluate it by comparing the performance of our developed system with the opinion of an expert (clinical pathologist) and assess it is potential. We have conducted a study using laboratory data with and without thalassemia to develop and evaluate a fuzzy prediction method for thalassemia. Thalassemia screening using fuzzy approach with CBC and PBS data input is our contribution in this study. The study results show that our model has a very good performance in identifying thalassemia.

2. METHOD

2.1. Frameworks

The classification of diseases with a fuzzy approach is designed according to a predetermined framework. The framework is a working conceptual description of the thalassemia classification system. The framework that we have developed is presented in Figure 1. The main parts of Figure 1 are the knowledge base, inference engine, and user interface. The knowledge base is built on the clinical pathologist's knowledge of blood disorders and thalassemia. The inference engine draws conclusions based on the information stored in the knowledge base. The inference engine is responsible for reasoning about the knowledge base and using it to solve problems or answer questions. The inference engine follows a set of rules or logical steps programmed into the system. The user interface is in the form of a program display that is designed according to its function. Doctors use the user interface to provide CBC and PBS input. Furthermore, the doctor will get information on predictions of blood disorders and Thalassemia according to the knowledge of a clinical pathologist.

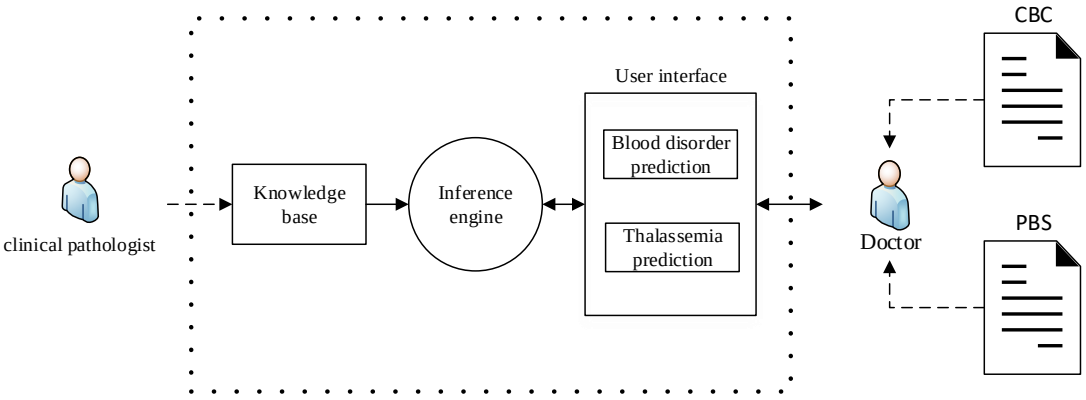


Figure 1. Framework of thalassemia screening

2.2. Prediction of blood disorders

Doctors usually perform an anamnesis, a physical examination of the patient, and are supported by the results of blood tests, i.e., CBC. This section uses a fuzzy approach to determine the suspected blood disorder. The fuzzy approach is used because the opinion of doctors about the standard threshold values on the CBC results has a tolerance. Based on previous literature [11], [16], CBC data: HGB, MCV, and MCH. Based on our interviews, clinical pathologists believe that HGB is the first indicator used to suspect the presence of blood disorders, then to assess other indicators.

2.3. Thalassemia prediction

The doctor's diagnosis leads to a blood disorder or not blood disorder. If the diagnosis leads to blood disorders, proceed with a more detailed blood test, namely PBS. Based on the results of the PBS, it will then be compared with the characteristics of thalassemia disease. In general, the characteristics of thalassemia based on PBS include microcytic, polychromasia, hypochromic, teardrop, and target cells [7], [29], [30]. The thalassemia prediction section will provide output in the form of patient information indicated by thalassemia or not thalassemia.

2.4. Knowledge based

This study uses CBC, including HGB, MCV, and MCH. The suspected presence of blood disorders such as thalassemia can be known based on these values [31]. Table 2 is a knowledge base on the prediction of blood disorders based on CBC.

