Review Article

A Non-invasive Methods for Neonatal Jaundice Detection and Monitoring to Assess Bilirubin Level: A Review

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Abstract: Neonatal jaundice is a frequent cause of substantial illness and mortality in newborns. The newborn infant's skin, eyes, and other tissues turn yellow because bilirubin contains a pigment or coloring. Jaundice that manifests in the first few days is highly dangerous and typically needs to be treated right away. It is typically "physiologic" when jaundice emerges on the second or third day. Hyperbilirubinemia refers to an abnormally high bilirubin level in the blood. During the decomposition of red blood cells, bilirubin is formed. Bilirubin can build up in the blood, bodily fluids, and other tissues of newborn babies because they are not naturally able to expel it. Kernicterus or irreversible brain damage can result from untreated jaundice if the abnormally high levels of bilirubin are not controlled. In cases of neonatal jaundice, there is currently a variety of estimating methods for measuring bilirubin levels. The goal of this research is to provide a thorough evaluation of various non-invasive frameworks for the identification of newborn jaundice. For this review article, a critical analysis has done by using 51 articles from 2009 to 2022 where all articles are based on the detection of neonatal jaundice. This literary work on non-invasive methods and neonatal jaundice results appear to be an understanding of the avant-garde procedures created and used in this domain. The review also compares and contrasts different non-invasive strategies for predicting an infant's state of serum bilirubin based on different data such as social media data, and clinical data. At last, the open issues and future challenges of using a non-invasive method to better understand as well as diagnose the neonatal jaundice state of any individual were discussed. From the literature study, usually apparent that the utilization of non-invasive methods in neonatal jaundice has yielded noteworthy fulfillment within the regions of diagnosis, support, research, and clinical governance.

Keywords: ***Bilirubin; Hyperbilirubinemia; Kernicterus; Neonatal Jaundice; Newborn***

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1. Introduction

About 70–80% of all newborn babies are affected by the disease, as evidenced by jaundice, and this is a significant factor in hospital admissions. Mothers typically are the first to notice jaundice in the great majority of affected newborns, especially outside of hospitals [1-2]. Rapid diversity between the mainstream of babies with jaundice who have no primary disease and those with pathological reasons is important to detect the underlying disease and prevent bilirubin encephalopathy and kernicterus [3]. Experts urge doctors not to depend on visual examination alone to assess the bilirubin concentration in an infant with jaundice [4]. Clinical review can distinguish jaundice, but not the bilirubin level itself. The other main suggestions, based on detailed examination and an orderly blend of accessible proof, incorporate outwardly looking at all babies for jaundice at each opportunity, particularly within the beginning of 72 hrs. Isolated data is given for guardians, proposing that they examine their baby carefully, seeking for yellowing of the whites of the eyes and gums, as well as of the skin, and to test for dark urine and pale stools. On the off chance that jaundice is suspected or self-evident to guardians or wellbeing experts, the

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bilirubin concentration ought to be measured. Lack of recognition of jaundice and delayed introduction to clinic visits are the major causes of the burden of bilirubin encephalopathy, high rates of unnecessary exchange transfusions, and associated negative outcomes [5].

To successfully implement community-based mediations needed to lessen the burden of extreme neonatal jaundice, maternal empowerment and education are crucial. This allows for the timely detection of jaundice. However, separating and coordinating the skin color of an infant with a few near shades of yellow may be troublesome for untrained spectators, counting mothers and caregivers beneath variable lighting conditions [6]. Once jaundice is distinguished, newborn children may be treated using daylight, phototherapy, or, in serious cases, trade transfusion. The conclusion of jaundice is time critical and the more prominent the chance of long-term neurological inability. In expansion, jaundice may be characteristic of basic sicknesses that require pressing, since the longer hyperbilirubinemia remains untreated [7]. Jaundice of the sacred is an uncommon malady that has a small impact on not the well-being but moreover the life span of the persistent it features a great premonition. Chronic hepatitis, in specific viral hepatitis, may be an ordinary clutter that is clinical, a few patients displayed few or need indications, and liver work tests moreover may be ordinary [8].

In newborn infants, a bilirubin level over 85 umol/l (5 mg/dL) indicates clinical jaundice, whereas, in adults, a level of 34 umol/l (2 mg/dL) would indicate icteric. Jaundice in newborn infants is detected by lightening the skin with computed weight to reveal the skin and subcutaneous tissue beneath the surface. Neonatal newborns with jaundice exhibit a clear icteric sclera, yellowing of the forehead and chest yellowing. The dermal icterus first becomes apparent in the newborn baby's face, then spreads caudally to the trunk and then to the limits as the bilirubin level rises [9]. Kawano *et al.* [10] publicized an image-processing-based non-invasive procedure for recognizing neonatal jaundice. The facial locale was removed using normalized Red, Green, Blue (RGB) color and restrained regard, taken after by the eye layout and mouth layout. Two picture highlights were associated with analyzing jaundice: the essential was an estimation of the typical regard to skin tone information. The next step was to examine the skin's hue, which in normal circumstances remains consistent but changes with jaundice. To determine whether or not skin color was disseminated, the eigenvalues of the variance-covariance configuration were determined. Although the proposed method is vital and can be enhanced to induce predominant comes almost, it was unable to eliminate skin extend because eyebrows and eyes could not be ordered using an eye chart, resulting in failure cases of comes almost.

