Discrimination between Iron Deficiency Anaemia (IDA) and β-Thalassemia Trait (β-TT) Based on Pattern-Based Input Selection Artificial Neural Network (PBIS-ANN)

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Abstract
Discrimination between iron deficiency (IDA) anaemia and β-thalassemia trait (β-TT) is a time consuming and costly problem. Because, they have approximate similar effects on routine blood test indices, in some cases, the complementary tests, which are expensive and time consuming, would be needed for differentiate the anaemia. Complete blood count (CBC) is a fast, inexpensive, and accessible medical test that is used as a primary test for diagnosis anaemia. However, when the CBC indices cannot exactly state the subject, more advanced tests such as electrophoresis of hemoglobin must be performed. In this study, the CBC indices have been considered as the inputs of classifier and the chosen architecture is pattern-based input selection artificial neural network (PBIS-ANN). For evaluation the proposed method, traditional methods, which are still using for the problem such as Mentzer Index (MI), and several automated anemia diagnostic systems such as artificial neural networks (ANN), adaptive neuro-fuzzy inference system (ANFIS) and multi-layer perceptron (MLP) have been compared with the proposed method. The results indicate that the proposed method significantly outperforms the mentioned methods.

Keywords: Iron Deficiency Anemia, β-Thalassemia Trait, Artificial Neural Network, Complete Blood Count, Hemoglobin

1. Introduction

Despite iron deficiency anaemia (IDA) that is not a genetic disease, thalassemia is a genetic trait that causes a reduction in the life span of a red blood cell [1]. Thalassemia disease is a result of an abnormality in the genes that regulate the formation of hemoglobin. Thalassemia screening is an action to detect the couples with the potential of having a thalassemic infant. To achieve this goal the subjects with the thalassemia trait of same type must be recognized. There are several types of thalassemia. When the parents of a child have the thalassemia trait of the same type, he or she has the disease, trait, or is normal with the probability of 25%, 50%, and 25%, respectively. One of the most common types of thalassemia trait is β-thalassemia trait (β-TT). CBC, a fast an inexpensive medical test, is the primary test in the thalassemia screening. The similarity of CBC indices in IDA and β-TT makes discrimination between them so difficult. Hence, in the subjects that couldn’t be stated with their CBC indices, the complementary tests, which are time consuming and expensive, would be needed. Additionally, these tests are not available in all laboratories and hospitals. As a result,
many researchers have tried to find methods for discrimination between IDA and β-TT with interpreting the CBC indices [2–14].

Historically, mathematical formulas were used for the problem [2–7,12,13,15]. In the past few decades there has been increasing interested in the automated medical diagnostic systems. Early attempts to formulate an automated diagnostic tool for anemia classification employed image analysis [16], statistical [17], and clustering techniques [18]. Later, the implementation protocol has shifted to the expert systems, in which both rule-based [19–21] and hybrid neural network/rule-based [22] systems have been successfully tested in clinical trials. The other studies on automated classification of anemia was performed using image analysis [23] and artificial neural networks (ANN) [24]. A comparison study on thalassemia screening in which support vector machine (SVM), K-nearest neighbor (KNN), and an MLP were investigated [25], reported that the MLP classifier gives slightly better results than the SVM. Another comparison study on diagnosis IDA [26] was performed between ANN, ANFIS, and a logistic regression model. The authors revealed that the ANN is superior to the others.

An investigation on genetic programming (GP) in thalassemia classification [27] discovered that a GP-based decision tree and an MLP with one hidden layer are approximately equal in accuracy. But, the MLP with two hidden layers is superior. Piroonratana et al. investigated three classifier in hemoglobin typing for thalassemia screening [28] that are: C4.5, random forest and MLP. They revealed that C4.5 is more suitable than the others when using high performance liquid chromatography (HPLC) as the input. Although, the previous studies have been successfully tested, there are two major reasons for further investigation into automated discrimination between IDA and β-TT. First, an increase in precision is required, because a high accuracy in thalassemia screening is vital for having healthy population in the next generation. Second, reduction cost and time is achievable by using the CBC indices as the inputs of the anemia classifier, while the most accurate previous studies used the time consuming and expensive medical tests such as the electrophoresis or HPLC. This study has been performed to satisfy these requirements. It compares the proposed method with the existing methods of discrimination IDA and β-TT.