Table 2. Knowledge-based for blood disorders based on CBC

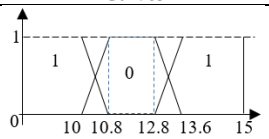
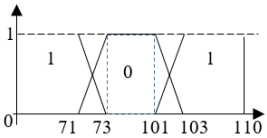
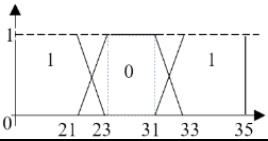
No	Parameters	References	Disorders	units
1	HGB	10.8-12.8	<10.8 or >12.8	g/dL
2	MCV	73-101	<73 or >101	fL
3	MCH	23-31	<23 or >31	Pg

CBC values that do not match the reference values indicate that patients are strongly suspected of having blood disorders. Doctors recommend that the patient undergo further examination, namely PBS, to ensure that there are suspected blood disorders. Based on PBS [29], [30], [32], thalassemia has several unique characteristics: microcytic, hypochromic, teardrop, polychromasia, and target cells. The opinion of expert states that the patient will be called a carrier if he is microcytic and hypochromic. At the same time, it is called thalassemia if it has other signs, such as teardrops, polychromasia, and target cells.

2.5. Fuzzy membership function

Based on the knowledge base on blood disorders, determine the parameters used and create a mathematical function in a fuzzy membership function [33]. The existence of expert tolerance for the reference value of each parameter used is why we use a fuzzy approach. We construct fuzzy membership functions and curves for each CBC parameter [11] based on laboratory data on blood disorders presented in Table 3.

Table 3. Membership function and curves

Parameter	Membership function	Curves
HGB	$x\,[7.2] = \begin{cases} 1 & x \le 10 \\ \frac{10.8 - x}{10.8 - 10} & 10 \le x \le 10.8 \\ 0 & x > 10.8 \end{cases}$	
MCV	$x\,[72] = \begin{cases} 1 & x \le 71 \\ \frac{73 - x}{73 - 71} & 71 \le x \le 73 \\ 0 & x > 73 \end{cases}$	
MCH	$x\,[22.2] = \begin{cases} 1 & x \le 21 \\ \frac{23 - x}{23 - 21} & 21 \le x \le 23 \\ 0 & x > 23 \end{cases}$	

For example, we consider patient x with CBC data with HGB values of 7.20, MCV of 72.00, and MCH of 22.20. Based on the membership function in Table 2, the fuzzy values for blood disorders are HGB: 1.00, MCV: 1.00, and MCH: 0.40. As for not blood disorders, the values are HGB: 0.00, MCV: 0.00, and MCH:0.60. Then we create fuzzy weights for 40% HGB, 30% MCV, and 30% MCH. So, we get a fuzzy weight for blood disorders of 0.82 and for not blood disorders of 0.18. Based on the fuzzy weights, it can be concluded that there is a suspicion that the patient has a blood disorder.

Furthermore, a PBS-based examination was carried out on patients suspected of having blood disorders. We put a "1" if the mark is found and a "0" if it is not found. Signs in question include microcytic, hypochromic, teardrop, polychromasia, and target cells [30]. The PBS data of patient x showed microcytic: 1, hypochromic: 1, teardrop: 1, polychromasia: 1, and target cells: 1. Based on the literature [29] and expert knowledge, PBS is a method commonly used by doctors to diagnose blood disorders. Therefore, the conclusion of the diagnosis based on the PBS value is that the patient suffers from thalassemia.

3. RESULTS AND DISCUSSION

3.1. Evaluation

The systems we have developed have been tested to evaluate the results of this study. We have as many as 30 lab data sets of CBC and PBS data. The trial was conducted using patient data obtained from the hospital. The results are compared to the opinions of experts (clinical pathologist at a public hospital in Lampung Indonesia). The results of this experiment are presented in Table 4.