Infant newborn children may create kernicterus when the abundance of bilirubin navigates from the circulation system to the brain tissue, which can cause passing, whereas survivors will endure cerebral paralysis and high recurrence of hearing misfortune [11]. The bilirubin of the newborn is handled by the mother's blood and liver structure while the baby is in the womb, but after delivery, the baby's liver prepares. Frequently, newborns experience problems due to their underdeveloped livers, which results in a dangerous accumulation of bilirubin [12]. A yellowish, water-soluble tetrapyrrole pigment called bilirubin can be seen in the blood. Chemicals in the liver must have glucuronidated bilirubin before it can be properly excreted [13]. In 1847, Jaques Hervieux discovered brain jaundice in 31 dissections of ungrateful newborn babies. In 1875, during an autopsy of a jaundiced term child, Johannes Orth noted an unusual yellowing of the basal ganglia, third ventricle divider, hippocampus, and central parts of the cerebellum. Christian Schmorl, after presenting the results of approximately 120 post-mortem examinations of jaundiced newborn children to the German Society of Pathology in 1903, was the first to adopt the term kernicterus (jaundice of the basal ganglia) [14]. In typical situations, the visual judgment of jaundice and the actual bilirubin concentration compare modestly, but the correlation is poor in late preterm infants. The concentration of chromophores such as melanin, collagen, hemoglobin, and bilirubin determines skin color, as is widely known [15].

The majority of the cutting-edge non-invasive techniques that have been suggested in the literature are surveyed in this research. These are the main contributions of this paper:

1. Review of the available jaundice detection techniques.
2. Compare the surveyed strategies so that they can be utilized as a benchmark for future work.

The remaining of this paper is arranged as follows: Section 2 shows literature work, Section 3 deals with the analysis of the previous work followed by the discussion in Section 4, and Section 5 draws the most conclusions from this paper.

2. An Overview of the Various Non-Invasive Techniques Used for Neonatal Jaundice Detection

Neonatal jaundice or neonatal icterus could be a yellowish coloring of the whites of the eyes and skin in infants due to elevated bilirubin levels combining excess lethargy or deficiency of boosting. Neonatal jaundice is seen when the bilirubin level surpasses 5 mg/dl (85 mmol/l) in modern infant blood. Bilirubin level rises in each infant within the, to begin with, a week of life. Beneath the world benchmarks, jaundice is recognized in nearly 60% of the sound full-term babies and 80% of the preterm babies [1]. An evaluated 84% of neonatal infants create jaundice is one of the most prevalent physiological disorders. The level of bilirubin in sound babies is typical. At any rate, on the off chance that not treated, the most extreme levels may be lethal and irreversible brain harm [3]. The standard gold strategy for measuring the bilirubin level is through a blood test, which recommends the collection of add up to total serum bilirubin (TSB). It isn't great practice or covetable to require blood on a regular premise from all newborn children for the primary weeks of their life. Since the method is time devouring, costly, agonizing for infants, and egregious for modern parents. A newborn child is in this manner screened for jaundice by neonatal medical attendants and birthing assistants, who take into consideration the clear degree of yellow discoloration and components such as gestational age and nourishing conduct [4].

Visual jaundice in neonatal babies, over 80% create within them, to begin with, a few days of life. Customary appraisal to identify infants with severe hyperbilirubinemia could be a central center of care amid birth hospitalization. As of late infant nurseries over the world detailed that all neonates are screened for all intents and purposes with either transcutaneous bilirubin (TcB) or add up to serum bilirubin (TSB) estimation sometime recently released by the clinic. Shockingly, bilirubin levels regularly crest in neonates in the fourth days of life, which is well after most babies are released. Precise evaluation of the seriousness of jaundice in outpatient newborns is risky. TSB estimation is more troublesome in newborns after release than amid the birth hospitalization. The tall fetched of TcB meters limits their broad utilization in outpatient settings, even though TcB estimation may be a practical alternative. Given these impediments, the outpatient evaluation of jaundice in neonates is mostly done by a visual review of an infant's skin to survey yellowness. There's plentiful proof that indeed experienced wellbeing care suppliers cannot precisely appraise the seriousness of jaundice [6].

Extreme hyperbilirubinemia, as defined by a serum bilirubin (TSB) level of 20 mg/dL, affects 1.1 million babies every year, whereas noteworthy hyperbilirubinemia (TSB 25 mg/dL) affects 481,000 newborns per year. In high-income nations, kernicterus has been abolished due to greater availability of early diagnosis and treatment with high-intensity phototherapy. In low- and middle-income countries, screening, observation, and treatment for hyperbilirubinemia are difficult to get. In these circumstances, an estimated 6 million newborns who need phototherapy do not receive it; around one-third of newborns with significant hyperbilirubinemia die, and 44% have severe encephalopathy [16].

