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Development of Model for Prediction of Thalassemia Disease

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Abstract: Thalassemia is known as one of the blood disorder diseases that is inherited by parents. There are several types of Thalassemia, namely as Thalassemia major, minor, and intermedia. Among them, Thalassemia major is the most dangerous and needs more attention. Generally, it can be detected since the child is one year old. Late detection of this disease can have adverse consequences and various complications. This study aims to develop a new model for the prediction of thalassemia for children. The model adopts a fuzzy-based rule. It can determine the thalassemia disease and also predict the emergency level of the disease. We validate the model by using some real data and information from thalassemia experts. The novelty in this article is that our model has 4 outputs, namely thalassemia major, intermedia, minor and not thalassemia. In the previous article it only had 3 outputs, namely thalassemia major, intermedia and minor. In addition, we have also built a better user interface to make it easier for users to analyze thalassemia based on Complete Blood Count data.

Keywords: Blood disorder diseases, Thalassemia, Fuzzy-based model, Thalassemia classification, Artificial Intelligence

1. Introduction

In many countries, there are many reports of blood disorders. One of them is thalassemia. The increase in thalassemia cases is due to the lack of genetic counseling and prenatal diagnosis [1][2][3]. Actually, thalassemia can be known after the baby is born through several visible symptoms. Currently, most of thalassemia parents only know after the child is two years old. In fact, thalassemia is very dangerous if it is not treated immediately [4]. Based on clinical manifestations, thalassemia is classified into several types, namely thalassemia major, thalassemia minor or trait or carrier and thalassemia intermedia [5][6][7]. Patients with thalassemia major require routine blood transfusions throughout their life. Patients with thalassemia intermedia also require blood transfusions, but not as often as thalassemia major. Meanwhile, thalassemia minor patients do not need blood transfusions but only carry thalassemia traits[8]. Thalassemia treatment in Indonesia is currently still supportive, it has not yet reached the level of cure. Supportive treatment given to thalassemia patients aims to treat the symptoms that arise due to

thalassemia. Symptoms include pale, yellowish or gray skin. In addition, there are also disturbances in growth. Lifelong routine transfusions, iron chelation administration, and psychosocial support are the main treatments for thalassemia major patients. [9][10].

A child becomes thalassemia due to genetic factors, namely a blood disorder that is inherited from parents[11][12][7]. Based on Mendel's law, it is known that if both parents or one of the two are characteristic carriers, the trait will be passed on to the child. Actually, thalassemia can be known based on visible physical symptoms. An easily seen disorder in thalassemia sufferers is that the child looks pale so that he experiences symptoms such as anemia[13][14]. In addition, thalassemia can also cause fatigue, dizziness, and shortness of breath because the blood vessels that supply the lungs are narrowed, forcing the heart to work harder to push blood in [15][16][17]. As a result, the activity of thalassemia sufferers will be disrupted. Thalassemia needs to be watched out for, especially thalassemia major because it can cause complications in the form of heart failure, stunted growth, liver problems, and even death[18]. Recent surveys show that thalassemia major occurs in infants between 300,000 and 400,000 babies born and it is known that up to 90% of births occur in poor and developing countries[5]. However, thalassemia is also very potential to occur in developed countries though.

The life of a thalassemia major patient is very dependent on blood transfusions of 1-3 bags per month. The existence of thalassemia major has a significant role in the blood supply needs of the Indonesian Red Cross. Doctors diagnose thalassemia through blood tests, including a complete blood test (CBC) and a special hemoglobin test. The CBC measures the amount of hemoglobin and various types of blood cells, such as red blood cells, in a blood sample. People who have thalassemia have fewer healthy red blood cells and less hemoglobin in their blood. People who have alpha or beta thalassemia traits may have red blood cells that are smaller than normal. The hemoglobin test measures the type of hemoglobin in a blood sample. People who have thalassemia have problems with the alpha or beta globin hemoglobin protein chains.

Usually moderate and severe thalassemia are diagnosed in early childhood. This is because the signs and symptoms such as severe anemia can be detected in the first 2 years of life. People who have mild thalassemia are usually diagnosed after routine blood tests show that they have anemia. Doctors will suspect thalassemia if someone is anemic and comes from an ethnic group at high risk of developing thalassemia.

The doctor will analyze the amount of iron in the blood to determine whether the anemia is due to iron deficiency or thalassemia. Iron deficiency anemia occurs because the body doesn't have enough iron to make hemoglobin. Anemia in thalassemia occurs due to problems with the alpha globin chain or hemoglobin beta globin, not due to iron deficiency. Through genes, thalassemia is passed from parents to children. Family genetic studies can also help diagnose the disorder.