Table 4. Test results predictive of blood disorders

No	Parameter			Expert	Proposed system	Results
	HGB	MCV	MCH			
1	12.90	73.70	25.90	Not	Not	True
2	5.90	49.30	12.00	Blood disorders	Blood disorders	True
3	7.20	72.00	22.20	Blood disorders	Blood disorders	True
4	9.20	98.30	30.80	Blood disorders	Blood disorders	True
5	13.00	82.30	29,10	Not	Not	True
6	11.70	59.90	18.80	Not	Not	True
7	11.80	74.30	27.60	Not	Not	True
8	8.80	90.50	28.90	Blood disorders	Blood disorders	True
9	4.50	85.70	29,20	Blood disorders	Blood disorders	True
10	13.70	79.20	27,60	Blood disorders	Blood disorders	True
11	11.20	83.50	28.00	Not	Not	True
12	12.60	78.80	26.80	Not	Not	True
13	11.30	76.40	25.50	Not	Not	True
14	15.50	83.60	29.90	Blood disorders	Blood disorders	True
15	13.80	82.20	28.60	Blood disorders	Blood disorders	True
16	12.50	77.50	27.60	Not	Not	True
17	7.30	53.50	14.90	Blood disorders	Blood disorders	True
18	8.70	72.90	23.30	Blood disorders	Blood disorders	True
19	9.70	82.10	26,40	Blood disorders	Blood disorders	True
20	16.70	65.90	21.70	Blood disorders	Blood disorders	True
21	3.60	91.70	27.30	Blood disorders	Blood disorders	True
22	11.30	69.00	10:60	Not	Not	True
23	10.00	92.20	30.10	Blood disorders	Not	False
24	13.90	84.00	28.90	Blood disorders	Blood disorders	True
25	4.90	110.10	38.00	Blood disorders	Blood disorders	True
26	6.70	77.20	25.00	Blood disorders	Blood disorders	True
27	3.50	80.20	27.80	Blood disorders	Blood disorders	True
28	5.00	66.70	20.30	Blood disorders	Blood disorders	True
29	10.80	62.50	19.90	Not	Not	True
30	14.00	74.00	25.60	Not	Blood Disorders	False

Table 4 shows that clinical pathologists believe that 8 patients have blood disorders and 11 do not. The system we developed also predicts the same number. However, there are differences in predictions from data 23 and 30. The predictions from the two data sets are contradictory to each other. The classification system for blood disorders that we developed gave results including 18 patients identified as having blood disorders (true positive), 1 patient with not blood disorder identified as a blood disorder (false positive), 1 patient with blood disorder identified as not blood disorder (false negative), and 10 patients with not blood disorder were identified as not blood disorder (true negative). We present the confusion matrix in Table 5.

Table 5. Confusion matrix for blood disorders

	Negative predictions	Positive predictions
Actual negatives	10	1
Actual positives	1	18

Table 5 shows that there were two inaccurate predictions, one wrong prediction for thalassemia and one wrong prediction for not thalassemia. We can evaluation metrics from these results, such as accuracy, sensitivity, and specificity. These show that the system has an accuracy value of 93.3%, a sensitivity or recall value of 94.7%, a specificity value of 90.9%, and a precision value of 94.7%. We illustrate the overall evaluation metric given by this system in the Figure 2.

We conducted another experiment to evaluate the prediction of thalassemia. The prediction is based on PBS information about the patient. We have already compared the results with those given by clinical pathologists. This comparison is presented in Table 6.