Advanced picture preparation and machine learning approaches have been embraced by many analysts. By acquiring color images of the palm, soles, and brow on a computer, the authors of [1] assessed RGB characteristics, which were then followed by a study of diffuse reflectance spectra to classify individuals as having jaundice or not. These characteristics were associated with the level of bilirubin. Patients were identified using a support vector machine that was both audible and silent. In this investigation, white balancing is employed to improve the clarity and sharpness of the collected images. Two techniques (KNN Regression and Support Vector Regression) are provided within the machine learning regressions to direct the machine in determining the bilirubin level. The compliance rate between the framework and the conventional blood test was 85% when KNN regression was utilized, as opposed to 75% when SVR regression was utilized. The success rate of F- statistical tests and ROC analyzes in determining the accuracy of the data and the execution of the framework appeared to be an astounding 85 percent. Castro-Ramos *et al.* [2] developed a similar method for identifying infant jaundice by acquiring digital images of neonates' palms, soles, and foreheads. Captured images are refined and analyzed in terms of RGB characteristics and diffuse reflectance spectra. To determine the proximity of jaundice, a support vector machine (SVM) was applied to the precomputed examination. With 20 spectra, the method yielded an affectability of 71.8% and a specificity of 78.8%. This prospective concept may be an excellent method for measuring the various bilirubin levels in infants.

The authors of [3] utilized a specialized computer program and data on color values within the pictures (“features”) which were extricated from pictures of patients. Machine learning algorithm investigation procedures were used to distinguish highlights for incorporation in models to expect an assessed bilirubin level for each infant. The relationship between assessed bilirubin levels and TSB levels was moreover calculated. A framework named BiliCam had been proposed in this paper, which could be a low-cost framework. Its employments smartphone cameras to survey infant jaundice. Creators assessed BiliCam on 100 newborns, yielding a 0.85 rank arrange a relationship with the gold standard blood test. The convenience challenges and plan arrangements had to be talked about forming the framework down to earth. A strategy to screen for jaundice in neonates employing an advanced picture of the sclera is proposed in the paper [4]. RGB pixel values from a crude arrange picture were used to derive an appraisal for the entire serum bilirubin (TSB). An inquiry at UCH Neonatal Unit found a relationship of $r=0.71$ ($p<0.01$) between measured TSB and TSB evaluated. The preferences of employing a smartphone camera as a portable screening gadget had to be discussed.

The authors of [5] gathered blood samples from infants with suspected jaundice throughout the first week of serum bilirubin levels. Within two hours, photos were obtained by placing a color calibration card over the breast and utilizing an app called Biliscan. Bilirubin was tested after color correcting, highlight extraction, machine learning regression, and blood values were compared. In 35 neonates, there was a significant correlation (0.6) between Biliscan bilirubin estimation and blood bilirubin levels (p0.0001). Biliscan thorax levels correlated significantly better than midsection values (0.6 vs 0.551) with serum values. BiliCam is a contemporary, low-cost framework for detecting jaundice in infants utilizing an iPhone 4S camera coupled to an 8-megapixel camera [6]. Utilizing a calibration card with an estimate of a regular commerce card positioned on the newborn's sternum and forehead time, the approach is effective. Recently, a collection of photographs is taken. BiliCam images from 530 neonates were compared to the gold standard blood test, resulting in a 0.91 correlation coefficient. Using 2 choice rules, the strategy's affectability in distinguishing infants with high TSB levels was 84.6% and 100%; specificities were 75.1% and 76.6%, respectively. This process may be a useful method for measuring bilirubin levels in infants. The method may underestimate the reading ability of infants with darker skin tones.

Leung *et al.* [7] provided a previously unrecognized method for screening for infant jaundice based on enhanced photography of scleral images. The Nikon D3200 camera has a large-scale focal point with a 60 mm central focal length and a 24.6-megapixel Complementary Metal Oxide Semiconductor (CMOS) sensor. The use of the scleral tone to determine the serum bilirubin concentration was validated in 110 babies’ sclera. MATLAB was used to analyze the collected images, and a bespoke color chart was used as a reference. The color reference was assumed to be white. This approach was demonstrated to be a promising screening tool for diagnosing newborn jaundice, especially in situations of TSB levels exceeding 205 mol/L. The Collector Working Characteristics (ROS) curve from the regulatory review indicated that the affectability was 1.00, and the specificity was 0.50, a result that was much superior to that of commercial Transcutaneous Bilirubinometers (TcB) such as the JM-103 and BiliCheck. In 110 neonates, the analysis of the link between scleral tints and the measured evaluation of TSB level revealed a rather high correlation of 0.75.

According to our study of the selected articles, it has been found that different techniques are used to detect and monitor neonatal jaundice. Blood serum, a transcutaneous bilirubin meter utilizing BiliCheck, and optical imaging utilizing BiliCapture, BiliCam, and Biliscan are utilized to measure the quantity of bilirubin-serum bilirubin in the laboratory (Figure 1).