Thalassemia in children can be detected after going through a series of blood tests in a medical laboratory or commonly called blood screening. The results of thalassemia screening contained several components of the blood test, including the complete blood count (CBC), High Performance Liquid Chromatography (HPLC) values and peripheral blood analysis. The CBC components consist of hemoglobin, hematocrit, erythrocyte, leukocyte, platelet and MC values, namely MCV, MCH, MCHC and RDW. While the HPLC components consist of HbA2 and HbF[19].

Many people think that the current cost of screening for thalassemia is quite expensive. In general, in Indonesia, not all health laboratories can provide blood screening services. Only health laboratories in big cities like Jakarta have blood screening testing facilities. In addition, it takes about 1 week to find out the results of a person's blood screening. The aim of this article is to propose a new model to determine thalassemia in children based on CBC values. Where almost every health laboratory in the area has this testing facility. Thus, thalassemia is known faster than the usual method so far. In this study, we used the fuzzy approach, which is one of the methods of artificial intelligence to solve the classification problem of thalassemia. Fuzzy approach is also known to be often used to solve various problems in health.

2. Literature Study

The first article discusses the Efficiency of Data Types for Classification Performance of Machine Learning Techniques for Screening Thalassemia [20]. This article compares the MultiLayer Perceptron, K-Nearest Neighbors, Bayesian networks, NaiveBayes, and Multinomial Logistic Regression methods for the classification of thalassemia. The results obtained in this first article show that the MultiLayer Perceptron, K-Nearest Neighbors, and Bayesian networks have the best accuracy. The second article discusses the design of a fuzzy model for thalassemia disease diagnosis. The type of fuzzy used in diagnosing thalassemia is mamdani [21]. In this second article, there are 3 input variables used, namely hemoglobin, MCV and MCH. Meanwhile, the results show that the Fuzzy Inference System can be used for the classification of thalassemia. The third article discusses the Thalassemia risk prediction model using fuzzy inference systems[22]. In this third article, 3 input variables are used, namely symptoms, HbA and Hba. The results obtained are in the form of a prediction model for the severity of thalassemia patients.

Wantoro in his article entitled Implementation of fuzzy-profile matching in determining drug suitability for hypertensive patients implementing artificial intelligence techniques in the health sector. He made an application to make it easier for doctors to analyze hypertension data then provide possible drug recommendations for patients. Based on the results of comparisons with expert 1 and expert 2, the results of the average system testing are obtained with a value of 100% precision, recall 96.6% and accuracy 96.5%. Tests show that the application with a fuzzy logic approach can increase the efficiency of 9.5% compared to the interpolation weighting method[23].

3. Method

Knowledge Base Development

Based on consultations conducted with experts and several literature reviews on blood screening, the criteria for developing a knowledge base for the classification of thalassemia are presented in Figure 1.

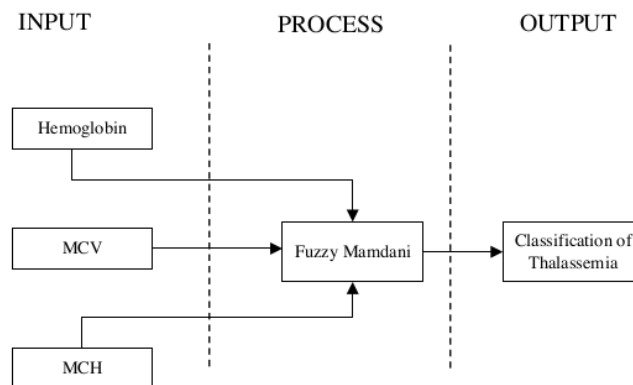


Figure 1 Knowledge for thalassemia classification

Variable

Experts think that the results of the CBC test may be used to determine thalassemia in children [18][24]. There are several values that are strongly thought to affect the results of thalassemia screening including hemoglobin, MCV, and MCH. Furthermore, these values are analyzed and used to determine the type of thalassemia in children. Meanwhile the variable names are presented in Table 1.