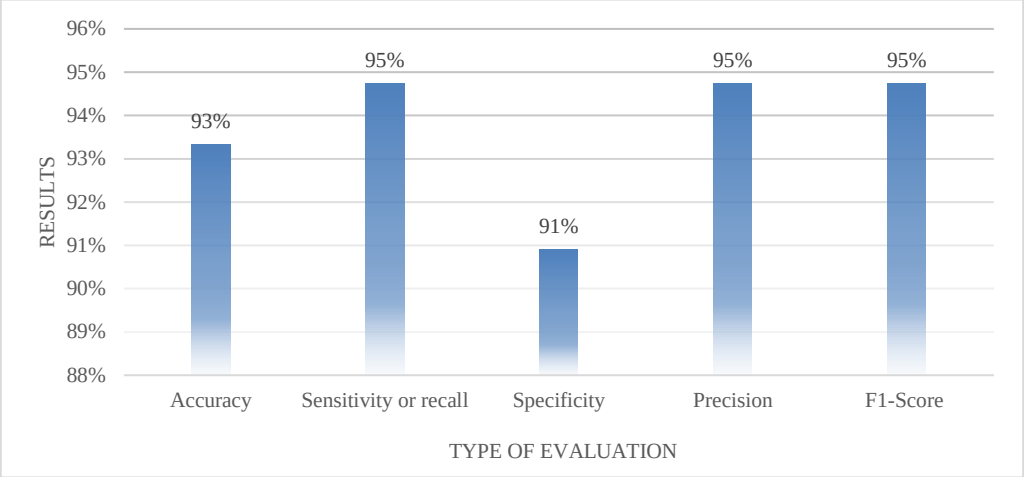


Figure 2. System evaluation metric for prediction of blood disorders

Table 6. Thalassemia prediction test results

No	Parameter					Expert	Proposed system	Results
	Microcytic	Hypochromic	Teardrops	Polychromasia	Target cells			
1	1	1	1	1	1	Thalassemia	Thalassemia	True
2	1	1	1	1	1	Thalassemia	Thalassemia	True
3	1	1	0	1	0	Thalassemia	Thalassemia	True
4	0	0	0	1	0	Not	Not	True
5	1	1	0	1	0	Thalassemia	Thalassemia	True
6	0	0	0	0	0	Not	Not	True
7	0	0	0	0	0	Not	Not	True
8	0	0	0	0	0	Not	Not	True
9	1	1	0	0	0	Thalassemia	Thalassemia	True
10	1	1	1	0	0	Thalassemia	Thalassemia	True
11	0	0	0	0	0	Not	Not	True
12	1	1	0	0	0	Thalassemia	Thalassemia	True
13	0	0	0	0	0	Not	Not	True
14	0	0	0	0	0	Not	Not	True
15	0	0	0	0	0	Not	Not	True
16	0	0	0	0	0	Not	Not	True
17	1	0	0	0	0	Not	Not	True
18	0	0	0	0	0	Not	Not	True
19	1	1	1	1	1	Thalassemia	Thalassemia	True

Evaluation must be done to measure the performance of the model we have developed. The evaluation of the thalassemia classification that we propose gives results including 8 patients who are thalassemia identified as thalassemia (true positive), 0 patients who are not thalassemia identified as thalassemia (false positive), 0 patients who are thalassemia identified as not thalassemia (false negative), and 11 patients who were not thalassemia were identified as not thalassemia (true negative). We show the confusion matrix in Table 7.

Table 7. Confusion matrix for prediction of thalassemia

	Negative predictions	Positive predictions
Actual negatives	11	0
Actual positives	0	8

Based on expert opinions as shown in Table 7, the accuracy of the test results of the system we developed to identify Thalassemia using PBS is 100%. However, we feel that this research needs to be developed further by using more datasets and developing models, for example with fuzzy ensembles [34], [35]. We hope that this work can be continued by using more actual data to test the quality and accuracy of the system that has been developed.

4. CONCLUSION

This study provides a novel fuzzy-based approach for thalassemia screening. It adopts a fuzzy-based approach based on CBC and PBS data. The knowledge used in this research is also based on information from clinical pathologists. The system has been evaluated using the hospital's actual patient data and comparing the results with those provided by experts. Based on CBC and PBS data, our system has very high accuracy in predicting blood disorders (93% accuracy) and thalassemia (100% accuracy). However, more data sets are needed to test this model. In the future, this model can adapt the fuzzy ensemble to improve model performance.

ACKNOWLEDGEMENTS

We thank to Universitas Teknokrat Indonesia for supporting this research. We also thank the Immanuel Hospital Bandar Lampung, Indonesia, especially Mr. Ns. Dwiantoro, for providing the laboratory data.

REFERENCES

[1] J. I. Johnsen, C. Dyberg, and M. Wickström, "Neuroblastoma—A neural crest derived embryonal malignancy," *Frontiers in Molecular Neuroscience*, vol. 12, pp. 1–11, 2019, doi: 10.3389/fnmol.2019.00009.

[2] S. Perera *et al.*, "Genotype-phenotype association analysis identifies the role of α globin genes in modulating disease severity of β thalassaemia intermedia in Sri Lanka," *Scientific Reports*, vol. 9, no. 1, pp. 1–9, 2019, doi: 10.1038/s41598-019-46674-y.

[3] M. K. Barker *et al.*, "Serum soluble transferrin receptor concentrations are elevated in congolese children with glucose-6-phosphate dehydrogenase variants, but not sickle cell variants or α-thalassemia," *The Journal of Nutrition*, vol. 147, no. 9, pp. 1785–1794, 2017, doi: 10.3945/jn.117.252635.

