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Classification of neonatal jaundice in mobile application with noninvasive image processing methods

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Abstract: This study aims a mobile support system to aid health care professionals in hospitals or in regions far away from hospitals to utilize noninvasive image processing methods for classification of neonatal jaundice. A considerably low processing cost is aimed to be attained by developing an algorithm that could work on a mobile device with low-end camera and processor capabilities within this study. In this context, an algorithm with low cost is developed performing detection of most meaningful parameters by a multiple input single output regression model and correlation.The advantage of the proposed method is that it can estimate bilirubin with the help of a simple regression curve. The reason for its low cost is that the noninvasive jaundice prediction is performed with a simple regression curve instead of many mathematical operations in morphological image processing methods. The study was performed on a total of 196 subjects, 61 of which were classified as severe jaundice while 95 of the newborns were mild jaundice cases, and other 40 cases are used for tests. As a result of this work, the two-group classification accuracy of the developed algorithm is observed to be 92.5% for the 40 subject test group.

Key words: Neonatal jaundice, Indirect hyperbilirubinemia, multiple regression analysis, image interpretation

1. Introduction

Neonatal jaundice is an illness known for a long time. There are some treatment methods available today. Phototherapy comes first among these. Phototherapy is the most common therapeutic intervention used for the treatment of hyperbilirubinemia [1]. The first information regarding jaundice in newborn babies were found in Metlinger's book, titled "Ein Regiment der Kinder" in 1473 [2]. Neonatal jaundice or neonatal hyperbilirubinemia can be observed clearly when the bilirubin level in the newborn's blood exceeds 5 mg/dL (85 mmol/l) [3]. In the first week of life, bilirubin level in every newborn increases. According to global census, jaundice is observed in almost 60% of healthy full-term newborns while it is observed in 80% of the premature newborns [4]. Jaundice is observed clinically in at least two thirds of newborns [5]. High bilirubin levels that are not detected or treated on time may cause to severe neurological sequels [5]. Today, it is possible to detect the jaundiced cases by transcutaneous bilirubinometry or observing the baby on a well-lit environment by the doctor. The main aim of this study is to create a decision support system that could detect the neonatal jaundice starting from the birth of the baby and aid the medical professionals in early detection and taking necessary

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action. Topaloglu and Sur created a decision support system to detect jaundice and reduce misdiagnosis in their study titled “Decision Tree application to Reduce Misdiagnosis in Jaundice Symptoms” [6]. The study was carried out to aid the medical practitioners in diagnosing patients with jaundice. In their study, data of 300 patients diagnosed with jaundice were used. Moreover, the data of patients diagnosed with jaundice earlier were collected in a database and organized. Using these organized data, the training dataset is formed. Later, in their comparative algorithms, decision tree models were created using data mining methods. The decision trees were formed using C5.0 and J48 algorithms. The aim of the decision trees were to reach 16 illnesses using 21 features. Here, diagnosing the illness with three different points of view was the main objective instead of creating a decision support system with a single decision tree. Relevant pruning processes were carried out for the decision trees created by algorithms. A total of 16 different illnesses were diagnosed with no error with the most robust pruning method. In their study titled “Neonatal Jaundice Detection System”, Aydın et al. [7] prepared a patient group consisting of babies with jaundice and a control group consisting of healthy babies, each containing 40 newborns within 24–48 h of birth. Advanced image processing techniques were used on images captured with a standard smartphone and a color calibration card. The color calibration card, in the method of Aydın et al., bilirubin estimation was performed with color charts, morphological image processing methods and decision mechanisms.The success rate of this study is 85%. Mansor et al. [11] predicted the crystalline prediction approach without using a chart. On the other hand, Olusanya et al. [13] aimed to detect newborn jaundice using a color chart. Segmentation, pixel similarity, and white balancing methods were used as image processing techniques, and the important information of pixels were obtained completely with RGB (red-green-blue) values. The next step consisted of the feature extraction stage, in which color mapping conversions and feature calculation were employed to carry out comparisons between color change values and specially designed 8-color calibration card on RGB plane. Finally, at the bilirubin level estimation stage, K-nearest neighborhood and support vector regression machine learning progressions obtained by feature extraction were used. According to the comparison made with control group, the success rate of the system is 85% based on the compliance rate of the proposed method's results with the results from the standard blood test. Arulmozhi and Ezhilarasi discovered that early detection of neonatal jaundice is possible using maximal information compression index and Kernel support vector machine [8]. Moreover, neonatal jaundice detection using noninvasive image processing methods were aimed by Greef et al. [9]; however, their classification accuracy remained at 76%. Polley et al. [10] carried out studies regarding jaundice detection in adults by checking the eye. Mansor et al. [11] analyzed features such as energy and entropy in images of newborn babies with and without jaundice to detect neonatal jaundice. Similar to these studies in recent years, Sammir et al. [12] aimed detection of neonatal jaundice by image processing. Moreover, Olunsaya et al. [13] carried out a classification study with a bicolor time sheet. Taylor et al.'s [14] bilicam smartphone application provided accurate estimates of total serum bilirubin (TSB) values, demonstrating that an inexpensive technology that uses common smartphones could be used to effectively scan newborns for jaundice. Swarna et al. [15] smart phone applications can be used as an alternative to measure bilirubin. "Biliscan" for scanning neonatal jaundice was reviewed in detail. Subramanian et al.'s [16] work is aimed at developing a noninvasive bilirubin meter using a smartphone to capture colour images, which are then processed and analysed to obtain an estimate of the bilirubin count using an estimation algorithm like artificial neural networks and can be further used to determine the jaundice level in the infant. This can allow continuous monitoring of the jaundice during the phototherapy sessions without the need for multiple pricks and blood tests for assessment. Padidar et al.'s [17] smartphone-based estimation of bilirubin levels had a sensitivity of 68% and specificity of 92.3% for estimating the bilirubin levels of less than