Figure 1. (a) Blood serum [16]; (b) Transcutaneous bilirubin meter [16]; (c) Optical imaging [16]; (d) BiliCam [3] and (e) Biliscan [5]

An accumulation of examiners made a non-invasive way to assess the bilirubin level in 61 babies in 2009, which was one of the essential exercises to communicate an elective conclusion strategy. Pictures of the newborn's chests were shot using a computerized camera, and the makers carefully studied and changed them in Photoshop using the proposed procedure. The photos were at that point surveyed, and the CMYK system's Y and M components were measured. The genuine regard for serum bilirubin was found by subtracting M from Y. Pearson's product-moment relationship and coordinate backslide was used to analyze the relationship between including up to serum bilirubin and the regard of Y-M. The makers found an interface between serum bilirubin levels and the expected bilirubin values gotten from pictures. Despite the truth that the strategy was imperfect, it was the herald of other non-invasive strategies [17].

Ali *et al.* [8] published a contemporary set of computations to examine acquired cases of protective jaundice, including Dubin-Johnson syndrome, Gilbert's syndrome, and Rotor's syndrome. Five clinical highlights for each infection were identified. The calculation consisted of two components: first, the use of Wavelet Change to segment images, and second, the determination of the rate of dark scales for each image using a histogram. This method employs three types of image enhancement techniques: image modification, logarithmic change, and histogram equalization. Develop Cut Strategy is utilized for the division of images while Fluffy Displaying Framework Structure is used for the classification to determine one of three situations of acquired safe jaundice. The study demonstrated that the fluffy reasoning method had a high degree of accuracy, ranging from 95% to 100%, in identifying the three aforementioned illnesses.

Mansor *et al.* [9] established a color detection technique for monitoring baby jaundice. In this study, three variations of the Jaundice discovery framework are utilized. The primary arrangement involves the extraction of skin highlight data from video recordings of the child, whereas the moment organization involves the selection of quantitative highlights of the infant's fascinating behavioral traits. The parameters cruel, standard deviation, skewness, kurtosis, vitality, and entropy are determined. The third organization was responsible for recognizing the proximity of jaundice. Luminance (Y) and chroma (CbCr) color spaces are utilized to determine the location of jaundice based on skin tone. Kurtosis information revealed a higher predictive value than the other components based on the feature extraction examination of an irritated and non-jaundiced child. Consequently, this highlight has been selected for use in the screening and observation of baby jaundice as a component of the active image localization instrument. The technique aimed to provide jaundice evaluations that are independent of the newborn's skin pigmentation, the irradiance of the surrounding lighting, and the color of the newborn's walled area. In the suggested method, the newborn's epidermis is exposed to a light source that emits the majority of its radiation at a predetermined frequency within the range of 425 nm to 525 nm. The reflected light is compiled from a predetermined occurrence to assist in the production of an electrical flag for handling assistance. A tungsten-halogen fiber light serves as the source of illumination.

Ali *et al.* [11] propose an optical technique for identifying jaundice in infants. The concept of light retention of oxyhemoglobin at different wavelengths has been linked by utilizing blue and green powered lights. The blue Driven is used as a light source to assess the bilirubin level, whilst the green Driven is used as a reference point to differentiate between bilirubin and hemoglobin. These light sources will pass through the skin and interact with certain particles, with a photodiode analyzing the reflected light. The photodiode will measure the reflected light and transfer the data to the Arduino Uno Microcontroller in order to determine the bilirubin concentration.

Rizbi *et al.* [16] proposed another method for using the image processing strategy in the identification of newborn jaundice. This considers using the transcutaneous bilirubin meter on the temple and getting optical imaging through checking of the conjunctiva of eyes, moreover alluded to as BiliChek and BiliCapture, separately. In a sample of 100 neonates, there was a significant correlation between Biliscan bilirubin estimation and serum bilirubin levels (p 0.0001). A standalone smartphone-based jaundice level location app has been proposed by Saini *et al.* [18]. This paper used the spectrophotometer and non-invasive estimations are, to begin with, done by using serum bilirubin coloration on strips and after that compared with those specifically from the skin. The strategy gives a 0.93 rank arrange relationship and can distinguish bilirubin concentration up to 24mg/dl to avoid hyperbilirubinemia. Leung *et al.* [19] provide a contemporary color metric titled "Jaundice Eye Color Index" (JECI) that predicts the yellowness of ocular sclerae for a given total to serum bilirubin level in newborn jaundice. This reflects on the employment of a Nikon D3200 computerized camera equipped with a large-scale focal point (60 mm focal length) to take advanced photographs of infants' eyes shortly after they underwent blood tests for TSB as part of their regular care.

The authors of [20] have described a noninvasive method for detecting bilirubin levels and jaundice using a device. The equipment device was made utilizing a color sensor (TCS3200), an ATmega328P-based Arduino Uno board, and a 16x2 LCD display. Adobe Color CC is used to extract the RGB component of skin from an image. TCS3200 may be a light-to-period converter that can be programmed. Padidar *et. al* [21] describe an Android OS-based application for identifying newborn jaundice. This considers utilizing the application to differentiate jaundice in 113 neonates, and smartphone-based assessment of bilirubin levels requires a smartphone, a color calibration card, and a 100X zoom magnifying instrument clip. The estimation of bilirubin levels had an affectability of 68% and specificity of 92.3% for assessing bilirubin levels of less than 10 mg/dL, and an affectability of 82.1% and specificity of 100% for assessing bilirubin levels of less than 15 mg/dL, as well as a correlation of 0.479 with the full serum bilirubin values. Leung *et al.* [7] suggest a novel screening approach for neonatal jaundice by exploiting the yellow discoloration within the sclera. It requires taking advanced photos of the eyes of infants (n = 110) and evaluating the pixel color values of the sclera in order to estimate total serum bilirubin (TSB) levels. The direct and rank correlation coefficients between this method and the measured TSB are 0.75 and 0.72 (both p0.01), respectively. The inhumane variance is 0.00 41.60 mol/l (SD). The collector operating characteristic curve suggests that this method can distinguish individuals with TSB levels greater than 205 mol/l with a sensitivity of 1.00 and a specificity of 0.50, demonstrating its potential as a screening device.

