

DEVELOPMENT OF LOW-COST PHOTOTHERAPY NEONATAL BILIBLANKET FOR DEVELOPING COUNTRIES

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Abstract. A study by WHO in 2020 shows an upsurge of neonate death in Africa due to lack of medical technology required to adequately treat hyperbilirubinemia. This study researches the use of Light Emitting Diodes in neonate phototherapy administration. The design used a categorized pulse sensor and a temperature sensor to monitor the neonate-health, a microcontroller regulated the wavelength of LEDs in the range of 450-500nm, $33\mu\text{W}/\text{cm}^2/\text{nm} \pm 15\%$ irradiance with an illumination area of 700cm^2 . A total of 375 LEDs were distributed appropriately along the body of the blanket at a matrix of 12 x15 green LEDs and 13 x 15 blue LEDs. The results indicated that the prototype lowers serum bilirubin among healthy term infants, as the bilirubin level of the neonate decrease; there is a corresponding decrease in the intensity of LED intensity. The developed prototype included smart safety control features which are automatically controlled by the microcontroller, with high reliability in responses. The phototherapy neonate was used on 4 cases of hyperbilirubinemia neonates, with the levels of urinary lumirubin (is a irreversible structural isomer of bilirubin gotten as the result of the photochemical reaction) being measured every 30mins during the trial test. The total rate of reduction of serum bilirubin (mol/L/hour) calculated averagely from the individual test subjects were at 6.7 ± 2.05 which is rather significant.

Keywords: *low-cost biliblanket, hyperbilirubinemia, developing countries, neonatal phototherapy*

Introduction

Neonatal hyperbilirubinemia was confirmed to be commonly experienced during the first week of the life of a newborn (Qattea et al., 2022; Kaplan and Hammerman, 2004). The effect of hyperbilirubinemia in most cases leads to sudden infant death syndrome (SIDS) (Cornet et al., 2022; Qattea et al., 2022; Seneadza et al., 2022). SIDS accounted for around 15,000 newborn fatalities globally in 2017 (Miahet al., 2019; Dzulkiifliet al., 2018; Mustafa et al., 2017) of which 8% to 11% of neonates develop hyperbilirubinemia (Mustafa et al., 2017). Neonatal jaundice is the discoloration of skin and sclera to yellowish in a newborn by the presence of bilirubin (Seneadza et al., 2022; Miahet al., 2019; Dzulkiifliet al., 2018). When the total serum bilirubin (TSB) rises to about 94% during the first week of life, it is considered hyperbilirubinemia (Coquery et al., 2022; Qattea et al., 2022). About 80% of preterm babies develop a common type of jaundice “physiological jaundice” (Gaafar et al., 2020; Begum and Afroze, 2018). Rai et al. (2022) cited that Dermal icterus i.e., change of skin pigmentation to either yellow or greenish is first noted in the face and when hyperbilirubinemia condition continues within the body, then the case might be pronounced as extreme. Moghadam et al. (2020) stated that an increase in red blood cell breakdown and reduced bilirubin excretion was observed to cause Hemolytic jaundice and also several metabolic diseases, linked to an

increased incidence of jaundice (Gaafar et al., 2020). According to Boskabadi et al. (2022), bilirubin reacts just like uric acid, as an important antioxidant in the biological system of the neonate (Turkmen, 2020). The development of the central nervous system of the patient become toxically impaired due to hyperbilirubinemia (Pranty et al., 2022), especially causing a neurotoxic condition because bilirubin could penetrate the blood-brain barrier resulting in acute or chronic encephalopathy (Boskabadi et al., 2022), which manifests clinically as a developmental delay, deafness, and convulsions. The presences of behavioral and neurological impairment are includes as stated above (Boskabadi et al., 2022; Conti, 2021; Wang et al., 2019).