10 mg/dL and sensitivity of 82.1% and specificity of 100% for estimating the bilirubin levels of less than 15 mg/dL. Their application-based estimation of bilirubin levels had the correlation of 0.479 with the total serum bilirubin values. Mannino et al. [18] introduced a paradigm of completely noninvasive, on-demand diagnostics that may replace common blood-based laboratory tests using only a smartphone app and photos.

In this study, classification is carried out by separating the neonatal jaundice cases into two groups, namely the control group, patients of which have a bilirubin level between 0 and 9.9 mg/dL and the mild jaundice group with bilirubin levels between 10 and 30 mg/dL. In the step following this classification, 30 points from the image of the baby, 5 from each of head, arms, feet, and body where symptoms of jaundice is more clear, were chosen using multiple input regression, and their RGB values are used as program input. Moreover, in order to alleviate the effect of ambient conditions on system operation, RGB values of 8 different points, one from each color region, were used as program input in order to carry out multiple input linear regression with a total of 38 points' RGB values. Linear regression is a linear approach to model the relationship between the dependent variable and one or more independent variables [19]. The process involving multiple descriptive variables is called linear regression [20]. This term is different than multivariable linear regression, in which multiple dependent variables are estimated instead of a single scalar variable [21].

The novelty of this study is revealed by the choice of a structure with a considerably low process load that could work even in the simplest android phone with image capturing capability. In this context, the advantages of the study can be given as follows: choice of multiple regression, employing this method in detecting neonatal jaundice, rapid and accurate operation of the system in Android compatible mobile applications, and a high accuracy even with a relatively low dataset size. 92.5% success was achieved with the two-class classifier with the mathematical formulation obtained by multiple regression analysis on the images of the baby with the mobile application, when compared to the results obtained by the blood test carried out on the baby.

The contribution of this study to literature is the development of a decision support system to aid doctors in a practical manner on mobile platform with new subjects. The study proposed an easy-to-use application on Android mobile platforms, employing multiple regression analysis to yield a rapid diagnosis algorithm.In the materials and methods Section, the materials used and the bilirubin estimation algorithm are presented. The results and detailed discussion of these results are provided in Results and Discussion part.

2. Materials and methods

2.1. Data acqusition and user interface

In this study, images and information, such as age and sex, belonging to 196 newborn babies and separated as control and case groups, are obtained by Prof. Dr. Mustafa Aydın from Fırat University, Faculty of Medicine between March 2018 and February 2020. The images of newborn babies in the incubator are obtained by the medical expert using an android compatible 8 megapixel camera mobile phone or tablet computer as seen in Figure 1.