Mansor *et al.* [22] proposed a PCA technique for analyzing the newborn child's behavior. The test reveals that the proposed technique can reduce the severity and mortality of the conventional strategy based on k-NN regression. This metric is based on images selected at random from a database generated by http://www.google.infantmonitoring.com. All obtained images differ in terms of light level, separation, and the focal point. This collection of photographs provides a more inquisitive test for locating a robust sample to detect jaundice in a newborn baby.

The modern noninvasive strategy uses a computerized camera and control paper used by Leartveravat *et al.* [23]. Take a photo of the infant and estimate by using L*a*b framework degree at sternum chest divider at delicacy = 70%, estimation esteem of Y and M by CMYK framework, use M subtract from Y to urge the genuine esteem of yellow of bilirubin. The relationship between adding up to serum bilirubin and the esteem of Y-M was evaluated by Pearson’s item moment correlation and straight relapse. The full transcutaneous advanced bilirubin (TcdB) can calculate by TcdB= 0.2(A + 0.58x(Y-M)12.9 mg%. The think-about gather comprised 61 newborns (31 male, 30 female). An arrangement of direct connections was found to exist between adding up to serum bilirubin concentration and the esteem of Y-M. The cruel adds up to serum bilirubin =12.55t4.2mg% and cruel adds up to computerized transcutaneous =72.921p.4 mg%, coefficient of relationship = 0.86, coefficient of determinate (f)=77.4, standard blunder of estimation = 1.38. Critical measurement between the esteem of serum bilirubin and the esteem of Y-M was found ($P < 0.05$) [24].

Althnian *et al.* [25] propose a thorough exchange learning technique based on eye, skin, and merged images. In addition, they created conventional machine learning models, such as multi-layer perceptron (MLP), decision tree (DT), support vector machine (SVM), and random forest (RF), and compared their performance to that of the exchange learning signal. They collected their dataset using a smartphone's camera. In addition, unlike the bulk of current claims, their research quantified the relevance of precision, accuracy, f-score, recall, and area under the curve (AUC) for all the tests. The findings of the study reveal that the transfer learning model worked best with photographs of skin, whereas traditional models performed best with images of eyes and combined highlights. The Transcutaneous Bilirubinometer (TcB) is ineffective for neonates born after 35 weeks of gestation and within 24 hours of birth. TcB levels below the 50th percentile for age nearly certainly exclude the possibility of developing hyperbilirubinemia in the future. TcB levels measured 12 hours apart have a greater predictive power than a single measurement [26]. Phototherapy's ultimate objective is to reduce or stop the existing bilirubin level from rising. This will be accomplished by altering the structure and development of bilirubin with light energy, allowing it to be converted into particles that can be emptied when the conventional transformation fails [27].

The demand for more cost-effective, convenient, and widespread screening measures for jaundice in neonates has been fulfilled in part by the proliferation of digital cameras and mobile phones. It has been proved that these cutting-edge technologies perform as well as or better than the current screening methods. The bulk of these methods identify jaundice through image processing and color analysis [28]. Observing the color of the exposed external skin layer is one of the most common ways for detecting jaundice and forecasting the bilirubin concentration. This could be achieved by establishing a correlation between skin color and bilirubin concentration by examining the skin's visual properties with a camera and image processing tools [29]. The authors of paper [30] created artificial intelligence-based algorithms for detecting jaundice in babies. In addition to ending their evaluation of several AI approaches, they released a report summarizing their achievements and the challenges they have faced in this industry.

In infants with jaundice, Liu *et al.* [31] evaluated the relationship between total serum bilirubin (TSB) levels and globus pallidus-related metabolic markers of proton magnetic resonance spectroscopy (1H-MRS). They examined the relationship between their hypothesized categories of globus pallidus-related 1H-MRS metabolic indices and TSB concentrations. In babies with neonatal jaundice, the serum TSB level is correlated with the 1H-MRS metabolic index Glx/Cr, and the TSB and Glx/Cr values serve as a diagnostic reference for bilirubin encephalopathy. Authors of [32] developed a mobile support architecture to facilitate the application of noninvasive image handling algorithms for the classification of infant jaundice by healthcare professionals in hospitals or remote places. The research revealed a new framework for jaundice identification contrasts in skin color analysis to address all the aforementioned issues. The authors of [33] provided a thorough review of the majority of these strategies, stressing their benefits and drawbacks and contrasting them in terms of the strategy employed, preferences, restrictions, and the region of interest selected for handling.