In physiological jaundice, Ifeanyi (2019) noted that neonates manifest between days 2 and 4 post-birth with immediate resolution after 1-2 weeks, but in the presence of risk factors, sometimes when it appears some indirect bilirubin could have already entered the basal ganglia of the central nervous system, because of the immature blood-brain barrier, leading to neuronal apoptosis and other neuronal defects (Rashwan et al., 2021). Five to ten percent of newborns diagnosed with jaundice require careful management to focus on hyperbilirubinemia (Long et al., 2022). According to Seneadza et al. (2022), Slaughter et al. (2022) as well as Gani and Ahmad (2021) the major causes of hyperbilirubinemia include race, genetic polymorphisms; inherited and acquired defects e.g., spherocytosis, and Gilbert's syndrome. Grossman et al. (2022) as well as Anderson and Calkins (2020) quoted The American Academy of Pediatrics' suggestion which states that "severe hyperbilirubinemia can be treated with phototherapy or transfusion if discovered early and handled promptly".

Etiology of jaundice

Characterization of hyperbilirubinemia which results from elevated total serum bilirubin defined by yellow discoloration of body tissue. The deposition of excessive bilirubin is gotten from the byproduct of hemoglobin or myoglobin, cytochrome, catalase, tryptophan, pyrolyze, and peroxidase catabolism, but 80% of bilirubin is gotten from hemoglobin metabolism (Cornet et al., 2022). At a nominal serum bilirubin content is usually less than 1miligram per deciliter (mg/dL). Characterized by the yellow coloration of the sclera also known as sclera icterus, it was discovered that whenever the serum bilirubin level exceeds 3 mg/dL there will be a further increase in skin discoloration progressively even to the extremities (Pettersson et al., 2022; Seneadza et al., 2022; Begum and Afroze, 2018). Statistics have shown 60% of term infants and 80% of preterm infants develop neonatal jaundice in their first week of life (El-Garhy and Gameel, 2021), and 10% of breastfed newborns developed jaundice before the end of the fourth week of birth, in summary about 24 million newborns are diagnosed with jaundice per year (Fathi et al., 2021).

Neonatal hyperbilirubinemia is the most common medical problem encountered in the first two weeks of life (Huda et al., 2021). Neonatal hyperbilirubinemia is divided into two types: (1) unconjugated hyperbilirubinemia (UHB); and (2) conjugated Hyperbilirubinemia (CHB). Unconjugated hyperbilirubinemia (UHB) is also known as indirect hyperbilirubinemia. According to Huda et al. (2021) UHB is the most common type of jaundice and can either be physiological or pathological. Healthy adults have 1mg/dl more total serum bilirubin compared to neonates because of the owing overload of bilirubin from the increased red blood cell (RBC) level after birth. Physiological jaundice appears 24 hours after birth and peaks 48-96 hours but resolves in full-term babies after 2-3 weeks. Hyperbilirubinemia is considered pathologic with an increased

serum bilirubin (TSB) level above 5 mg/dl/day or 0.2 mg /dl/hour after birth or when it persists for more than 2-3 weeks after birth (Cozzi et al., 2022). El-Masry et al. (2020) highlighted the evolution mechanism of bilirubin elevation, the cytology of unconjugated hyperbilirubinemia is grouped into the following three categories: Increased Bilirubin Production, Decreased Bilirubin Clearance, and also the presence of other miscellaneous causes like diabetic mother, congenital hypothyroidism, drugs like sulfa drugs, breast milk jaundice (Bratton et al., 2019).

Conjugated Hyperbilirubinemia (CHB) also known as Direct Hyperbilirubinemia. It is usually due to hepatocellular or cholestatic diseases (Neonatal cholestasis) and characterized by increased serum-conjugated bilirubin above 1.0 mg/dL (Feldman and Sokol, 2020). It is mandatory to distinguish between UHB and CHB for easy diagnosis and prompt treatment, especially for CHB. The cytology of conjugated hyperbilirubinemia is also grouped based on the following categories: Obstruction of biliary flow, Infections e.g., CMV, HIV, herpes virus, syphilis, urinary tract infection (UTI), etc., Genetic causes (e.g., Alagille syndrome, galactosemia, fructosemia (Long et al., 2022) and Miscellaneous (e.g., Idiopathic neonatal hepatitis, parenteral nutrition induced cholestasis and hypotension).