Mobile software is designed to be consisting of four interfaces, as seen in Figure 2. These interfaces are sign in/up screen, main screen in which earlier logs are held and new images can be added, the screen at which data can be chosen over the image of the baby, and the screen to which baby information will be entered. After the information about the baby is entered, the estimated bilirubin value is displayed on the screen.

After user login, the application is launched with the screen displaying earlier logs as can be seen on Figure 3a. New measurement adding screen, in Figure 3b, can be launched for bilirubin measurement. Here, for user convenience, either previously or newly captured neonatal jaundice images can be used. After the image

Figure 1. Neonatal Jaundice Images

selection, the current neonatal image shown in Figure 3c is obtained, and the selection is confirmed by tapping on the confirmation button at the upper right corner of the screen. In order to make the system invariant to the differences in ambient lighting, resolution or color differences due to the camera and so on, the calibration card consisting of 8 colors seen on Figure 3c is used.

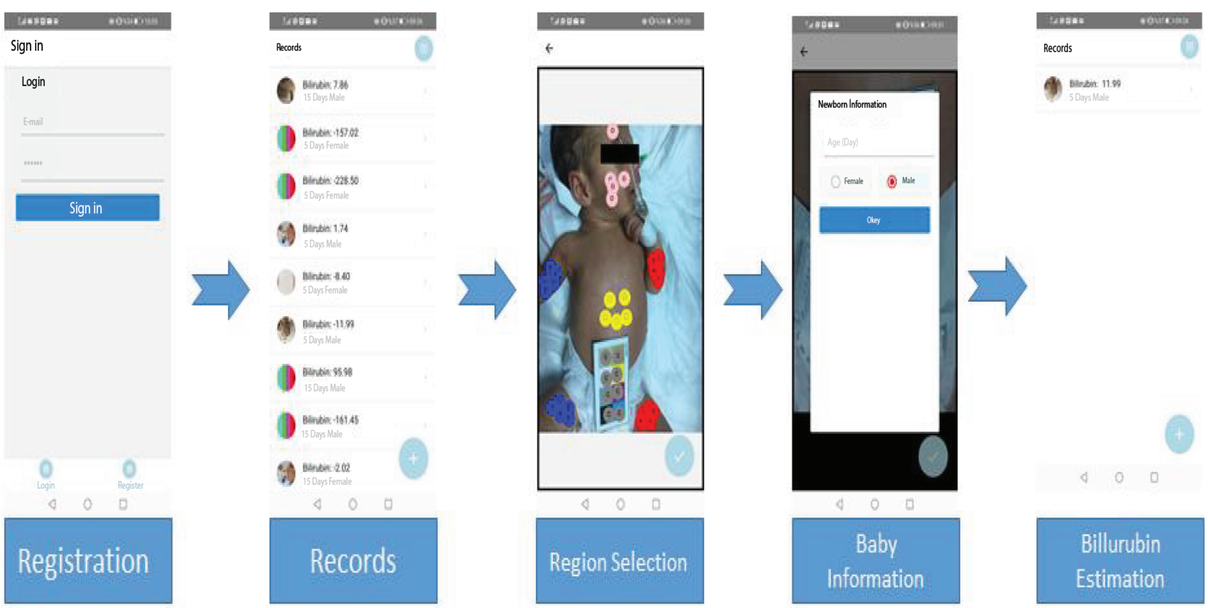

Figure 2. Screenshots of Mobile Bilirubin Estimation Application Stages

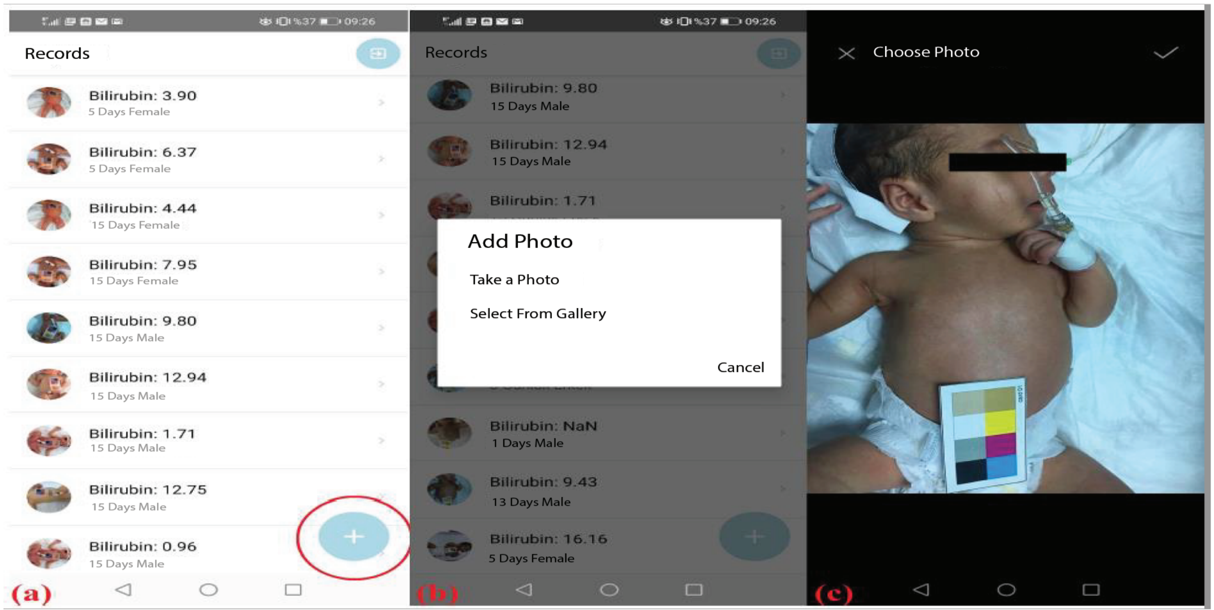

Figure 3. Mobile application log and image selection screenshots.**a.**Log screen. **b.** New log creation screen. **c.** Neonatal image addition screen.

In order to perform classification, the medical expert marks 5 points from each of the body parts: head, arms, middle body and feet, making a total of 30 points. One color from the eight colors on the chart and points to prevent the effect of lighting are also obtained as can be seen in Figure 4.

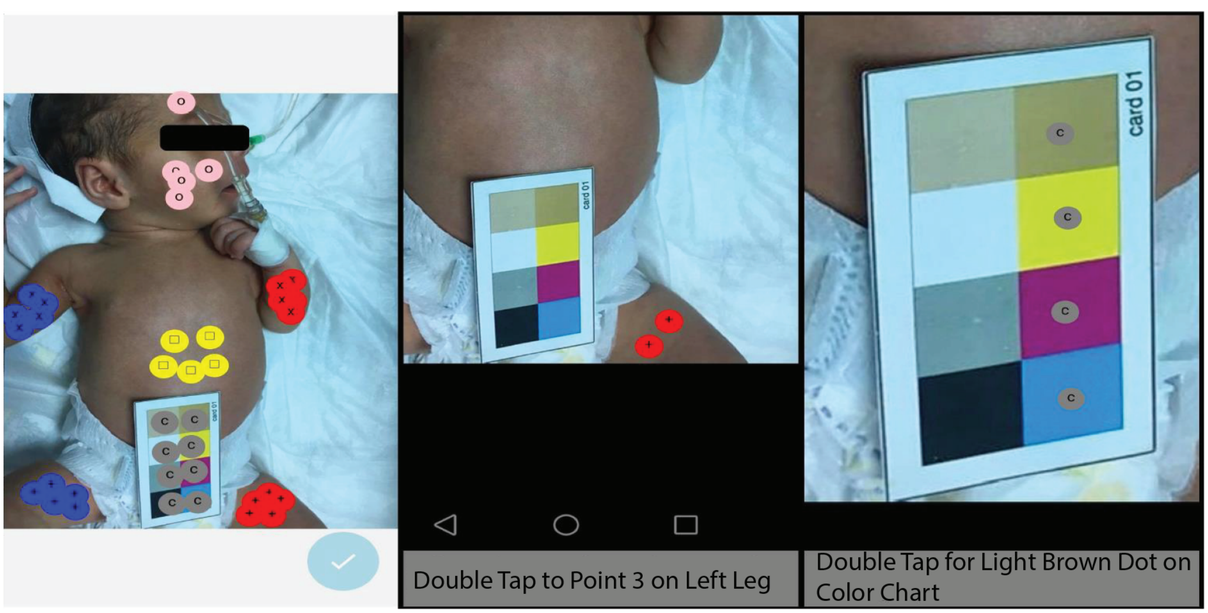

Figure 4. Bilirubin estimation screenshot of the mobile application.**a.** Data selection screen **b.** Region Selection screen. **c.** Chart color selection screen.