The remaining of the article is organized as follows. Section 2 explains some scientific information on the structure of hemoglobin and its formation, and the relations between the anemia and hemoglobin. In section 3, the collected data will be analyzed. Section 4 introduces the proposed method and section 5 compares the obtained results of the proposed method with the other methods in literature. Finally, section 6 concludes the study and gives some suggestions for further works.

2. The Effects of Anemia

Hemoglobin, which is a core component of a red the blood cell, consists of four poly peptide chains (globin) and the other component that is called ‘heme’ [1]. First component is affected by thalassemia and the second one is affected by IDA. There are four types of globin chains that are: alpha (α), beta (β), gamma (γ), and delta (δ). Regarding to the types of globin chains in the structure of hemoglobin, it can belongs to one of the three major types of hemoglobin, including HbA (α2β2), HbA2 (α2δ2), and HbF (α2γ2). HbF or fetal hemoglobin is the main constructor of a fetus’ red blood cells, which after born gradually exchanges with HbA. The proportions of the HbA, HbA2,
and HbF in a mature and healthy person’s blood are approximately, 97%, 2-3%, and less than 1%, respectively.

Thalassemia disease stems from the defects on the genes that regulate the formation of globin chains. The type of thalassemia and the severity of disease are depended on the type and the number of defective genes, respectively. In fact, persons with thalassemia trait do not have the disease but inherit genes that cause the disease. Generally, the incidence of β-thalassemia is more than α-thalassemia. Therefore, detection of β-TT to avoid of having the β-thalassemia infants is a major purpose of screening. In the other hand, when the subject has IDA disease, because of deficiency of the iron, the concentration of the component ‘heme’, which is an iron-based molecule, will be reduced. Hence, the quantity and quality of hemoglobin will be affected in the presence of IDA. In the next subsection more details of the effects of anemia on blood indices will be explained.

2.1. CBC indices

Each red blood cell contains approximately 300 million molecules of hemoglobin. Hence, a change in the structure of globin affects the structure and functionality of the red blood cells. As previous discussed, IDA and β-TT both lead to decrease hemoglobin’s quality and quantity. With the difference that the first one affects the ‘heme’ component and the later affects the globin formation. As a result, thalassemia changes the CBC indices in the following manner: Hemoglobin concentration (Hb), which denotes the quantity of hemoglobin in blood, reduces in presence of thalassemia disease or trait. The red blood cell count (RBC) is the other index of CBC that in a thalassemic subject might be increased for compensation of the hemoglobin reduction. The other significant indices of CBC that are usually employed in diagnosis thalassemia are: mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red blood cell distribution width (RDW), and hematocrit (HCT). These indices would also be reduced in the presence of thalassemia disease or β-TT.

In the other hand, IDA has similar effects on CBC indices except that in the β-TT subjects, we have increased RBC while in the IDA subjects the RBC index would be decreased. This is the most important difference between those anemia. In spite of the difference on RBC volume on different cases, it is so difficult to discriminate IDA from β-TT subjects.

3. Data Analysis

The samples were collected from the archives of the several thalassemia screening centers where situated in five northern cities of Iran. Total number of collected CBC tests is 750, which were obtained from the blood specimen of 390 males in ages 20-35 and 360 females in ages 17-32 years old. The information has been organized as follows.

1. The samples that their CBC indices obviously are in the normal ranges (218 samples).
2. The samples that their CBC indices are abnormal and definitely show β-TT or IDA on them (98 samples, IDA = 38, β-TT = 60).
III. The samples that their CBC indices cannot exactly determine them. They were stated by complementary tests such as electrophoresis (434 samples, IDA = 231, β-TT = 203).

According to the above issues total number of β-TT and number of IDA subjects are 269 and 263, respectively. Table 1 shows some examples of different categories of collected samples. Abnormal values are shown in bold face (Table 1). It is undeniable that the samples in the cat. III are so similar and there is a complex relation that a simple mathematical formula cannot distinguish between IDA and β-TT subjects in this category as well. Because, the study’s purpose is differentiate between IDA and β-TT subjects, we excluded the normal subjects from the collected samples and the remaining samples (532 samples including IDA and β-TT) were randomly divided into the training and the testing patterns with 132 and 400 samples, respectively.

Table 1. Some examples of different classes of collected samples.