3. Method of Non-invasive Techniques

The major aim of this study is to investigate the suitability, restrictions, and challenges of detecting and monitoring neonatal jaundice issues using non-invasive techniques based on clinical data and a variety of other information sources. We also investigated the reasonableness of this neonatal jaundice detection system by analyzing the methods of data analysis, data extractions, outcomes, and limitations. The sources of information, including extraction strategies and the execution of the classifiers in non-invasive approaches, were investigated in this research. The literature search was conducted primarily using major investigation databases, such as Scopus, Pub- med, and WoS (Web of Science). Articles distributed from 2009 to 2022 were included in the survey of this literature. The following section (3.1) discusses the methodologies of neonatal jaundice detection from the selected research, while the results or outcomes of those studies have been discussed.

3.1. Methodologies of Neonatal Jaundice Detection

Non-invasive methods are getting to be an unmistakable instrument for identifying neonatal jaundice issues. Many strategies for dissecting information, used within the location of different neonatal jaundice issues, have been created. Diverse sections of a neonate's body, including the face [34], forehead [2, 17-18, 21, 35], sternum [5-6, 18, 35], abdomen [5, 36], or other body parts such as the arm, palm and sole [2] and face, feet, arms and central body [37] have been utilized for skin-based conclusions. The authors adopted various methodologies for highlight extraction, including mean, skewness, standard deviation, energy, kurtosis, and entropy [34], YCbCr and lab color spaces [6, 35-36], RGB [2, 6, 21, 36, 37], hue and saturation values [5, 18], and diffuse reflection spectral characteristics [2]. Diverse machine learning models, such as KNN [36, 38], SVR/SVM [2, 36], regression [5, 21, 37], and an ensemble of classifiers, counting KNN, LARS-Lasso elastic net, LARS, SVR, and RF [6, 35], have been used to determine jaundice.

Effectively, a smartphone camera has been utilized to record images of enraged and solid neonates, such as those in [2, 6, 16-17, 21, 34-40]. To determine if a smartphone camera can be utilized as a screening device for jaundice, the work described in [17] employed several tactics, including a coordinate camera strategy, a yellowish-green gelatin channel strategy, and dermatoscopy. The scientists determined that the last technique for jaundice detection is the most compelling. The items in [5-6, 21, 35, 40], but not [34, 38], utilized a calibration card for color adjustment in advance. In [35], the authors developed a revolutionary white-adjustment technique with an active edge for modifying various color temperatures without a calibration card. The works cited in [18, 34] gathered bilirubin coloring in stripes from serum. In [36], the authors captured images of the eyes using two distinct methods, namely closed boxes and colored glasses, but in [38], only closed boxes were used to take images of the eyes.

Several works depicted the hue of serum bilirubin on location strips. For instance, Saini *et al.* [18] identified infant jaundice by correlating images of temple and sternum skin with images of serum bilirubin coloring on discovery strips. Singla *et al.* [39] have utilized bilirubin strip images to examine the efficacy of homomorphic filtering on jaundice detection. In their research, the authors linked homomorphic sifting to the estimated blue color force of images. The link between actual and predicted bilirubin levels was computed. The darkening of the sclera of the eyes indicates the imminence of newborn jaundice due to the accumulation of bilirubin in the body and the inability of the liver to expel it. There are numerous attempts in the literature to find jaundice in adults by utilizing photographs of the sclera and a box to restrict eye exposure to light. For instance, Laddi *et al.* [38] utilized a 3CDD camera and a light source covered by an aphotic housing composed of acrylic paper to acquire eye images that were then augmented to CIE Lab color presentation. The images in [36] were captured using an iPhone SE with two accessories, a head-worn box and paper glasses with colored squares for calibration. It appeared that their outcomes were significantly superior to those of the box. For infant jaundice, the authors of [7] utilized a Nikon camera to capture ocular images, from which RGB highlights were extracted and fed to a straight relapse display to predict TSB levels. Rizvi *et al.* [16] used photographs of the eyes of neonates to determine bilirubin levels using the Diazo method with dichloroaniline (DCA). The authors of [4, 41] caught two variations of each photograph, namely flash and non-flash images. In the preceding study, images were used to implement the encompassing subtraction technique, which yielded encouraging outcomes. In this method, the RGB values of the two image formats are subtracted to approximate the values without light. Several studies, such as [7], evaluated skin and ocular images for the direct relapse diagnosis of jaundice. Their outcomes suggested that the latter can provide significantly superior outcomes.

