Non-Invasive Bilirubin Detection

Satyawan Mishra*, Lalit Mohan Saini[&], Jasbinder Kaur[#]

[&]*School of Biomedical Engineering, National Institute of Technology, Kurukshetra, Haryana, India*

[#]*Govt. Medical College and Hospital, Chandigarh, India*

ABSTRACT

Jaundice is a condition in where an abnormal state of bilirubin is available in the blood. In infants, jaundice is quite common as all the organs are not sufficiently developed. And it is called Neonatal Jaundice. Bilirubin is processed in the liver and it is formed because of the breakdown of hemoglobin. There are two methods of Bilirubin detection namely invasive and non-invasive. Invasive method is painful and in this method some blood is taken for the analysis purpose. A non-invasive method that can reduce pain as compared to the old method. One of the most popular techniques of non-invasive methods is by using a particular wavelength of electromagnetic spectrum, Bilirubin will absorb the light and photodiode will capture the reflected light from bilirubin. This reflected light is converted into voltage by the photodiode and this voltage is processed by Arduino Uno. The doctor can monitor the babies' bilirubin level all the time which might be useful in subsequent investigations.

Keywords—bilirubin;jaundice;TcB;TSB

I. INTRODUCTION

Jaundice is a common problem in new born babies. Jaundice occurs due to breakdown of RBC's. Breaking down of RBC's is known as Hemolysis. If Hemolysis occurs at a rate faster than the liver's ability to get it out of the body then the level of Bilirubin in the body increases and leads to Jaundice. Neonatal jaundice is found more in Asian countries than the European countries.

*A. **Bilirubin Production And Excretion***

Bilirubin is a yellow color byproduct of hemoglobin metabolism First of all hemoglobin is broken into heme and globin. Heme is then oxidized and converted into bilverdine Bilverdine is finally converted into bilirubin, globin, on the other hand, is converted into amino acid. If kidney is not able to excrete bilirubin then problem of jaundice occurs.

In bloodstream albumin binds bilirubin and complex is carried to liver. This bilirubin-albumin complex is called as indirect or unconjugated bilirubin which is water insoluble. In liver hepatocytes take up bilirubin and hepatic microsomes conjugate bilirubin with glucuronic acid. Conjugation occursvia UDP glucouronyl transferase enzyme. This enzyme is synthesized slowly after birth, hence causing newborn jaundice.

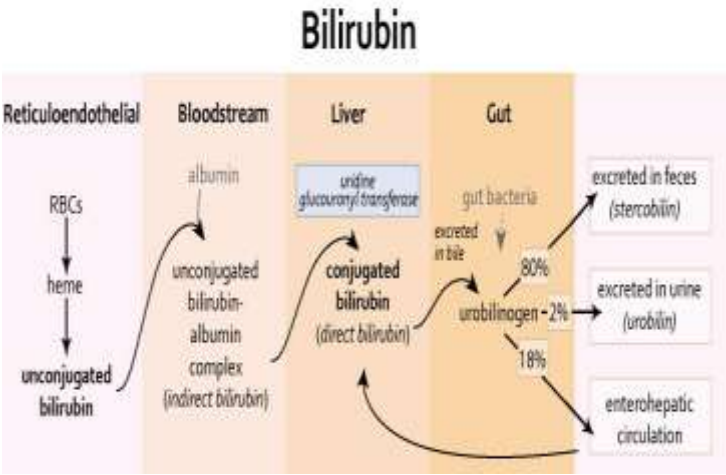

Fig.1: Bilirubin production and excretion

Conjugated bilirubin is also known as direct bilirubin which is water soluble. A portion of conjugated bilirubin is excreted in urine remainder is secreted into bile and then into small intestine. In gastrointestinal tract, in terminal ileum and colon, bilirubin is deconjugated by bacterial enzymes and metabolized to urobilinogen. 18 percent of urobilinogen is absorbed via enterohepatic circulation and delivered back to liver. 80% of urobilinogen is converted into stercoblin and excreted in feces. Stercoblin gives characteristic color of feces. 2% of urobilinogen is converted into urobilin and excreted in urine. Urobilin gives characteristic color of urine.