<table>
<thead>
<tr>
<th>Sample number</th>
<th>RBC (M/mm³)</th>
<th>HD (g/dL)</th>
<th>HCT (%)</th>
<th>MCV (fL)</th>
<th>MCH (pg)</th>
<th>MCHC (%)</th>
<th>Category number</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5.43</td>
<td>10.2 ↓</td>
<td>34 ↓</td>
<td>62.6 ↓</td>
<td>18.8 ↓</td>
<td>30 ↓</td>
<td>II</td>
<td>β-TT</td>
</tr>
<tr>
<td>2</td>
<td>6.13</td>
<td>12.5 ↓</td>
<td>40.1</td>
<td>65.4 ↓</td>
<td>20.4 ↓</td>
<td>31.2 ↓</td>
<td>II</td>
<td>β-TT</td>
</tr>
<tr>
<td>3</td>
<td>6.8 ↑</td>
<td>12.6 ↓</td>
<td>43.4</td>
<td>63.8 ↓</td>
<td>18.5 ↓</td>
<td>29 ↓</td>
<td>II</td>
<td>β-TT</td>
</tr>
<tr>
<td>4</td>
<td>4.73</td>
<td>10.1 ↓</td>
<td>38.7 ↓</td>
<td>69.9 ↓</td>
<td>19.7 ↓</td>
<td>30.3 ↓</td>
<td>II</td>
<td>IDA</td>
</tr>
<tr>
<td>5</td>
<td>4.13 ↓</td>
<td>8.2 ↓</td>
<td>38.4 ↓</td>
<td>71.8 ↓</td>
<td>19.9 ↓</td>
<td>28.9 ↓</td>
<td>II</td>
<td>IDA</td>
</tr>
<tr>
<td>6</td>
<td>4.61</td>
<td>12.8 ↓</td>
<td>38.9 ↓</td>
<td>84.4</td>
<td>27.8</td>
<td>32.9</td>
<td>I</td>
<td>normal</td>
</tr>
<tr>
<td>7</td>
<td>4.36 ↓</td>
<td>13.1 ↓</td>
<td>39.7</td>
<td>91.1</td>
<td>30</td>
<td>33</td>
<td>I</td>
<td>normal</td>
</tr>
<tr>
<td>8</td>
<td>4.77</td>
<td>13.3 ↓</td>
<td>39.7</td>
<td>83.2</td>
<td>27.9</td>
<td>33.5</td>
<td>I</td>
<td>normal</td>
</tr>
<tr>
<td>9</td>
<td>3.99 ↓</td>
<td>11.4 ↓</td>
<td>35.1 ↓</td>
<td>88</td>
<td>28.6</td>
<td>32.5</td>
<td>I</td>
<td>normal</td>
</tr>
<tr>
<td>10</td>
<td>4.4 ↓</td>
<td>13.7</td>
<td>40.5</td>
<td>92</td>
<td>31.1</td>
<td>33.8</td>
<td>I</td>
<td>normal</td>
</tr>
<tr>
<td>11</td>
<td>6.62 ↑</td>
<td>13.1 ↓</td>
<td>43.9</td>
<td>65.9</td>
<td>19.7</td>
<td>29.8</td>
<td>III</td>
<td>β-TT</td>
</tr>
<tr>
<td>12</td>
<td>4.56</td>
<td>10.3 ↓</td>
<td>34.7 ↓</td>
<td>76.1</td>
<td>22.6</td>
<td>29.7</td>
<td>III</td>
<td>β-TT</td>
</tr>
<tr>
<td>13</td>
<td>5.95</td>
<td>12.5 ↓</td>
<td>43.4</td>
<td>72.8</td>
<td>21</td>
<td>28.9</td>
<td>III</td>
<td>β-TT</td>
</tr>
<tr>
<td>14</td>
<td>4.65</td>
<td>10.5 ↓</td>
<td>35.6 ↓</td>
<td>76.6</td>
<td>22.6</td>
<td>29.5</td>
<td>III</td>
<td>β-TT</td>
</tr>
<tr>
<td>15</td>
<td>5.12</td>
<td>10.6 ↓</td>
<td>36.7 ↓</td>
<td>71.7</td>
<td>20.7</td>
<td>28.9</td>
<td>III</td>
<td>β-TT</td>
</tr>
<tr>
<td>16</td>
<td>4.81</td>
<td>11.6 ↓</td>
<td>37.6 ↓</td>
<td>78.2</td>
<td>24.1</td>
<td>30.9</td>
<td>III</td>
<td>IDA</td>
</tr>
<tr>
<td>17</td>
<td>5.05</td>
<td>11.5 ↓</td>
<td>38.8 ↓</td>
<td>76.8</td>
<td>22.8</td>
<td>29.6</td>
<td>III</td>
<td>IDA</td>
</tr>
<tr>
<td>18</td>
<td>4.88</td>
<td>12.1 ↓</td>
<td>38.8 ↓</td>
<td>79.5</td>
<td>24.8</td>
<td>31.2</td>
<td>III</td>
<td>IDA</td>
</tr>
<tr>
<td>19</td>
<td>5.03</td>
<td>12.7 ↓</td>
<td>39.9</td>
<td>79.3</td>
<td>25.2</td>
<td>31.8</td>
<td>III</td>
<td>IDA</td>
</tr>
<tr>
<td>20</td>
<td>5.1</td>
<td>13.2 ↓</td>
<td>39.7</td>
<td>77.8</td>
<td>25.9</td>
<td>30.7</td>
<td>III</td>
<td>IDA</td>
</tr>
</tbody>
</table>