Epidemiology of jaundice

Physiological jaundice is the most frequent clinical jaundice. About 50% of hyperbilirubinemia can be attributed to physiological jaundice, with 10% considerably under unconjugated hyperbilirubinemia that requires phototherapy treatment (Nokhsorova et al., 2022). ABO compatibility system serves as one of the major causes of identification followed by G6PD deficiency (Karabulut and Şimşek, 2019). Bilirubin encephalopathy is found in 65 of every 100 live birth in Nigeria has 80% likelihood of Bilirubin (Diala et al., 2018). Another effect of neonatal hyperbilirubinemia is Biliary Atresia, which leads to cholestatic jaundice and can be identified in 25%-40% of all-cause of hyperbilirubinemia. Biliary atresia is a common indicator of liver transplant because the patient with Biliary Atresia would eventually need a liver transplant to survive, even in childhood (Boskabadi et al., 2022). It is estimated that 60% to 70% of patients with Biliary Atresia will eventually require liver transplantation in childhood, and Biliary Atresia remains the most common indication for a pediatric liver transplant (Diala et al., 2018).

Method of diagnosing and treatment of jaundice

Feldman and Sokol (2020) iterated various invasive and non-invasive methods of diagnosing jaundice, but the optimal method involves blood sampling, which is a painful and stressful process that requires direct blood collection from the neonate. It is performed by the caregivers, though the results are not always immediate. Early detection with appropriate treatment is crucial for preventing major neurological hormones. The 20th century is lucky to witness these two major advancements in the treatment of jaundice. They include Exchange transfusion and Phototherapy. Phototherapy came after the discovery of the exchange transfusion method. The major essence of this second intervention is to avoid blood transfusion through the exchange transfusion method.

Materials and Methods

The materials used for the construction of this Bili blanket are a Temperature sensor, Pulse sensor, LCD screen, Buzzer, Arduino board, Blue-green light emitting diode, Wires, Switch, Battery, Timer, Cotton, Ac/dc converter, and Relay.

Temperature sensor

The temperature sensor used during this research is a phototherapy control unit recommended temperature sensor which measures using a digital temperature sensor, the DS1820, with an accuracy of 0.5°C, the DS1820 can measure temperatures between -55°C and 125°C. User-programmable resolution is another feature of the DS1820. Utilizing a unique form of serial connection known as 1-wire, the DS1820 would output the measured temperature to the microcontroller. The protocol is known as 1-Wire because it uses a sensor to transmit temperature data as a serial data stream over a single wire. The microcontroller would output a HIGH (5V) to the transistor-relay switching stage, which switches power to the phototherapy light when the temperature detected is lower than the set/desired temperature and the microcontroller would output a LOW (0V) to the transistor-relay switching stage, which turns power away from the phototherapy light when the temperature detected is at the set or desired temperature.

Liquid Control Display (LCD) (HD44780)

The 14 pins used to connect all HD44780-based character LCD panels are made up of three power lines, three control lines, and eight data pins (D0-D7) (Vdd, Vss, Vee). Some LCDs offer an LED backlight function that makes it easier to read the data on the display in dimly lit areas. They, therefore, have two extra connectors (LED+ and LED-), totaling 16 pins. Actual character data or command/status data are transferred between the LCD module and an external microcontroller depending on the value of the control pin RS. The microcontroller indicates low to read the state of the LCD then transmit commands to it. The R/W pin controls the direction of data flow with the commands/character data written to the LCD module if it is pulled low. Additionally, the character data or status information from the LCD registers is read when it is pulled high. The R/W pin will always be grounded in this arrangement because one-way data communication, from the microcontroller to the LCD module, is employed. The actual data transfer is started by the enable pin (E). Only the high-to-low transition of the E pin is used to send data when writing to the LCD. The LCD module data sheets calls for a +5V d.c. supply to operate, some LCDs may function effectively with a wider range of voltages (3.0 to 5.5V). It is recommended to connect the Vss pin to the ground and the Vdd pin to the positive power source. Vee, which is located on pin 3, is used to modify the display's contrast. The pre-set potentiometer is used to link this pin to a voltage of between 0 and 2V. Data lines are pins 7 through 14 (D0-D7). Either an 8-bit mode or a 4-bit mode can be used to transmit data to and from the display. A byte is conveyed using all eight data lines in the 8-bit mode, whereas a byte is split into two 4-bit values in the 4-bit mode.

Pulse sensor

A 24-inch color code cable, an ear clip, Velcro dots, and transparent stickers are all included with the pulse sensor. A color code cable is attached to header connections.