[4] A. Tamaddoni, S. K. Astaneh, R. Tabaripour, and H. A. -Niaki, "Krüppel-like factor 1 gene mutations in thalassemia patients from north iran: report of a new mutation associated with β-thalassemia intermedia," *Hemoglobin*, vol. 43, no. 1, pp. 12–17, 2019, doi: 10.1080/03630269.2019.1567528.

[5] I. K. Kwaifa, M. I. Lai, and S. M. Noor, "Non-deletional alpha thalassaemia: A review," *Orphanet Journal of Rare Diseases*, vol. 15, no. 1, pp. 1–12, 2020, doi: 10.1186/s13023-020-01429-1.

[6] G. Kakourou *et al.*, "The clinical utility of PGD with HLA matching: A collaborative multi-centre ESHRE study," *Human Reproduction*, vol. 33, no. 3, pp. 520–530, 2018, doi: 10.1093/humrep/dex384.

[7] V. Viprakasit and S. Ekwattanakit, "Clinical classification, screening and diagnosis for thalassemia," *Hematology/Oncology Clinics of North America*, vol. 32, no. 2, pp. 193–211, 2018, doi: 10.1016/j.hoc.2017.11.006.

[8] K. Tari, P. V. Ardalan, M. Abbaszadehdibavar, A. Atashi, A. Jalili, and M. Gheidishahran, "Thalassemia an update: molecular basis, clinical features and treatment," *International Journal of Biomedicine and Public Health*, vol. 1, no. 1, pp. 48–58, 2018, doi: 10.22631/ijbmph.2018.56102.

[9] I. Mustafa *et al.*, "Genetic epidemiology of beta-thalassemia in the Maldives: 23 years of a beta-thalassemia screening program," *Gene*, vol. 741, 2020, doi: 10.1016/j.gene.2020.144544.

[10] R. Das *et al.*, "A decision support scheme for beta thalassemia and HbE carrier screening," *Journal of Advanced Research*, vol. 24, pp. 183–190, Jul. 2020, doi: 10.1016/j.jare.2020.04.005.

[11] S. Thakur, S. N. Raw, and R. Sharma, "Design of a fuzzy model for thalassemia disease diagnosis: Using mamdani type fuzzy inference system (FIS)," *International Journal of Pharmacy and Pharmaceutical Sciences*, vol. 8, no. 4, pp. 356–361, 2016.

[12] S. Thakur and S. N. Raw, "Thalassemia risk prediction model using fuzzy inference systems : an application of fuzzy logic," *Research Journal of Mathematical and Statistical Sciences*, vol. 5, no. 7, pp. 1–8, 2017.

[13] I. L. Roth, B. Lachover, G. Koren, C. Levin, L. Zalman, and A. Koren, "Detection of β-thalassemia carriers by red cell parameters obtained from automatic counters using mathematical formulas," *Mediterranean Journal of Hematology and Infectious Diseases*, vol. 10, no. 1, pp. 1–10, 2018, doi: 10.4084/MJHID.2018.008.

[14] S. L. Mendiratta, S. Bajaj, S. Popli, and S. Singh, "Screening of women in the antenatal period for thalassemia carrier status: comparison of NESTROFT, red cell indices, and HPLC analysis," *Journal of Fetal Medicine*, vol. 2, no. 1, pp. 21–25, 2015, doi: 10.1007/s40556-015-0036-0.

[15] T. Munkongdee, P. Chen, P. Winichagoon, S. Fucharoen, and K. Paiboonsukwong, "Update in laboratory diagnosis of thalassemia," *Frontiers in Molecular Biosciences*, vol. 7, pp. 1–12, 2020, doi: 10.3389/fmolb.2020.00074.

[16] S. Sadiq *et al.*, "Classification of β-thalassemia carriers from red blood cell indices using ensemble classifier," *IEEE Access*, vol. 9, pp. 45528–45538, 2021, doi: 10.1109/ACCESS.2021.3066782.

[17] F. R. Aszhari, Z. Rustam, F. Subroto, and A. S. Semendawai, "Classification of thalassemia data using random forest algorithm," *Journal of Physics: Conference Series*, vol. 1490, no. 1, Mar. 2020, doi: 10.1088/1742-6596/1490/1/012050.