Table 1. Some examples of different classes of collected samples.

4. Proposed Method

ANN, which is inspired by human organism, first considered by Warren McCulloch and Walter Pitts [29] in decade 40. After that, Donald Hebb introduced a training algorithm for ANN. Classification, pattern recognition, prediction, function approximation and data processing are some applications for ANNs [30–33]. In this study a new method based on ANN has been proposed to differentiate between IDA and β-TT subjects. In the next subsections we explain the architecture of the proposed method.

4.1. The architecture of the proposed method

To understand the idea behind the proposed method, consider the abnormal values in Table 1, which are marked with the symbols “↑” or “↓”. It is clear that some indices...
have approximately the same patterns of abnormal values and supposed to be redundant. Thus, to choose the most suitable indices as the inputs of the ANN, we proposed an architecture naming pattern-based input selection artificial neural network (PBIS-ANN). A briefly illustration of the proposed method has been shown in Fig. 1.

The dataset that were used for implementing the proposed method has been explained in the previous section. This dataset contains 532 CBC samples from IDA and β-TT subjects.

![Figure 1](image)

**Figure 1. Briefly illustration of the proposed method**

**Table 2. The algorithm for finding the pair of CBC indices with the most similarity.**

<table>
<thead>
<tr>
<th>Inputs</th>
<th>Indices as matrix $A_{m\times n}$ &amp; Array $B$ in size of $m$ ($B_i$ is the lower band of normal ranges for $i^{th}$ CBC index)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Output</td>
<td>$R_1, R_2$: the indices for the pair of rows with the most similarity;</td>
</tr>
</tbody>
</table>

1. $Max = 0$
2. **FOR** $i = 1$ TO $m-1$ **DO**
3. **FOR** $j = i+1$ TO $m$ **DO**
4. $COS =$ Calculate similarity between rows $i$ and $j$;
5. **IF** $COS > max$ **THEN**
6. $max = COS$;
7. $R_1 = i, R_2 = j$;
8. **END IF**
9. **END FOR**
10. **END FOR**

$m$ is the number of indices & $n$ is the number of samples;

1 calculate similarity regarding Eqs. (1,2):

As seen in Fig. 1, the most suitable indices of CBC are achieved with an iterative algorithm. To achieve the goal, first, the pair of indices with the most similarity (with
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respect to the abnormal pattern) must be found with the algorithm that is shown in Table 2. Then, one CBC index between that pair must be eliminated. To find the best choice for elimination a coefficient that is called coefficient of interference (COI) will be calculated with the algorithm that is shown in Table 3. The index with higher COI from the most similar pair must be eliminated.

**Table 3. The algorithm to calculate coefficient of interference (COI) for an index of the CBC tests.**

| Input: the values of an index of the collected CBC tests as a one dimensional array 'I' with the size of N |
| Output: the coefficient of interference (COI) for the input (I) |