The size of an ear clip is the same as that of a heart rate monitor. Transparent strikers are layers of protection used to shield the sensor from perspiring fingers and earlobes. This sensor has three holes towards its outer border so that accessories can be connected to it with ease.

Specification

The biliblanket diameter of 0.625m and a thickness of 0.125, this is a biometric pulse rate sensor that can detect heartbeats, with an operational voltage of +5V and +3.3V otherwise, and 4mA of current is used by circuits like amplification and noise cancellation. The microcontroller based used was Arduino Uno Rev 3 on the ATmega 328P (datasheet) having a 16 MHz ceramic resonator (CSTCE16M0V53-R0), 6 analog inputs, 14 digital input/output pins (of which 6 can be used as PWM outputs), a USB port, a power jack, an ICSP header, and a reset button. The control design uses an ATmega328P microcontroller with a 5V operating voltage and a 7V to 12V suggested input voltage range. The I/O consist of digital input and output pins total 14, analog input and output pins total 6, and the DC used for the 3.3 V pin is 50 mA. The controller is enclosed within a concealment which weighs 25g, measures 68.6 mm by 53.4 mm in size, and has an integrated LED. The design ingenuity key benefit of this design is that the microcontroller may be changed if we make a mistake. The DIP (dual-inline package), detachable, and ATmega328 microprocessor are the key features of this board. This board's code may be loaded with ease using an Arduino computer application.

Phototherapy design

The light source was created using an LED, an LED circuitry with automatic intensity regulation based on microcontroller differentiation, the light array was designed with blue LEDs with a wavelength of 460 nm and green LEDs with a wavelength of 500 nm to lower the concentration of bilirubin, the LED blanket was created with dimensions of 16 inches in width by 7 inches according to the Donel prototype in length to allow proper penetration of illumination to cover the entire child's body. The embedded system was designed with an LCD, pulse sensor, temperature sensor DS18B20, and buzzer is connected to the Arduino UNO Rev 3 throughout this process. The LCD pin 15 was linked to the microcontroller 5V pin to test the LCD's functionality initially. Pin 16 of the LCD was next linked to the GND pin of the Arduino. The LCD's backlight is powered by these pins. The experiment was initially run on a breadboard, and the first stage involved soldering a 16-wire connector to an LCD. The LCD's pin 1 and pin 2 were linked to the Arduino's GND and 5V pins, respectively, to set up the LCD's logic. The regulation mechanism of the design uses a potentiometer for adjusting contrast. The terminal of the 10K potentiometer was attached to the Arduino's 5V pin, the middle terminal to the LCD's pin 3, and the third terminal to the Arduino's GND pin. Next, the Arduino was powered up and the backlight on the LCD turns ON. Additionally, the character blocks on the LCD changed brightness and darkness as the potentiometer's knob was twisted.

The GND pin of the Arduino was attached to the LCD's pin 5 (RW). This pin serves as the Read/Write pin and is not used. Next, the digital pin 7 of the Arduino was linked to the LCD's pin 4 (RS). The LCD may be informed if we are sending data or commands via the RS pin (to change the position of the cursor). Next, the digital pin 8

of the Arduino was linked to the LCD's pin 6 (EN). The LCD's EN pin, which is used to signal that data is ready for reading, whereby is the LCD's enabling pin. The LCD's four data pins were then linked, with pin 14 (DB7) of the LCD being attached to pin 12 of the Arduino.

Temperature sensor operational dynamics

The three wires of the DS18B20 sensor are black, red, and yellow. The black pin is used for GND, the red pin is used for Vcc, and the yellow pin is a signal pin. A 4.7K resistor was used for this step. The sensor's Vcc pin, or its red wire, was connected to the 5V supply after the GND pin, or the sensor's black wire, was linked to the ground. The signal pin, commonly known as the yellow wire, was linked to the Arduino's Digital Pin No. 12 and the 5V supply through a 4.7kohm resistor. A buzzer of 5V was incorporated with the ground is connected to "-", whereas the positive voltage is connected to "+." The analog signal output from the sensor is carried on the third "S" wire, which is connected to the Arduino's A0 analog input. A 100-ohm resistor was used to connect the buzzer's Supply wire (RED) to the Arduino's Digital Pin 9. The buzzer's Ground wire (BLACK) was attached to any Arduino Ground Pin. The control circuitry is illustrated in *Figure 1*.