[18] N. Radakovich, M. Nagy, and A. Nazha, "Artificial intelligence in hematology : current challenges and opportunities," *Current Hematologic Malignancy Reports*, vol. 15, no. 3, pp. 203–210, 2020, doi: 10.1007/s11899-020-00575-4.

[19] Y. E. Alaoui, A. Elomri, M. Qaraqe, R. Padmanabhan, and R. Y. Taha, "A review of artificial intelligence applications in hematology management : current practices and future prospects," *Journal of Medical Internet Research*, vol. 24, no. 7, pp. 1–24, 2022, doi: 10.2196/36490.

[20] L. A. Zadeh, "The role of fuzzy logic in the management of uncertainty in expert systems," *Fuzzy Sets Systems*, vol. 11, no. 1–3, pp. 197–198, 1983, doi: 10.1016/S0165-0114(83)80081-5.

[21] P. Lialiou, D. Zikos, and J. Mantas, "Development and evaluation of an expert system for the diagnosis of child autism," in *Studies in Health Technology and Informatics*, 2012, pp. 1185–1187, doi: 10.3233/978-1-61499-101-4-1185.

[22] N. C. E. -Chukwu, "Applications of artificial intelligence in agriculture: a review," *Engineering, Technology and Applied Science Research*, vol. 9, no. 4, pp. 4377–4383, 2019, doi: 10.48084/etasr.2756.

[23] S. Santini *et al.*, "Using fuzzy logic for improving clinical daily-care of β-thalassemia patients," in *2017 IEEE International Conference on Fuzzy Systems (FUZZ-IEEE)*, IEEE, Jul. 2017, pp. 1–6, doi: 10.1109/FUZZ-IEEE.2017.8015545.

[24] T. Siswantining, A. Kamalia, Z. Rustam, F. Subroto, and A. S. Semendawai, "Classification of thalassemia data using K-nearest neighbor and naïve Bayes," *International Journal of Advanced Science and Technology*, vol. 28, no. 8, pp. 15–19, 2019.
[25] P. Paokanta, M. Ceccarelli, and S. Srichairatanakool, "The effeciency of data types for classification performance of machine learning techniques for screening thalassemia," in *2010 3rd International Symposium on Applied Sciences in Biomedical and Communication Technologies (ISABEL 2010)*, IEEE, Nov. 2010, pp. 1–4, doi: 10.1109/ISABEL.2010.5702769.
[26] A. Wantoro, A. Syarif, K. Muludi, and K. Nisa, "Implementation of fuzzy-profile matching in determining drug suitability for hypertensive patients," *IOP Conference Series: Materials Science and Engineering*, vol. 857, no. 1, 2020, doi: 10.1088/1757-899X/857/1/012027.
[27] M. Seera and C. P. Lim, "A hybrid intelligent system for medical data classification," *Expert Systems with Applications*, vol. 41, no. 5, pp. 2239–2249, Apr. 2014, doi: 10.1016/j.eswa.2013.09.022.
[28] E. R. Susanto, A. Syarif, K. Muludi, R. R. W. Perdani, and A. Wantoro, "Implementation of Fuzzy-based Model for Prediction of Thalassemia Diseases," *Journal of Physics: Conference Series*, vol. 1751, no. 1, Jan. 2021, doi: 10.1088/1742-6596/1751/1/012034.
[29] V. Villatoro and M. To, *A laboratory guide to clinical hematology*. Edmonton: University of Alberta Library, 2019, doi: 10.29173/oer1.
[30] F. Wang *et al.*, "Differential diagnosis of thalassemia and iron deficiency anemia using the CellaVision advanced red blood cell software," *International Journal of Laboratory Hematology*, vol. 43, no. 4, pp. 853–858, 2021, doi: 10.1111/ijlh.13424.
[31] R. Risoluti, S. Materazzi, F. Sorrentino, C. Bozzi, and P. Caprari, "Update on thalassemia diagnosis: New insights and methods," *Talanta*, vol. 183, pp. 216–222, 2018, doi: 10.1016/j.talanta.2018.02.071.
[32] S. Ali *et al.*, "Current status of beta-thalassemia and its treatment strategies," *Molecular Genetics and Genomic Medicine*, vol. 9, no. 12, pp. 1–14, 2021, doi: 10.1002/mgg3.1788.
[33] G. Selvachandran *et al.*, "A new design of mamdani complex fuzzy inference system for multiattribute decision making problems," *IEEE Transactions on Fuzzy Systems*, vol. 29, no. 4, pp. 716–730, 2021, doi: 10.1109/TFUZZ.2019.2961350.
[34] C. Mahanty, R. Kumar, P. G. Asteris, and A. H. Gandomi, "COVID-19 patient detection based on fusion of transfer learning and fuzzy ensemble models using CXR images," *Applied Sciences*, vol. 11, no. 23, Dec. 2021, doi: 10.3390/app112311423.
[35] C. Mahanty, R. Kumar, and S. G. K. Patro, "Internet of medical things-based COVID-19 detection in CT images fused with fuzzy ensemble and transfer learning models," *New Generation Computing*, vol. 40, no. 4, pp. 1125–1141, Dec. 2022, doi: 10.1007/s00354-022-00176-0.