1. Insert the values of 'I' that are related to IDA and β-TT subjects into the arrays A & B, respectively;
2. \( N_1 = \text{size of } (A) \) & \( N_2 = \text{size of } (B) \);
3. \( \text{Max}_1 = \text{max of } (A) \) & \( \text{Max}_2 = \text{max of } (B) \);
4. \( \text{Min}_1 = \text{min of } (A) \) & \( \text{Min}_2 = \text{min of } (B) \);
5. \( S = 0 \);
6. IF \( \text{Min}_1 < \text{Min}_2 \) THEN
7. FOR \( i = 1 \) TO \( N_1 \) DO
8. IF \( A(i) > \text{Min}_2 \) THEN
9. \( S = S + 1 \);
10. END IF
11. END FOR
12. ELSE
13. FOR \( i = 1 \) TO \( N_2 \) DO
14. IF \( B(i) < \text{Max}_1 \) THEN
15. \( S = S + 1 \);
16. END IF
17. END FOR
18. END IF
19. FOR \( i = 1 \) TO \( N_2 \) DO
20. IF \( B(i) > \text{Max}_1 \) THEN
21. \( S = S + 1 \);
22. END IF
23. END FOR
24. FOR \( i = 1 \) TO \( N_1 \) DO
25. IF \( A(i) < \text{Max}_2 \) THEN
26. \( S = S + 1 \);
27. END IF
28. END FOR
29. END IF
30. \( \text{COI} = S / N \);
31. END.

As seen in Table 2, to find the most similar pair of indices, a coefficient that is called coefficient of similarity (COS) must be calculated. The COS could be obtained by Eq. (1) as follows.

\[
\text{COS} = 1 - \frac{\sum_{i=1}^{n} |\text{LB}_i (\text{Row}_i^k) - \text{LB}_j (\text{Row}_j^k)|}{n}
\]  

(1)

Where \( n \) is the number of samples, \( \text{Row}_i^k \) is \( k \)'th value for \( i \)'th CBC index, and \( \text{LB}_i (r) \) is a function that denotes: whether \( r \) is an abnormal value or not, with respect to the lower band of normal ranges for \( i \)'th CBC index, and it can be obtained by Eq. (2) as follows.
After running the proposed method, four CBC indices have survived in the final ANN that are: Hb, RBC, HCT, and MCV. For implementation the ANN, the collected samples were randomly divided into two groups with 132 and 400 samples for training and test, respectively. The chosen training algorithm was Levenberg–Marquardt and the error function was sum square errors (SSE), which could be obtained by Eq. (3) as follows.

\[ SSE = \sum_{i=1}^{n} \sum_{j=1}^{m} (d_j^{(i)} - a_j^{(i)})^2 \]  

Where \( n \) and \( m \) are the number of training patterns and the number of network’s outputs, respectively. \( a_j^{(i)} \) denotes the \( j \)’th output of the network for \( i \)’th training pattern, and \( d_j^{(i)} \) represents its corresponding desired output.

**4.2. Training the employed ANN**

In this subsection the structure of ANN and the designing issues are explained. As previous discussed the methodology for choosing the inputs of ANN is performed by the PBIS algorithm. The algorithm includes several iterations. In each iteration of the algorithm, whole procedure of designing and the test of ANN will be performed.

As previous studies have proven, the most suitable neural network for the anemia classification problem is multi-layer perceptron (MLP) [22,25–28,34,35]. To choose the number of layers and neurons in each layer, we used trial and error method. Finally, the MLP with one hidden layer as shown in Fig. 2. Has been chosen as discriminator between IDA and β-TT.

As seen in Fig. 2, signed sigmoid is used as the activation function in the input layer and the hidden layer of MLP. The output layer takes a linear function as the activation function. Each MLP has trained several times. Fig. 3 shows the best obtained error diagram, which is SSE function, in the training of the designed MLP.
5. Results and Comparisons

For evaluation the proposed method, we compared the obtained results with the existing methods of discrimination IDA and β-TT. This section has been organized in two subsections. In the first one, some traditional methods, which are still used for the problem, have been introduced and the CBC samples were applied to them. In the second subsection several recent works have been compared with the proposed method.

5.1. Comparison with traditional methods

Several popular traditional methods, which is still using in discrimination IDA and β-TT, have been shown in Table 4. For better comparison, the samples that used in evaluation traditional methods were same as the test samples of our proposed method.