B. Detection of Bilirubin level

The visual inspection with the help of Kramer's rule is shown in Figure-2. The body part can be divided into five zones as depicted in the figure. The five parts are palms and soles, lower trunk and thighs, upper trunk, arms and lower legs and head and neck [11]. Yellowness of skin decides the valueof bilirubin concentration assessment. The yellowness of skin is due to bilirubin itself. This bilirubin can be identifying as unconjugated bilirubin that bound with albumin that flow around the blood system. The rule states that each prediction value of total serum bilirubin (TSB) concentration for each yellowness zone. The first yellowness will be from the head and end at soles shows the increasing TSB. Each zone will represent the jaundice level condition by normal, medium and critical. The Kramer's rule is generally used by pediatrics department in order to predict the TSB concentration value based on physical color of skin (Randev and Grover 2010) as shown in Fig.2. As an example, if the yellowness of skin reaches to upper trunk of babies, TSB is >15mg/dl and need to be monitored under phototherapy light.

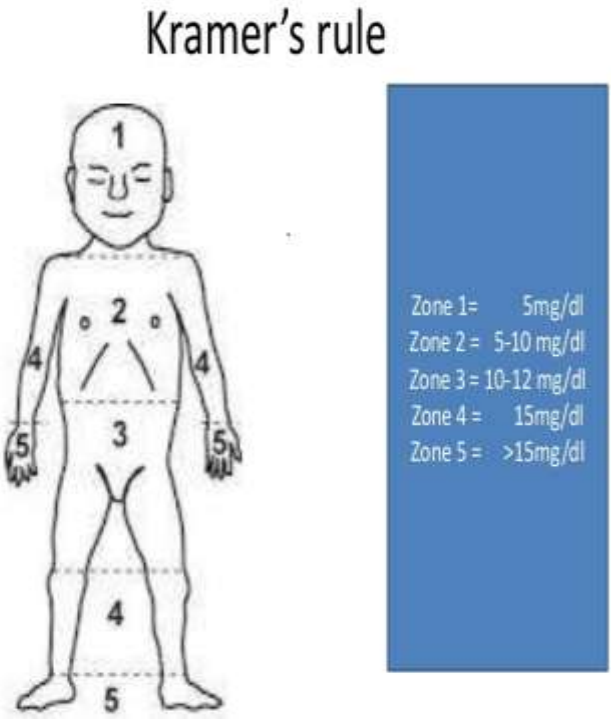

Fig.2: Zones of Kramer's rule

Although this method is non-invasive but this method is not very reliable. If the level of bilirubin reaches greater than 15mg/dl, other method is needed to detect the jaundice level.

Other non-invasive techniques

Other non-invasive techniques include optical methods to detect bilirubin level in the blood. Transcutaneous bilirubin detection device introduced by James W. Kornberg [1] is based on the absorption of light by the skin. More is the absorption of light by the skin more is the illness. Steven L. Jacques [8] studied a device which is based on the principle of refraction of red, yellow and orange light and reflection of blue light. Buttita developed a device which employs two lights, one which is fully absorbed and the other which is either partially absorbed or not absorbed. The other one which partially absorbed or not absorbed at all determines concentration of bilirubin in the blood. Vinod K. Bhutani [9] developed a device that depends on multicolor spectral reflectance analysis. This device focuses on the babies who have high risk of hyperbilirubinemia. Gagan Mahajan studied the correlation between the transcutaneous bilirubin meters and TSB reading without using phototherapy. Yu-Hsun Chang assessed the convenience of JM-103 in Taiwanese infants.

There are different measures accessible for non-invasive measurement with the help of transcutaneous bilirubinometer like Spectrx Bilicheck, ColormateTLc-Bilitest, Minolta Air Shield JM-102, and Minolta Air

Shield JM-103. The table depicted different benchmarks such as clinical practice with standards for bilirubin devices. Two-channel outline strategy on which a portion of the gadgets are rely for example Air Shield JM-102, ColormateTLc-Bilitest and Minolta. Few depend on reflectance information at numerous wavelengths for example Minolta Air Shield JM-103 and Spectrx Bilicheck. Generally, these gadgets help a lot where large samples are required the blood taken out invasively causes huge amount of blood loss hence these non-invasive devices are required in order to safely detect the bilirubin in the neonates. Minolta Air Shield JM-102 and ColormateTLc-Bilitest in light of configuration which is two-channeled quantify hemoglobin rectified yellow shading on account of the inconstancy of the relationship of TcB readings and serum bilirubin connection. The strategy has been most valuable to enable clinical to choose. To diminish these abnormalities of two machines Minolta Air Shield JM-103 and Spectrx Bilicheck has been produced utilizing reflectance data with the help of numerous wavelengths. Various transcutaneous bilirubinometer are listed in the table 1.