Subramanian *et al.* [40] point to making a noninvasive bilirubin meter that employments a smartphone to capture color pictures, which are then extricated and analyzed to attain a bilirubin check expectation using a calculation called counterfeit neural systems, which can at that point be used to recognize the infant’s jaundice level. This may permit for compelling observing of jaundice throughout phototherapy sessions with no requirement for visit finger pricks and blood tests. Angelico *et al.* [37] created a user-friendly app for Android cellphones. The application used machine learning to develop a stool color recognition algorithm according to the infant stool color card with seven different grades of color, which served as the reference model. The smartphone's camera was used to take a series of photographs of feces, which were then assessed as "normal" or "acholic" by the program. Based on the analysis of 165 photos, the application's sensitivity, specificity, and accuracy were determined to be 100, 99.0, and 99.4%, respectively. Aune *et al.* [41] designed a method for assessing bilirubin levels in newborn infants. The framework integrates a color analysis of digital photos with a physics-based model of light transmission through the skin. Using a scientific demonstration based on the diffusion hypothesis, the authors replicated the reflectance spectra of newborn skin and compiled them into a library. Red, green, and blue were the three hues used by the authors' mobile camera when they captured digital photographs. The colors on each image's accompanying reference card were utilized to calibrate the hues. The degree of each card was determined using a color spectrometer, and the results were saved and compared to a massive database of color and bilirubin. The database may be downloaded to the device and utilized even when the device is not connected to the internet. It looked like the researchers had a high correlation. Juliastuti *et al.* [42] suggested a risk-zone estimation framework. The framework employs an advanced camera to collect photographs of infants, a middle filter to remove grain from the images, and color rectification to lower color saturation by using a color card containing the three primary colors of RGB. The images were then converted to RGB, HSV, and YCbCr color spaces, with measurement parameters derived from the histograms of each channel. These values were used as input parameters for the validation and modeling of linear regression with an estimated bilirubin level as the output variable. In fact, despite the proposed framework's simplicity and robust relationship category, its error rate was 17% and its precision was 66%.

Tomtsis *et al.* [43] developed a chromatic modulation imaging method to detect transcutaneous bilirubin; the results can be used to evaluate serum bilirubin levels in neonates; they discovered a significant association between hue angle and transcutaneous bilirubin level. Hasim *et al.* [44] proposed a camera-based method for identifying jaundice in newborns. The technology uses advanced image processing techniques to extract and evaluate the captivating characteristics of gathered photographs in real time. This includes skin recognition using edge value and color space conversion, Region of Interest (ROI) selection, and skin color analysis in RGB and YCbCr color schemes. Based on the data gained via image processing, the system determines if the infant requires therapy. In addition, jaundice may be treated with an Arduino Uno microcontroller that controls a blue LED light for phototherapy. The suggested framework has been proved to be a realistic, cost-effective, and uncomplicated technique for the identification and treatment of infant jaundice. provided a method for identifying jaundice using sclera photos. The images were obtained with a webcam camera and a webcam-mounted LED flashlight. The flashlight was calibrated to provide the same degree of illumination independent of the ambient lighting conditions. During the preparation for picture collection, the participant was required to wear goggles that filtered ambient light and improved the precision of region of interest extraction. To reduce noise, the pictures were then subjected to a 3D median filter. Since the proposed technique depends on sclera pictures, sclera extraction must be performed using bounding box calculation and color thresholding to remove the skin surrounding the eye. In addition, the scientists calculated the bilirubin concentration utilizing RGB, HSV histogram, and random forest regression. The method proposed in [45] might promptly measure jaundice severity and deliver findings. In addition, it did not require particularly qualified personnel to operate; yet, only adults may use it. Angelico *et al.* [37] created an Android app that is user-friendly. The program uses machine learning to construct a stool color identification algorithm using the newborn child stool color card, which served as the reference model. The smartphone's camera was used to require a series of images of feces, which were then classified as "normal" or "acholic" by a computer. The application's affectability, specificity, and accuracy were 100%, 99.0%, and 99.4%, respectively, based on a study of 165 photos.

Strong newborns who are enraged and determined have successfully been photographed using a smartphone camera. Related tires have employed other regions of a neonate's body, including the forehead, sternum and face, limbs, feet, and chest, in skin-based conclusions [46]. They understood evolving highlight extraction methods like YCbCr and lab color schemes. Different machine learning methods, such as an ensemble of different classifiers, checking KNN, LARS- Lasso elastic net, LARS, SVR, and RF, have been employed to ensure jaundice. Using methods for sophisticated digital image processing and data mining, Dissaneevate *et al.* [47] suggested a Mobile Computer-Aided Diagnosis (mCADx) tool to diagnose the Neonatal Hyperbilirubinemia symptom. They explored data mining approaches using the dataset, including Decision Trees, k Nearest Neighbors, and the Conventional Neural Network, on picture data of 178 infant participants with varying degrees of jaundice severity. The accuracy of the classification results on CNN was 0.8099, 0.9251, and 0.8086. Table 1 represents a comparison of the existing research projects on neonatal jaundice detection and monitoring using various methods.

Table 1. Analyses of Non-Invasive Bilirubin Studies Based on Various Neonatal Jaundice Detection Techniques