**Table 4. Mathematical formulas for discrimination between IDA and β-TT.**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Symbol</th>
<th>Year</th>
<th>Formula</th>
<th>IDA</th>
<th>β-TT</th>
</tr>
</thead>
<tbody>
<tr>
<td>England &amp; Fraser [2]</td>
<td>E&amp;FI</td>
<td>1973</td>
<td>MCV − RBC − 5×Hb − 3.4</td>
<td>≥0</td>
<td>&lt;0</td>
</tr>
<tr>
<td>Shine &amp; Lal [5]</td>
<td>S&amp;LI</td>
<td>1977</td>
<td>MCV × MCH × 0.01</td>
<td>≥1530</td>
<td>&lt;1530</td>
</tr>
<tr>
<td>Green &amp; King [6]</td>
<td>G&amp;KI</td>
<td>1989</td>
<td>MCV × RDW × Hb × 0.01</td>
<td>≥72</td>
<td>&lt;72</td>
</tr>
<tr>
<td>Sirdah et al. [12]</td>
<td>SI</td>
<td>2008</td>
<td>MCV − RBC − 3×Hb</td>
<td>≥27</td>
<td>&lt;27</td>
</tr>
<tr>
<td>Ehsani et al. [13]</td>
<td>EI</td>
<td>2009</td>
<td>MCV − 10×RBC</td>
<td>≥15</td>
<td>&lt;15</td>
</tr>
</tbody>
</table>

In all of the experiments six popular medical indices namely: sensitivity (SENS), specificity (SPEC), positive predictive value (PPV), negative predictive value (NPV), accuracy (ACC) and Youden’s index (YI), were used to comparison. The mentioned indices are obtained by Eqs. (4–9) as follows:

\[
SENS = \frac{TP}{TP + FN} \times 100
\]

(4)
\[
SPEC = \frac{TN}{TN + FP} \times 100
\]  
(5)

\[
PPV = \frac{TP}{TP + FP} \times 100
\]  
(6)

\[
NPV = \frac{TN}{TN + FN} \times 100
\]  
(7)

\[
ACC = \frac{TP + TN}{TP + TN + FP + FN} \times 100
\]  
(8)

\[
YI = SENS + SPEC - 100
\]  
(9)

Where TP, TN, FP and FN are true positive, true negative, false positive and false negative, respectively. Currently, several well-known traditional methods in the field of diagnosis anemia (Table 4) have been compared with the proposed method. Table 5 indicates that the proposed method gives significantly better results than traditional methods.

Table 5. Comparison between the proposed method and traditional methods for diagnosis IDA.

<table>
<thead>
<tr>
<th>Method</th>
<th>TP</th>
<th>TN</th>
<th>FP</th>
<th>FN</th>
<th>SENS (%)</th>
<th>SPEC (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>ACC (%)</th>
<th>YI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI [3]</td>
<td>196</td>
<td>173</td>
<td>13</td>
<td>18</td>
<td>91.6</td>
<td>93.0</td>
<td>93.8</td>
<td>90.6</td>
<td>92.2</td>
<td>84.6</td>
</tr>
<tr>
<td>E&amp;FI [2]</td>
<td>191</td>
<td>171</td>
<td>15</td>
<td>23</td>
<td>89.3</td>
<td>91.9</td>
<td>92.7</td>
<td>88.1</td>
<td>90.5</td>
<td>81.2</td>
</tr>
<tr>
<td>S&amp;BI [4]</td>
<td>197</td>
<td>174</td>
<td>12</td>
<td>17</td>
<td>92.1</td>
<td>93.5</td>
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<td>85.6</td>
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<td>S&amp;LI [5]</td>
<td>203</td>
<td>179</td>
<td>7</td>
<td>11</td>
<td>94.9</td>
<td>96.2</td>
<td>96.7</td>
<td>94.2</td>
<td>95.5</td>
<td>91.1</td>
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<td>SI [12]</td>
<td>192</td>
<td>171</td>
<td>15</td>
<td>22</td>
<td>89.7</td>
<td>91.9</td>
<td>92.8</td>
<td>88.6</td>
<td>90.7</td>
<td>81.6</td>
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<tr>
<td>EI [13]</td>
<td>195</td>
<td>174</td>
<td>12</td>
<td>19</td>
<td>91.1</td>
<td>93.5</td>
<td>94.2</td>
<td>90.2</td>
<td>92.2</td>
<td>84.6</td>
</tr>
<tr>
<td>G&amp;KI [6]</td>
<td>202</td>
<td>175</td>
<td>11</td>
<td>12</td>
<td>94.4</td>
<td>94.1</td>
<td>94.8</td>
<td>93.6</td>
<td>94.2</td>
<td>88.5</td>
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<tr>
<td><strong>Proposed method</strong></td>
<td><strong>209</strong></td>
<td><strong>183</strong></td>
<td><strong>3</strong></td>
<td><strong>5</strong></td>
<td><strong>97.7</strong></td>
<td><strong>98.4</strong></td>
<td><strong>98.6</strong></td>
<td><strong>97.3</strong></td>
<td><strong>98.0</strong></td>
<td><strong>96.1</strong></td>
</tr>
</tbody>
</table>

Total number of samples 400 (214 IDA & 186 β-TT).