BIOGRAPHY OF AUTHORS

Erliyan Redy Susanto Doctoral student at the Faculty of Mathematics and Natural Sciences, Lampung University. Currently he is a lecturer at the Faculty of Engineering and Computer Science, Universitas Teknokrat Indonesia. He has his Bachelor of Computer Science, Ahmad Dahlan University, Yogyakarta in 2006. He has his Master degree in Computer Science from Bogor Agriculture University in 2016. His research interests are primarily in the field of artificial intelligence for medicine. He can be contacted at email: erliyan.redy@teknokrat.ac.id.

Admi Syarif Professor at the Dept. of Computer Science, Faculty of Mathematics and Sciences, Lampung University, Indonesia. He received a Bachelor of Science in Mathematics from Padjadjaran University, Indonesia, in 1990 and his Ph.D. in Industrial and Information System Engineering from Ashikaga Institute of Technology, Japan, in 2004. He was a director of the research center of Lampung University from 2010 to 2016; and has been a national research reviewer of the Ministry of Education and Culture, Republic Indonesia, since 2014. He can be contacted at email: admi.syarif@fmipa.unila.ac.id.

Warsito Professor at the Department of Physics, Faculty of Mathematics and Natural Science, Lampung University. He completed his bachelor's degree at the Department of Physics, Brawijaya University, Malang in 1995. Meanwhile, his master's degree was completed in 2000 at Universite De Caen, France. For doctoral education he completed in 2004 at the same university in France. His other experience is as the Education and Culture Attache at the Indonesian Embassy in Paris. Currently he serves as Deputy for Coordinating Education Quality Improvement and Religious Moderation. He can be contacted at email: warsito@fmipa.unila.ac.id

Khairun Nisa Berawi is a professor candidate from the Faculty of Medicine, University of Lampung. He earned his medical degree from Sriwijaya University, Palembang in 1999. In 2008, he completed his master's degree in public health at Padjadjaran University, Bandung. She successfully completed her doctoral program in 2018 at Andalas University, Padang. She is a Sports Physiology Expert in Indonesia with an AIFO degree. She can be contacted at email: khairun.nisa@fk.unila.ac.id.

Putu Ristyaning Ayu Sangging is a lecturer at the Faculty of Medicine, University of Lampung with expertise in Clinical Pathology. She completed medical education in 2002 at Hang Tuah University, Surabaya. Then she successfully completed her master's degree in health and clinical pathology specialist in 2012 at Hasanuddin University, Makassar. Furthermore, he completed his sub-specialist education at Diponegoro University, Semarang. She can be contacted at email: ristya.ayu@gmail.com.

Agus Wantoro is a Faculty of Engineering and Computer Science lecturer at the Universitas Teknokrat Indonesia. He obtained a bachelor's degree in computer from the College of Informatics Management and Computer Teknokrat Lampung in 2009. He completed a master's degree in computer in 2015 from Budi Luhur University, Jakarta. Then in 2022 complete his doctoral education at the University of Lampung. The field currently occupied is artificial intelligence in the medical field. He can be contacted at email: agus.wantoro@teknokrat.ac.id.