Table 1 Variables for determining the type of thalassemia

Hemoglobin	MCV	MCH
g/dL	fL	pg

The Evaluation of Thalassemias Classification

Based on the results of the CBC, data is needed as a basic reference for measuring the severity of thalassemia. For example, to find out a thalassemia major child has a hemoglobin value less than 7 g/dL, has an MCV value of 50 to 70 fL, and has an MCH value of 12 to 20 pg. In this case, we divide the data for each variable into four types including high, medium, low and very low. So that the ideal data used to determine the classification of thalassemia are obtained in Table 2.

Table 2 Classification data for thalassemia

Type	Hemoglobin	MCV	MCH
Mayor	<7[18]	50-70[18]	12-20[18]
Intermedia	7-10[18]	50-80[18]	16-24[18]
Minor	10-11	53-71[24]	17-25[24]
Not Thalassemia	10.8-12.8	73-101	23-31

Based on the data in Table 2, it is then used as a basis for determining the type of thalassemia using the Profile Matching evaluation method.

Input

Based on the thalassemia classification data in Table 2 and this data has been confirmed by a thalassemia specialist. Furthermore, the model for thalassemia are made using fuzzy Mamdani which is presented in Table 3.

Table 3 Model for input



Figure 2 Model for hemoglobin variable

Variable	Model
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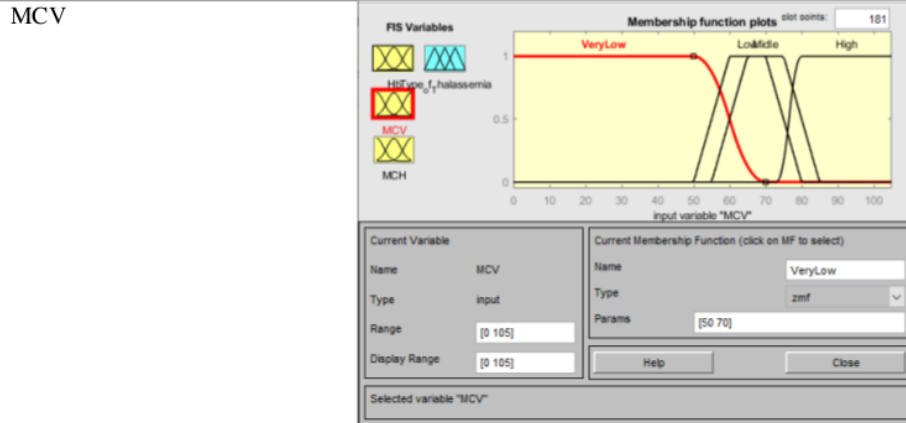


Figure 3 Model for MCV variable



Figure 4 Model for MCH variable

Output

After the input model is created, then we also create a model to display the results of the analysis using Mamdani fuzzy. The output of the model is adjusted according to the rules as in Table 4.

Table 4 Classification of output

Linguistic Variable	Ranges	Fuzzy Set
Type_of_Thalassemia	≤ 3	Not Thalassemia
	$\geq 3; \leq 4$	Minor
	$> 3.5; \leq 8$	Intermedia
	≥ 7	Major

The output model is presented in Figure 5.

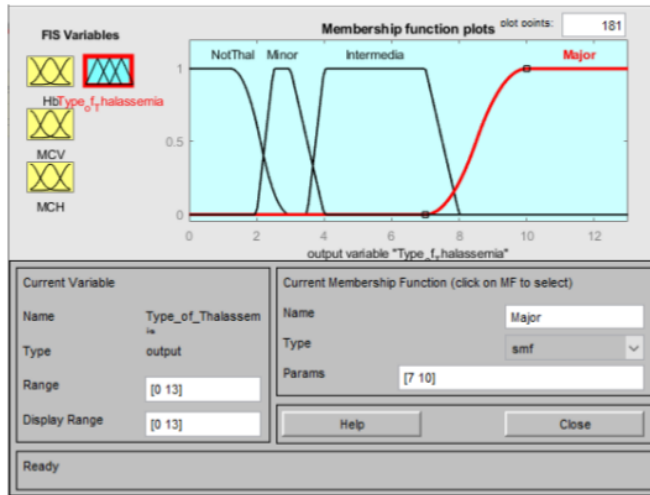


Figure 5 Model for output

Based on the membership function, the membership value for each variable is then calculated. As an example the membership values for Thalassemia Major. In this case we used data from pediatrician regarding thalassemia screening which are presented in Table 5.

Table 5 Fuzzy membership values for thalassemia major

P-001	Data	Membership values
Hemoglobin	5.0	Value (x) = (x<7) then x=1
MCV	66.7	Value (x) = (x>=50; x<=70) then x=1
MCH	20.3	Value (x) = (x>=12; x<=20) then x=0

Based on these data, it is then tested on a model that has been made. The results of the model trials are presented in Figure 6.