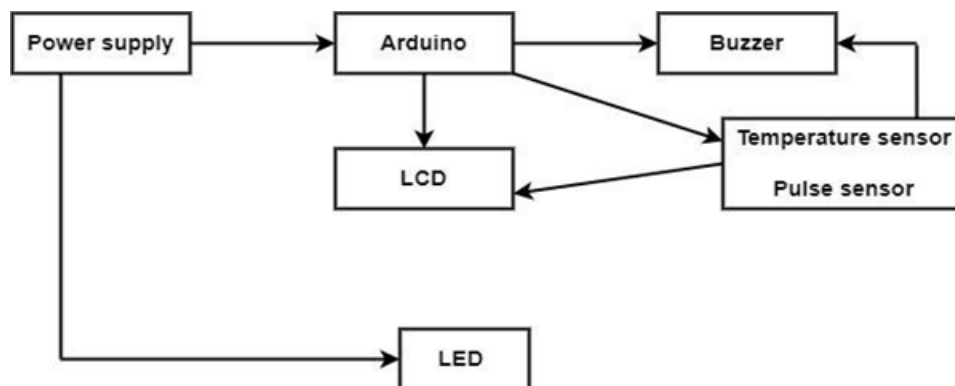


Figure 1. Controller circuitry schematics.

Principle of operation

Arduino Uno Rev 3 was used to programme the control of the design to manage the entire phototherapy session serves as the foundation of the programmable temperature control for phototherapy lamps. The infant's temperature is displayed using a temperature sensor (DS18B20) communication with the internal microprocessor is accomplished using the one-wire bus protocol, which employs a single line. A pulse sensor (SEN 11574) was used to gauge the newborns' blood flow by monitoring variations in light absorption and reflection onto the skin. This design uses a liquid crystal display (LCD) to show the time input as well as the timer's countdown (*Figure 2*). The phototherapy lights can be switched into the manual mode of operation using this digitally controlled light control, which allows manual operation of the phototherapy lights. Additionally, a buzzer that sounds an alarm and notifies the caregiver whenever an infant's temperature rises above 37.8°C is a part of this digitally regulated phototherapy (*Figure 3*).

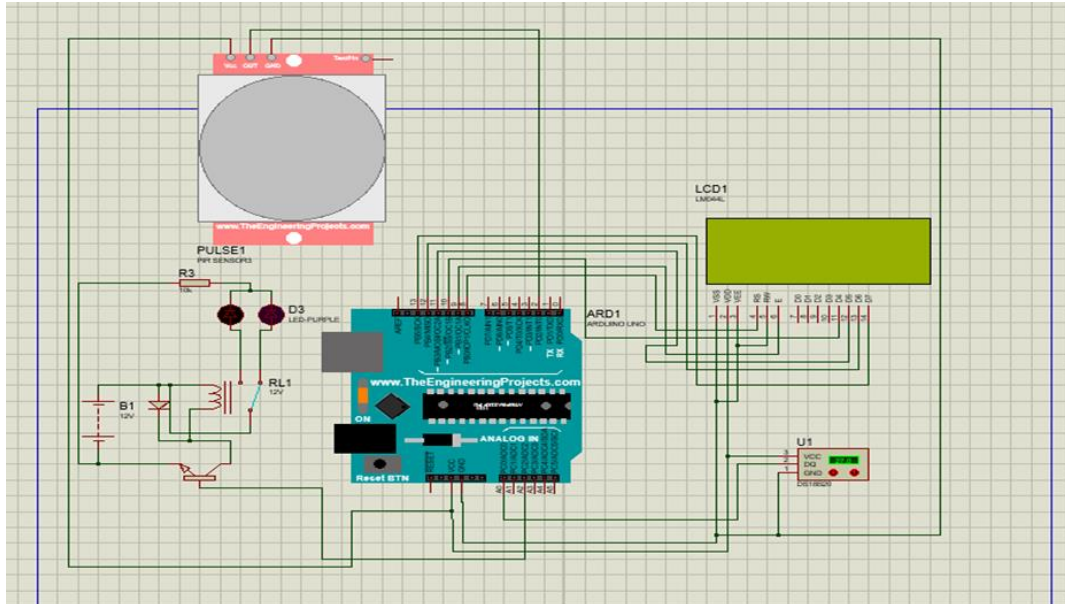


Figure 2. Overall circuit diagram of the embedded system.