The software containing the mobile interface and estimation module is developed using "Native React" which is an open source mobile software developed by Facebook and provided under MIT licence. While "Native

React" platform could be used to develop applications for Android, iOS, Web or UWP(Universal Windows Platforms, in this study, Android platform was chosen. The interface development was carried out with Native React V0.61.

In this study, the training set consists of the data from 95 babies, bilirubin levels of which are below 10 mg/dL, and 61 babies, bilirubin levels of which are above 10mg/dL. These data are obtained by Prof. Dr. Mustafa Aydın from Fırat University Faculty of Medicine Department of Child Health and Diseases with necessary permissions, and ethical committee approval is obtained. The images of the babies were separated into two classes depending on their bilirubin levels: one class with bilirubin levels between 10–30 mg/dL and the other class with bilirubin levels between 0–10 mg/dL.

The color charts placed on the baby during image acquisition consist of black, gray, white, light brown, brown, yellow, pink, and blue colors in order to alleviate the effect of lighting during image analysis. The chart was designed to contain both primary and secondary colors and to be easily placed on the baby.The 38 points on baby (30 from the different regions of baby's body and 8 from the chart) are chosen by the medical expert. After that, regression line is formed by inputting the color values obtained as well as the sex and age of the baby (in hours). Multiple input regression line is chosen as the regression method. The color data is obtained by using RGB color space.

The application developed with this study is designed to have a simple algorithm that could work even on a very simple mobile phone. In this study, all of the data entries are performed via the Android based mobile application, only the user log on/in tasks are designed to be defined on the server.

2.2. Method

It is aimed with this study to classify the newborn babies in hospital into two groups according to their bilirubin levels: $<$10 mg/dL and $\geq$10mg/dL. Bilirubin estimation is provided with the relation between the variables by performing multiple linear regression analysis with images and data obtained. The main objective in realizing multiple input linear regression is to achieve a rapid and accurate operation in mobile environment.

Early literature studies revealed that neonatal jaundice starts to be visible from the head region [22, 23]. With this information, a structure that is independent of the lighting level of the medium is designed to be used with the regional data obtained from the baby.

The first stage of the bilirubin estimation module consists of determination of 5 points each from the most prominent parts of the baby, which are face, arms, feet and middle body. Secondly, one pixel value is obtained from each of the 8 colors on the color calibration chart placed on the baby. By averaging the colors obtained from each region of the baby's body, RGB median values are calculated for each region. Bilirubin level estimation is obtained by performing multiple input linear regression method using RGB and chart values obtained from 156 babies within the scope of this work. The decision support system is created to aid the medical expert using this linear equation as can be seen in Figure 5.

In this study, the main input of the system is set to be the image data obtained by photographing the babies from the Neonatal Service of Fırat University Faculty of Medicine Department of Child Health and Diseases department on a flat and white surface, with the prepared color charts placed on their body. The training set bilirubin values were obtained from the blood tests from the babies.

RGB values were obtained from all 156 images, 5 points from each of the head, arms, feet, and middle body parts, making a total of 30 points for each image. In order to analyze the medium in which the baby is placed, RGB values are also obtained from the color chart, one from each of the 8 colors, constituting 8 points

Figure 5. Bilirubin estimation stages.

per chart. The regression line is generated using the RGB values of 38 points and bilirubin value, in mg/dL, obtained from blood test.The value of bilirubin that causes jaundice in newborn babies can be identified by the TSB (total serum bilirubin) and TCB (transcutaneous bilirubin) method. TSB value is determined by blood analysis results in terms of mg/dL in the blood. Multiple linear regression is a mathematical tool that measures the relationship between a dependent variable and one or more independent variables [24]. In the problems with multiple dependent variables, F statistic multiple regression will be used to compare the following hypothesis:

$$H_0 : y = b_0 \qquad (1)$$
$$H_1 : y = b_0 + \sum_{i=1}^{N} b_i . x_i$$

Each coefficient is checked according to the hypothesis provided in (2) to choose the independent variables.