Body Part	Method	Dataset	Result
Abdomen skin [1]	KNN and SVM	80 images collected from Fırat University	KNN accuracy = 85% SVR accuracy = 75%
Sternum and abdomen skin [5]	Regression	35 images collected from Chennai, India	Sternum correlation = 0.6
Sternum skin [6]	Regression	530 images collected from the different races in the US	Sensitivity = 84.6% Specificity = 75.1%
Sternum and forehead skin [8]	KNN, LARS, LARS-Lasso Elastic Net, SVR, RF	100 images collected from the University of Washington	A linear correlation of 0.84 with TSB, with a mean error of 2.0 mg/dL
Sternum and forehead skin [18]	Matching	A standard set of serum bilirubin coloration on detection strips	Correlation = 0.93
Forehead skin [17]	Linear regression model	64 images at Aalborg University Hospital	Green sensitivity = 100%, specificity = 62% Blue sensitivity = 90%, specificity = 60%
Forehead skin [21]	Regression	113 images at Hafez and Shoushtari hospitals	Sensitivity = 68% Specificity = 92.3%
Soles, palm, forehead, and arm skin [2]	SVM	20 images of infants in Mexico	Sensitivity = 71.8% Specificity = 78.8%
Face, arms, feet and middle body skin [35]	Linear regression	196 images at Firat university,	Accuracy = 92.5%
Face skin [34]	KNN	120 random images from Google infant monitoring	Accuracy = 90–96%
Eye [4]	Regression	86 images taken at the London UCH Neonatal Unit	Correlation = 0.71
Eye [7]	Linear regression	110 images collected at University College London Hospital	Correlation = 0.75
Eye [16]	Diazo method with dichloroaniline (DCA)	100 images at King Khalid Hospital	Sensitivity = 90% specificity = 75.6%
Eye [48]	Jaundice Eye Color Index Scleral-Conjunctival Bilirubin (JECI-SCB) and SCBxy model	51 images from the UCL Hospital	Correlation = 0.75
Skin [25]	MLP, SVM, DT, and RF	Data acquired at King Khalid University on newborns with and without jaundice	Average values Accuracy: 64.77% Precision: 67.39% Recall: 64.39%
Eye [25]			Accuracy:73.53% Precision: 74.64% Recall: 73.36%
Fusion [25]			Accuracy: 73.49% Precision:74.91% Recall: 73.49%
Skin [49]	Linear, Lasso, KNN, SVR	9 different observations of bilirubin level	Actual Value: approx. 15 Predicted Value: approx. 15.8
Bilirubin sample strips [50]	Correlation between actual and expected bilirubin concentrations	8 images of bilirubin sample strips	After filtering, the correlation coefficient improved from magnitude 0.5261 to magnitude 0.6974

4. Discussions, Limitations, and Future Research Directions

This paper has critically reviewed various non-invasive techniques used for diagnosing neonatal jaundice and initiatives to offer successful treatment. The survey covers a wide extend of articles distributed between 2009 and 2022. We examined the results concurring with the dataset of the articles which incorporates: social media data, overview survey data, and clinical data. The selected studies have been outlined in Table 1, according to their used object or body part, methods, dataset, and results.

The main shares of the publications studied in this article are concerned with diagnosing and detecting neonatal jaundice. We note an expanding number of investigative articles using non-invasive methods to investigate jaundice locations based on the previous findings. We have entirely taken after the set consideration and prohibition criteria, keeping this consideration restricted to the look that comes about hence created. In the future, we conduct an orderly writing survey to explore diverse other viewpoints on the approaches in this domain.

5. Conclusion

Infant newborns may experience jaundice frequently, especially if certain factors are present in the first week of life. Additionally, jaundice may be a sign of other potentially fatal illnesses. For instance, liver disorders, neonatal illnesses, and baby hemolytic anemia can all result in elevated bilirubin levels [4, 51]. The current gold standard for measuring serum bilirubin is the Diazo method, however, an invasive method and non-invasive alternative may be provided by specialized equipment known as a transcutaneous bilirubin meter, which is expensive and not readily available in various hospitals and clinics [5]. There's a requirement for an inexpensive, non-invasive strategy for observing jaundice. Since smartphones with web networks are accessible to nearly everybody, portable phone-based well-being detection may be a great arrangement for this problem. Smartphones with picture handling procedures for identifying jaundice may be an inexpensive choice that may be used indeed for home-based observing by guardians [5]. It is trusted that smartphone innovation-based solid apps can get to be a compelling substitution for transcutaneous bilirubin meters within the near future intrusive strategies within the clinical setting for the administration of neonatal jaundice [24]. For surveying and settling neonatal jaundice issues, a few diverse techniques and strategies have been concocted and created. There are without a doubt different openings and arrangements for ceaseless enhancement in this respect. There are still various troubles in finding and exploring the jaundice discovery and checking by using a wide run of basic truths and criteria in a non-invasive method. The reason for this paper was to examine current inquiries about the utilization of non-invasive methods in neonatal jaundice studies. To whole up, inquire about within the field of non-invasive technology for jaundice detection has made a significant advance, especially within the latter a long time. We have analyzed the systems developed for predicting neonatal jaundice and presented a detailed comparison amongst them.

The major shares of the articles have centred on non-invasive approaches which comprise various information sources, diverse include extraction strategies and execution of different classifiers. Our survey of the chosen articles uncovered that most of the analysts used various image processing techniques, smartphone technology, SVM classifier and regression, and kNN regression among the different prescient machine learning algorithms. In reality, many studies have broadly embraced using online social media information sources, since social media is one of the foremost used stages for communicating one's jaundice issues. Hence, analysts used information sources like Google and GitHub. In most cases, analysts received different datasets produced from clinical data. It is profoundly likely that the non-invasive method can dramatically improve the identification and diagnosis of neonatal jaundice.

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