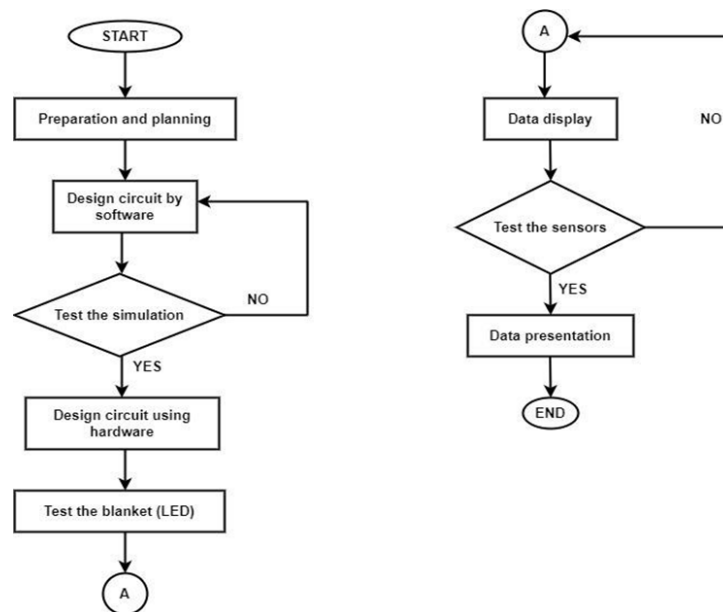


Figure 3. Functionality flow chart.

Results and Discussion

This research was conducted in three phases namely; the simulation phase (i.e a process of implementing on a breadboard), the assembly phase where soldering of the circuits on a printed circuit board, and lastly coupling and reliability test phase which process of different parts and components on the frame. All required materials were incorporated according to specification, a standard requirement of 450-500nm wavelength, $33\mu\text{W}/\text{cm}^2/\text{nm} \pm 15\%$ irradiance, and about 700 cm^2 illumination area this corresponds with the result presented by (Cozzi et al., 2022; El-Masry et al., 2020). The formula below is the eligible equation used in calculating how the LEDs generate illumination:

$$E = \frac{I \cos(\theta)}{R^2} \quad \text{Eq. (1)}$$

Where, E is the illumination in lux, I is light intensity (cd), $\cos\theta$ is the angle generated between the light source and irradiation, and R is the radius between the light source and irradiation area. The conventional phototherapy light with a florescent bulb emits heat of about 1400 which tends to increase the neonate's body temperature. A total of 375 LEDs were distributed appropriately along the board at a matrix of 12 x15 green LEDs and 13 x 15 blue LEDs (Pace et al., 2019). Part of the effectiveness of the LEDs (blue-green) is the ability to not emit a high temperature even when switched on for a long period. The timer also helps to buzz the time giver and automatically turn off the device after 2-3hours as conveniently specified by the medical practitioner. Although research has shown that the blue-green LEDs heat cannot significantly increase the neonatal body temperature, should in case the pulse or body temperature increases above the 100 beats/min and 37°C the buzzer sound comes up and the respective reading is displayed on the screen. As shown in *Figure 4*, the illumination angle for each of the LEDs for higher level of luminance was as 140o as calculated from the Eq. (1). The research is a low-cost development therefore its simulation and testing were done using a breadboard and a circuit simulation platform (proteus). The power supply was initially taken from a standard power supply for circuit designers provided in the laboratory to verify the bibliblanket functionality before being soldered. The project's circuit design performed well on a breadboard and achieved its goals at each level of the design process as shown in *Figure 5*.