$$H_0 : b_i = 0 \qquad (2)$$
$$H_1 : b_i \neq 0$$

It is assumed that there is a linear relationship between the variables in model selection and output value, and each variable can be controlled according to the regression model by Shapiro–Wilk test [25]. In this test model, each variable's weight is analyzed depending on the regression model. If the test result is close to zero, the given variable is assumed not to have an effect on the output and, therefore, removed from the equation system. By this way, it is possible to reduce the workload of the system by omitting the parameters that have little or no effect on the system. The multiple linear regression equation obtained with the study is given in (3).

$$y_{est} = 12.048 - 0.272^{*}CardW_G + 0.259^{*}CardW_B + 0.314^{*}Arm_R \qquad (3)$$
$$-0.413^{*}Arm_G - 0.326^{*}Chest_R + 0.767^{*}Chest_G - 0.401^{*}Chest_B$$

Here Yest, CardWG, CardWB, ArmR, ArmG, ChestR, ChestG and ChestB stand for estimated bilirubin level, the green component of the white color on chart, blue component of the white color on chart, mean value of red on arms, mean value of green on arms, mean value of red component on chest, mean value of green component on chest and mean value of blue component on chest, respectively.

3. Results

In this study, first of all, 30 points are taken on the image of the newborn baby, 5 points from each of the head, arms, feets, and trunk. Along with these 30 points, 8 points were selected (1 point from each of the 8 different colors in the color chart), and they were created by feeding the classification algorithms as input. The MLR (multiple linear regression) equation obtained from the bilirubin estimation module is tested using 40 images that were not used in the estimation module, consisting of 20 cases with bilirubin levels less than 10 mg/dL and 20 cases with bilirubin levels greater than 10 mg/dL. In the test stage, the data were used in the multiple regression equation, and the outputs are classified into two groups. Table 1 provides a comparison of the obtained model. When the test data is analyzed, it is seen that 18 samples out of 20 are classified correctly for the $<$10mg/dL set, while 19 of the 20 samples are classified correctly for the $\geq$10mg/dL set.

Table 1. TSB (total serum bilirubin) and estimated values of the test data.

Sample No:	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
TSB value$_{(mg/dL)}$:	12.2	6.4	7.6	3	0.1	11	4	7.2	3.9	8.7	3.4	7.5	0.2	8.2	19.8	12.5	8.5	5	13.5	11
MLR value$_{(mg/dL)}$:	11.1	7.1	7.1	3.7	1.7	11.6	4.5	7.3	4.5	9.7	3.5	7.4	1.1	8.2	21.9	14.8	8.8	5.2	14.5	12
Sample no:	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
TSB Value$_{(mg/dL)}$:	8.4	12.7	2.4	11	18	8	21	11.2	27	7.3	14.6	7.4	15.6	8	10.8	11.3	13	12	10.8	30
MLR value$_{(mg/dL)}$:	8.1	13.2	2.3	9.7	17.3	8.7	26.1	13.9	34	7.6	17.1	7.0	15.7	8.5	11.3	12.6	14.1	13	9.4	37

As a result of these studies, it is observed that total true negative and false positive rate is 7.5%. The bilirubin levels of the training set in the infants and the estimated value, error, and error percentage are given in Table 2.

Table 2. Bilirubin level estimation and error rates for training set.