Table1: Various devices and its principles.

Gadget	**Clinical Practice**	**Method Based**
Spectrx Bilicheck	2002	Reflectance principle of multiple wavelengths.
ColormateTLc-Bilitest	1998	Principle of two filters design method.
Minolta Air Shield JM-102	2004	Principle of two filters design method.
Minolta Air Shield JM-103	2008	Multiple wavelength reflectance data.

II. OPERATION OF NON-INVASIVE OPTICAL DEVICES

With the assistance of experiments continued, absorbance is inspected within the range of 300 nm to 900 nm and the result obtained from the spectra gives information about the metabolites of the skin. The metabolites found under the skin are hemoglobin, bilirubin and melanin. The melanin which is found in the epidermis layer of the skin is the main obstruction in the way of light. Melanin blocks most of the light of visiblespectrum. Hemoglobin found in the dermis layer of skin also absorbs light. Absorbance versus wavelength graph is given in the figure 4.

From the figure, it is evident that the bilirubin has the spectral range of 400nm to 520nm whereas hemoglobin has a different range of spectrum. In the range of 400nm to 800nm melanin is the main absorber of light. In this range, hemoglobin and bilirubin do not come in the way of melanin.

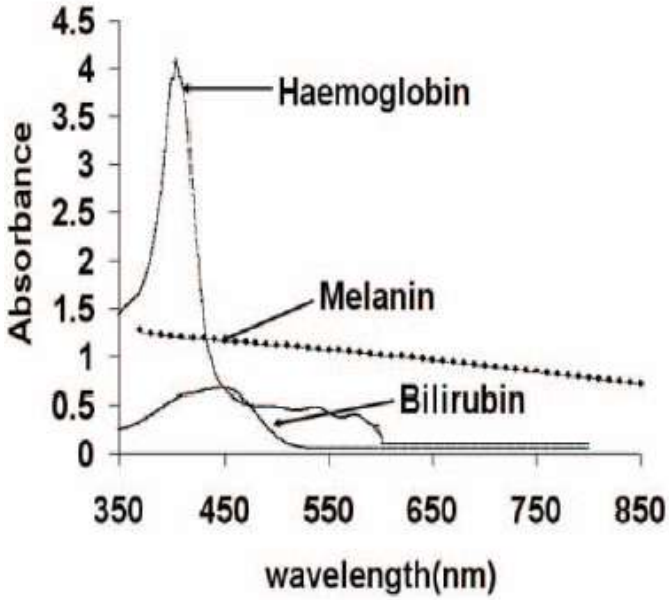

Fig.3: Wavelength versus Absorbance

A. ***Basic Idea***

The usage of artificial skin has been done at the beginning of the experiment. The mock skin was used initially which is a Sprague Dawely rat skin which resembles human skin in lot of ways (Osman, Ahmad *et al.* 2014) [12]. The rat skin has been shaved and kept in the solution of bilirubin with different concentration level. The rat skin had been soaked in the solution for ten minutes. The voltage value obtained after the reflectance of blue light from the different solutions has been recorded and obtained. The arrangement of six different solutions had

been done and the concentration levels are 1.0 mg/dl, 4.5 mg/dl, 6.5 mg/dl, 7.5 mg/dl, 15.0 mg/dl, 20.2 mg/dl. Now the blue light is incident on these solutions from LED. According to the bilirubin level in the blood, light is absorbed or reflected. Higher the concentration of bilirubin in the blood higher is the absorption. The photodiode converts light into voltage according to the intensity of light reflected from the solution. Thus a set of values is obtained which relates between bilirubin concentrations in the solution and voltage output by the photodiode. With the help of curve fitting tool of MATLAB an equation of straight line isobtained which is used to determine bilirubin concentration in blood when this device is used on human subjects.