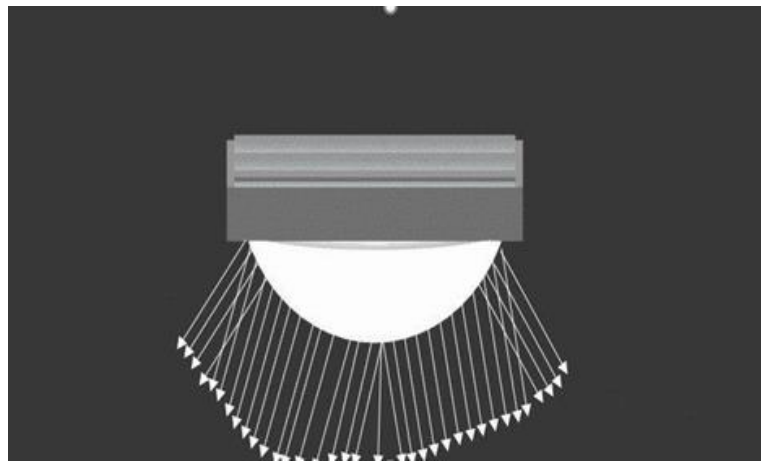


Figure 4. Illumination angle of the LEDs.

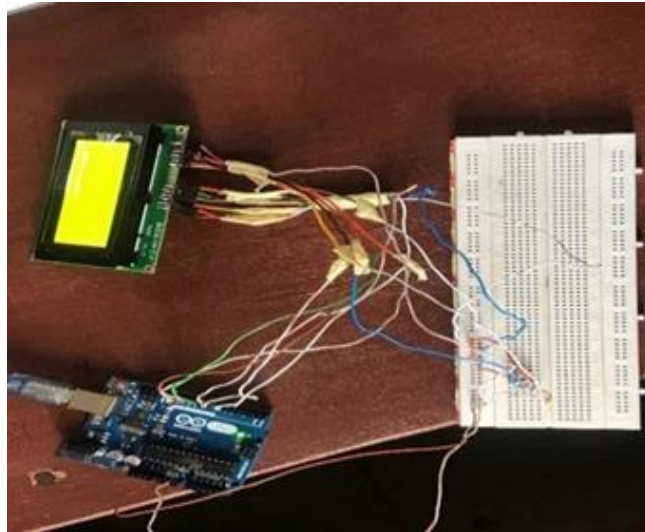


Figure 5. Arduino with LCD.

The components necessary for the developed biliblanket's operation were soldered together following the soldering instructions and relevant safety precautions in a well-ventilated area to keep airborne contaminants out of the breathing zone. Before soldering the digital display, transistor-relay switching, and micro-controller unit, the circuit that powers the power supply unit were initially assembled. On a printed circuit board, the project's soldering was completed. Due to its ability to facilitate communication between various units and components, the printed circuit board is crucial. The project's casing constitutes the third stage of construction. A plastic casing as shown in *Figure 6* was connected to this project. The hardwood case material was constructed with unique vents and perforations, and it was also properly labeled to provide ecstatic value.



Figure 6. Developed low-cost phototherapy neonatal biliblanket.

The electrical setup was evaluated for any errors starting from the power supply unit to the micro-controller unit. Additional runs were carried out to examine collectively and ensure correct feedback and communication from one unit to the next. The following equipment was used during the testing procedure: (1) standard power supply:

Before soldering the project's power source, the breadboard test was conducted using this to deliver voltage to the circuits various stages. The power supply was still used to test various stages before they were finally soldered even during the soldering of the project; and (2) digital multimeter: In essence, the digital multi-meter measures transistor, voltage, resistance, continuity, current, frequency, and temperature. Measurements of parameters such as component voltage, continuity, current, and resistance values, as well as frequency measurements, were necessary for the process of implementing the design on the board. The output of the voltage regulators utilized in this project was evaluated using the digital multimeter.

Upon completion of assembly and in-casing implementation with further evaluation of the electrical unit are undergoes. A hospital situated in a rural area was visited which had at that time 4 cases of hyperbilirubinemia neonates. After proper documentation and different permission requests, the 4 neonates were individually tested at a bound time of 2 hours while being enclosed in the developed biliblanket. The initial levels of bilirubin were measured and the final levels of bilirubin were checked before and after treatment with the bili-blanket. With a simple evaluation metrics, it was shown that bilirubin reduction was at the rate of 79.02% with substantial physical changes being noted in the neonate. To further indicate the efficacy of the prototype, the levels of urinary lumirubin (is an irreversible structural isomer of bilirubin gotten as the result of the photochemical reaction that the native bilirubin undergoes) was checked because of its relation to the clearance of creatin. The urinary lumirubin was tested and the lumirubin fluorescence was analyzed which showed an increasing fluorescence with regular measurements with 30 minutes interval during the phototherapy process using the prototype. The total rate of reduction of serum bilirubin (mol/L/hour) calculated averagely from the individual test subjects was at 6.7 ± 2.05 which is rather significant and reported to deliver an excellent result with further improvements.