Baby	Bilirubin	Estimated error	Error	Percentage of error	Baby	Bilirubin	Estimated error	Error	Percentage of error
1	3.4	2.91	0.49	14.41	21	5.4	3.26	2.14	39.63
2	4.1	1.23	2.87	70	22	4	2.48	1.52	38
3	2.8	0	2.8	100	23	4.1	4.08	0.02	0.49
4	2.9	1.98	0.92	31.72	24	4.3	2.19	2.11	49.07
5	5.1	2.44	2.66	52.16	25	4.5	1.7	2.8	62.22
6	3.1	0.78	2.32	74.84	26	10.2	6.6	3.6	35.29
7	3.4	2.66	0.74	21.76	27	13.6	8.92	4.68	34.41
8	3.6	2.54	1.06	29.44	28	15	13.55	1.45	9.67
9	3.9	2.26	1.64	42.05	29	24	19.18	4.82	20.08
10	7.1	5.2	1.9	26.76	30	13.6	9.88	3.72	27.35
11	7.3	5.64	1.66	22.74	31	14	7.5	6.5	46.43
12	11.1	8.92	2.18	19.64	32	9.5	8.39	1.11	11.68
13	2.8	0.55	2.25	80.36	33	20	16.2	3.8	19
14	3.2	1.4	1.8	56.25	34	29	22.85	6.15	21.21
15	3	1.22	1.78	59.33	35	17.8	16.77	1.03	5.79
16	3.2	2.56	0.64	20	36	4.7	1.2	3.5	74.47
17	6.2	3.35	2.85	45.97	37	9.2	7.91	1.29	14.02
18	6.4	5.88	0.52	8.13	38	3	1.11	1.89	63
19	6.3	4.45	1.85	29.37	39	4	2.88	1.12	28
20	5.2	3.76	1.44	27.69	40	10	6.5	3.5	35

Test samples values TSB with the data obtained, in the light neonatal jaundice data, estimated bilirubin value obtained shows the values of bilirubin obtained by image processing in the presented methodology. Matlab 2018b (MathWorks, Inc., Natick, MA, USA) was used in the analyzes.

4. Discussion

In this study, the success rate of the system is evaluated by comparing the bilirubin levels obtained from blood tests of the babies with the estimated bilirubin levels from the images provided to the mobile application. As a result of these analyzes, it is seen that the system is able to attain a classification accuracy of 92.5% with the test data used in the mobile application to detect neonatal jaundice. This study is believed to aid the medical professionals to diagnose patients easily and rapidly in the future as well as contributing to the literature considerably thanks to the speed, practicality, and noninvasive operation of the proposed system. A total of 196 newborn's data, data of 156 newborn babies for training set and 40 for test set, are obtained anonymously from Neonatal Intensive Care Unit (NICU) with the permission from ethical committee. Linear regression is employed in this study due to its reliability and simplicity, allowing it to work on even a very basic phone. Effective parameters are determined using type F statistical analysis during multiple linear regression bilirubin estimation work and, therefore, the number of parameters, which was initially considerably large, is reduced. When the resulting equation is analyzed, it is seen that jaundice detection is possible by considering the data only from the white component of the white region of the color chart, arm, and chest regions. 20 of the 40 test data for the verification stage of the study have bilirubin levels less than 10 mg/dL. Among these, the 10th patient is observed to be misclassified. Patient numbers 24 and 39 from the 20-patient group with bilirubin levels higher than 10 mg/dL are also misclassified as they were classified as "mild/no jaundice" instead of "severe jaundice". When the misclassifications are evaluated, it is noted that misclassification is likely to occur for patients having bilirubin levels that are on the vicinity of 10 mg/dL threshold. Moreover, the error rate is observed to be higher for high bilirubin estimation model. This can be explained by the fact that there are relatively fewer examples with high bilirubin levels in the dataset.

4.1. Conclusion

With this study, it is revealed that neonatal jaundice can be estimated by multiple linear regression method. In this study, a noninvasive mobile decision support system that could assist health care professionals was developed, and its results were evaluated. When the results of this work are analyzed, it is demonstrated that neonatal jaundice can be detected by optical control systems.

Mobile device based optical control systems should be used for medical decision support systems for doctors. One of the applications presented in this study is believed to enlighten future researches for medical applications.

Advanced methods that can perform calculations in workstation with higher accuracy are believed to be attainable considering the present state of the study. Furthermore, deep learning based classification could help better results for server based application.

4.2. Conflicts of interests

The authors declare that they have no conflicts of interests.

4.3. Authors' contributions

Mustafa AYDIN and Atika ÇAĞLAR performed the gathering the newborn data in the hospital, discussed & reported the results, and drafted the manuscript. Fırat HARDALAÇ created the study hypothesis with Uğurhan KUTBAY and helped to draft the manuscript. Uğurhan KUTBAY, Kubilay AYTURAN, and Anıl AKYEL participated in the alignment sequence and evaluated the algorithms. Bo HAi and Fatih MERT supervised the mobile application interface for a user-friendly design. All authors read and approved the final manuscript.

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