The results that are shown in Table 5 give the performance indices of diagnosis IDA. Because, the number of β-TT subjects is depended on the number of IDA in Table 5, we can obtain the performance indices for β-TT diagnosis with Eqs. (10 – 15) as follows:

\[
\beta TT_{SENS} = IDA_{SPEC}
\]  
(10)

\[
\beta TT_{SPEC} = IDA_{SENS}
\]  
(11)

\[
\beta TT_{PPV} = IDA_{NPV}
\]  
(12)

\[
\beta TT_{NPV} = IDA_{PPV}
\]  
(13)

\[
\beta TT_{ACC} = IDA_{ACC}
\]  
(14)

\[
\beta TT_{YI} = IDA_{YI}
\]  
(15)

5.2. More comparisons

The second part of the tests is aimed to compare the performance of the proposed method with some recent works. As can be observed in Table 6, the proposed method is more accurate than the other works in this area.
Table 6. Comparison between the proposed method and the other works.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Method</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azarkhish et al.</td>
<td>2012</td>
<td>ANFIS</td>
<td>87.1</td>
<td>95.6</td>
<td>90.7</td>
</tr>
<tr>
<td>Azarkhish et al.</td>
<td>2012</td>
<td>ANN</td>
<td>96.8</td>
<td>95.6</td>
<td>96.3</td>
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<tr>
<td>Amendolia et al.</td>
<td>2002</td>
<td>MLP</td>
<td>95.0</td>
<td>92.0</td>
<td>93.5</td>
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<tr>
<td>Amendolia et al.</td>
<td>2003</td>
<td>SVM</td>
<td>95.0</td>
<td>83.0</td>
<td>89.0</td>
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<tr>
<td>Amendolia et al.</td>
<td>2003</td>
<td>KNN</td>
<td>77.0</td>
<td>93.0</td>
<td>85.0</td>
</tr>
<tr>
<td>Masala et. al.</td>
<td>2013</td>
<td>RBF</td>
<td>93.0</td>
<td>91.0</td>
<td>-----</td>
</tr>
<tr>
<td>Masala et. al.</td>
<td>2013</td>
<td>PNN</td>
<td>89.0</td>
<td>73.0</td>
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</tr>
<tr>
<td>Masala et. al.</td>
<td>2013</td>
<td>KNN</td>
<td>80.0</td>
<td>91.0</td>
<td>-----</td>
</tr>
<tr>
<td>Bordbar et al.</td>
<td>2015</td>
<td>Math</td>
<td>84.7</td>
<td>87.9</td>
<td>94.3</td>
</tr>
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<td>Proposed method</td>
<td></td>
<td>PBIS-ANN*</td>
<td>97.7</td>
<td>98.4</td>
<td>99.5</td>
</tr>
</tbody>
</table>

*Adaptive neuro-fuzzy inference system; 1 artificial neural network; 2 multi-layer perceptron; 3 support vector machine; 4 K-nearest neighbor; 5 Radial Basis Function; 6 Probabilistic Neural Network; 7 mathematical formula; 8 pattern-based input selection artificial neural network;

6. Conclusion

In this study, based entirely on fast and inexpensive blood test, we developed an accurate medical diagnostic system for discrimination between iron deficiency anemia (IDA) and β-thalassemia trait (β-TT). The model that is called pattern-based input selection artificial neural network (PBIS-ANN) has been compared with traditional methods of discrimination diagnosis IDA and β-TT and the recently published works such as ANFIS, ANN, MLP, SVM, and KNN. The results indicate that the proposed method significantly outperforms the mentioned methods. The proposed method stems from a combination of human expert decision making and ANN. Before running the proposed method the patterns of abnormal values in each input must be stated by an expert human, on a set of inputs. The method could be employed in many medical problems in which the medical indices are used for diagnosis a disease. Since nationality and the ages of population, which is considered in the tests, is severely limited. Hence, it is suggested that a wider population would be considered for the future works.

References