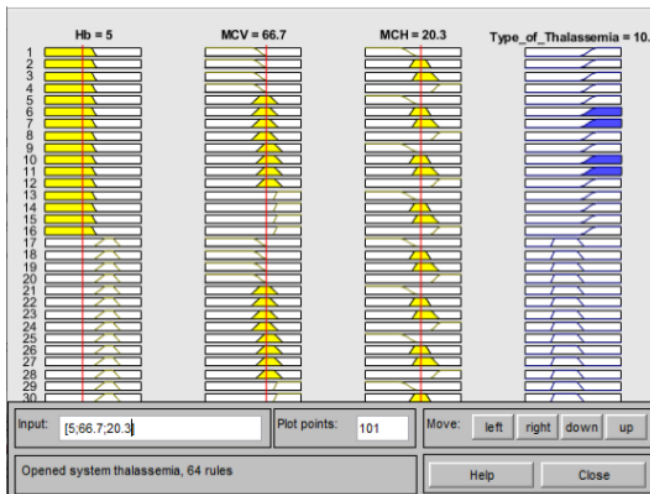


Figure 6 Tested the model using thalassemia major data

Based on the results of testing on the model, it can be seen that the results of the fuzzy calculation show a value of 10.7, so it can be concluded that the data includes thalassemia major.

4. Result and Discussions

After the model has been built, the next step is create a graphical user interface. In this case, we create a user interface as an implementation of the model we have developed. The software display is presented in Figure 7.

The screenshot shows a web-based application titled "Thalassemia Classification Using Complete Blood Count (CBC) Data". It features an "Input" section with three text boxes for "Hb Hemoglobin (g/dL)", "MCV Mean Corpuscular Volume (fL)", and "MCH Mean Corpuscular Hemoglobin (pg)". Below these are "Analyze!" and "Reset" buttons. The "Output" section contains two text boxes for "Value of Fuzzy" and "Classification". A copyright notice at the bottom reads "Copyright © 2020 - Eriyan Redy Susanto, Admi Syarif, Agus Wantoro".

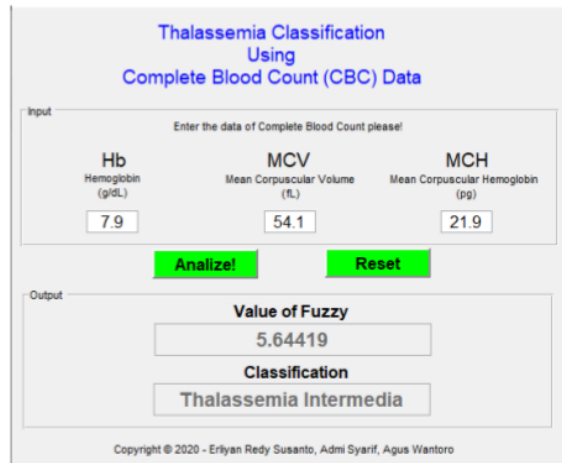
Figure 7 Software display for thalassemia classification

In testing the model we used 4 variables from CBC data. The first data contained several variable values including hemoglobin = 5.0 g / dL, MCV = 66.7 fL and MCH = 20.3 pg. The data inputted into the software as shown in Figure 8.

This screenshot shows the same software interface as Figure 7, but with test data entered. The input fields contain the values 5, 66.7, and 20.3. The "Analyze!" button has been clicked, and the output fields now display "Value of Fuzzy" as 10.7413 and "Classification" as "Thalassemia Major". The copyright notice remains the same.

Figure 8 Display software on data testing for thalassemia major

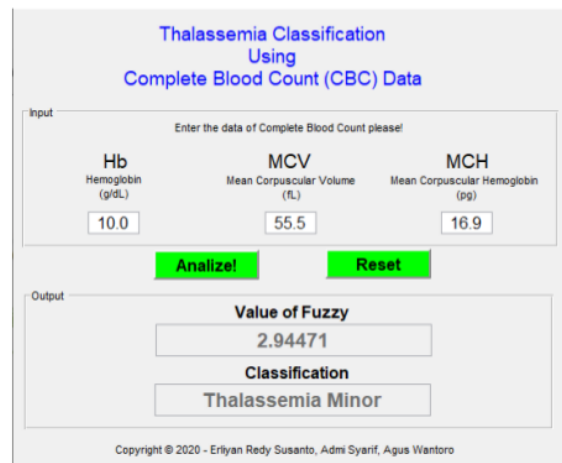
Based on the analysis results as figure 8, the fuzzy value = 10.7413 is obtained so that the classification of thalassemia is classified as major. Second data contained several variable values including hemoglobin = 7.9 g/dL, MCV = 54.1 fL and MCH = 21.9 pg. The test results are presented in Figure 9.