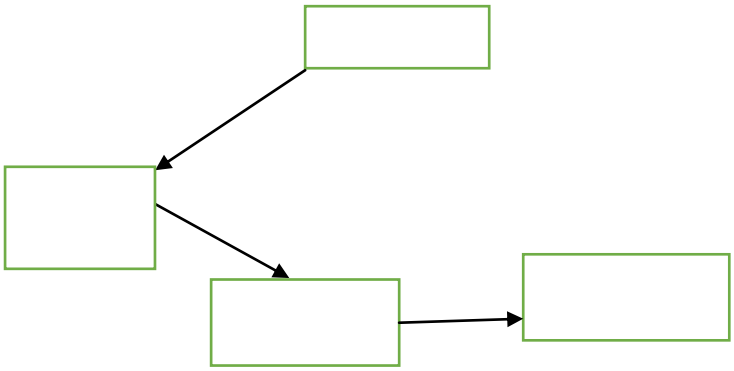

Fig.4: Basic Principle

The basic setup was created in which Gallium Nitride LED was used with wavelength 455 nm. The light was passed to the mock skin. The light after getting reflected from the mock skin was sent to the photodiode. The photodiode used is TSL 257 which converts light into voltage as it has a photodiode transimpedance amplifier on a single monolithic complementary metal oxide semiconductor (CMOS) integrated circuit is used to obtain voltage range of light reflectance from mock skin. Texas Advanced Optoelectronic Solution makes these photodiodes which is easily available in the market.

Jaundice monitoring can be also be done by using image processing. The images required for this process were obtained randomly from http://www.google.infantmonitoring.com [4]. The difference in the images was from illumination level, distance and angle of the image taken. The treatment of neonatal jaundice using colored light is called phototherapy. In this method of jaundice monitoring the captured image of the infant is processed through the image processing toolbox of MATLAB and then classifier makes the comparison whether the infant is suffering from the jaundice or not. With the help of image processing toolbox of MATLAB, the captured

image is brought in the MATLAB environment then image segmentation is done followed by feature extraction. After feature extraction bilirubin level is estimated (Nainika Saini et al).

Acknowledgment

This research is funded by MHRD, Government of India.

REFERENCES

[1] James W Kronberg, "Optical transcutaneous Bilirubin,",US Patent 52952.

[2] Ankan Gupta, Ashok Kumar, Preeti Khera, "Method and Model for Jaundice Prediction Through Non-Invasive Bilirubin Detection Technique" www.ijert.org.

[3] http://dx.doi.org/10.1016/j.proeng.2012.01.185

[4] Mansor, M. N. ,Yaacob, S. , Hariharan, M. , Basah, S. N. , " Jaundice in Newborn Monitoring using Color Detection Method" J PROENG 2012, vol. 29, pp-1631-1635.

[5] Suresh K. Alla*, Adam Huddle, Joshua D. Butler, Peggy S. Bowman, Joseph F. Clark, and Fred R. Beyette Jr.," Point-of-Care Device for Quantification of Bilirubin in Skin Tissue" *IEEE Trans Biomed. Eng*, vol. 58, no. 3, pp. 777–780, 2011.

[6] Nurashlida Ali ,Siti Zarina Mohd Muji ,Zuhairiah Zainal Abidin," A Review of Non –Invasive Jaundice detection using Optical Technique in Neonates" .

[7] Zulfadhli Osman, Afandi Ahmad-IEEE Member and Azlan Muharam-IEEE Student Member," Rapid Prototyping of Neonatal Jaundice Detector Using Skin Optics Theory" Conference IEEE 2014, pp 328-331.

[8] Steven L. Jacques,. David G. Oelberg,Iyad Saidi, "Method And Apparatus For Optical Measurement Of Bilirubin In Tissue". United States Patent. 5,353,790, 1994, pp. 1-79.

[9] Vinod K. Bhutani, Glenn R. Gourley, Saul Adler, Bill Kreamer, Chris Dalin and Lois H. Johnson ,"Noninvasive Measurement of Total Serum Bilirubin in a Multiracial Predischarge Newborn Population to Assess the Risk of Severe Hyperbilirubinemia,"the American Academy of Pediatrics. Vol. 106, 2000, pp. 1-9.

[10] Mustafa Aydın & Fırat Hardalaç & Berkan Ural & Serhat Karap," Neonatal Jaundice Detection System" J Med Syst 2016,40,166.

[11] Suresh A. Kumar,Prashant R. Bhadri,Fred R. Beyette Jr, "Non-Invasive Biomedical System for the Quantification of Bilirubin in Neonates" *IEEE*, pp. 1778– 1781, 2005.

[12] N. Ali, S. Z. M. Muji, A. Joret, R. Amirulah, N. Podari and N. F. Dol Risep, "OPTICAL TECHNIQUE FOR JAUNDICE DETECTION" Vol. 10, no. 20, 2015.