The screenshot shows a web-based application titled "Thalassemia Classification Using Complete Blood Count (CBC) Data". It has an "Input" section with three text boxes for "Hb Hemoglobin (g/dL)", "MCV Mean Corpuscular Volume (fL)", and "MCH Mean Corpuscular Hemoglobin (pg)". The values entered are 7.9, 54.1, and 21.9 respectively. Below the input fields are two green buttons: "Analyze!" and "Reset!". The "Output" section displays "Value of Fuzzy" as 5.64419 and "Classification" as "Thalassemia Intermedia". At the bottom, there is a copyright notice: "Copyright © 2020 - Eriyan Redy Susanto, Admi Syarif, Agus Wantoro".

Figure 9 Display software on data testing for thalassemia intermedia

Based on the analysis results as figure 9, the fuzzy value = 5.64419 is obtained so that the classification of thalassemia is classified as intermedia. Third data contained several variable values including hemoglobin = 10.0 g/dL, MCV = 55.5 fL and MCH = 16.9 pg. The test results are presented in Figure 10.



The screenshot shows the same web-based application as Figure 9. The input values are now Hb: 10.0, MCV: 55.5, and MCH: 16.9. The "Analyze!" and "Reset!" buttons are still present. The output section shows "Value of Fuzzy" as 2.94471 and "Classification" as "Thalassemia Minor". The copyright notice at the bottom remains the same: "Copyright © 2020 - Eriyan Redy Susanto, Admi Syarif, Agus Wantoro".

Figure 10 Display software on data testing for thalassemia minor

Based on the analysis results as figure 10, the fuzzy value = 2.94471 is obtained so that the classification of thalassemia is classified as minor. Fourth data contained several variable values including hemoglobin = 10.0 g/dL, MCV = 55.5 fL and MCH = 16.9 pg. The test results are presented in Figure 11.

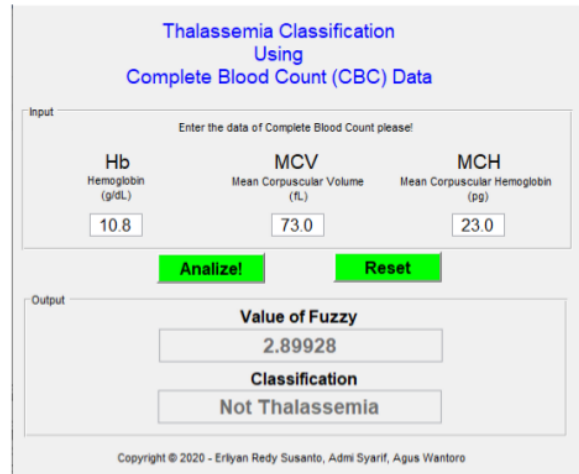


Figure 11 Display software on data testing for not thalassemia

Based on the analysis results as figure 11, the fuzzy value = 2.89928 is obtained so that the classification of thalassemia is classified as not thalassemia. The test result data is then matched with the opinion of the pediatrician. The test results on the four data are presented in Table 6.

Table 6 The Result of Testing

No	Variable			Value of Fuzzy	Classification	Result
	Hemoglobin	MCV	MCH			
1	5.0	66.7	20.3	10.7413	Major	Correct
2	7.9	54.1	21.9	5.64419	Intermedia	Correct
3	10.0	55.5	16.9	2.94471	Minor	Correct
4	10.8	73.0	23.0	2.89928	Not Thallasemia	Correct

The results of testing on 4 CBC data show that the model we developed is proven to be in accordance with the opinion of pediatricians regarding thalassemia.

5. Conclusion

Finally, the results show that the model we developed works well for detecting thalassemia. The type of thalassemia can be determined based on the results of the CBC examination based on the hemoglobin, MCV and MCH values. We have 4 output models, namely Major, Intermedia, Minor and Not Thalassemia. The results of the model prediction against 4 data were tested in accordance with the opinion of doctors about thalassemia. In order to know better accuracy, our model needs to be tested with more real data.

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