This shows that with further amount of time under the bili-blanket, there can be further reduction of bilirubin and elimination of hyperbilirubinemia. The result also shows that the current development of the biliblanket will do a great job in curing hyperbilirubinemia. However, it will perform better with further improvement.

Conclusion

The blue-green smart Bili blanket is designed to enhance bonding between the mother and neonates affected with hyperbilirubinemia. Its efficacy for long hours of phototherapy treatment with safety monitoring and easy therapeutic procedure cannot be over- emphasized. The pulse rate and body temperature value which are pointers to the pathophysiological condition are readily placed on the LED screen of the master device. This would assist the caregivers to monitor hyperthermia, dehydration, and skin lesion, diapers change without stopping the procedure become easy because neonates are now handy and can be easily accessed.

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Conflict of interest

The authors declare that there is no conflict of interest involve in this research study.

REFERENCES

- [1] Anderson, N.B., Calkins, K.L. (2020): Neonatal indirect hyperbilirubinemia. – *Neoreviews* 21(11): e749-e760.
- [2] Begum, N.A., Afroze, S. (2018): An overview of neonatal unconjugated hyperbilirubinemia and it's management. – *Bangladesh Journal of Child Health* 42(1): 30-37.
- [3] Boskabadi, H., Akhondian, J., Taghipour, A., Hashemi, N., Esmaeilzadeh, M., & Nejad Shahrokh Abadi, R. (2022) Neonatal Hyperbilirubinemia and Neurodevelopmental Delay Assessment at 6 Months of Age. – *SSRN Official Portal*. Retrieved from:
- [4] <https://www.ssrn.com/index.cfm/en/>
- [5] Bratton, S., Cantu, R.M., Stern, M. (2019): Breast milk jaundice. – National Cancer Institute 1p.
- [6] Conti, C.S. (2021): Bilirubin: the toxic mechanisms of an antioxidant molecule. – *Arch Argent Pediatr* 119(1): e18-e25.
- [7] Coquery, S.S., Georges, A., Cortey, A., Floch, C., Avran, D., Gatbois, E., Mehler-Jacob, C., de Stampa, M. (2022): Discharge of newborns with risk factors of severe hyperbilirubinemia: description of a hospital at home-based care monitoring and phototherapy. – *European Journal of Pediatrics* 181(8): 3075-3084.
- [8] Cornet, M.C., Kemper, A.R., Maisels, M.J., Watchko, J., Newman, T.B. (2022): Neonatal hyperbilirubinemia and bilirubin neurotoxicity: what can be learned from the database analysis? – *Pediatric Research* 1p.
- [9] Cozzi, L., Nuti, F., Degrassi, I., Civeriati, D., Paoletta, G., Nebbia, G. (2022): Gilbert or Crigler–Najjar syndrome? Neonatal severe unconjugated hyperbilirubinemia with P364L UGT1A1 homozygosity. – *Italian Journal of Pediatrics* 48(1): 1-5.
- [10] Diala, U.M., Wennberg, R.P., Abdulkadir, I., Farouk, Z.L., Zabetta, C.D.C., Omoyibo, E., Emokpae, A., Aravkin, A., Toma, B., Oguche, S., Slusher, T. (2018): Patterns of acute bilirubin encephalopathy in Nigeria: a multicenter pre-intervention study. – *Journal of Perinatology* 38(7): 873-880.
- [11] Dzulkipli, F.A., Mashor, M.Y., Khalid, K. (2018): Methods for determining bilirubin level in neonatal jaundice screening and monitoring: A literature review. – *Journal of Engineering Research and Education* 10: 10p.
- [12] El-Garhy, M.A., Gameel, A. (2021): Antenatal Corticosteroid Exposure As a Risk Factor For Neonatal Hyperbilirubinemia. – *Fayoum University Medical Journal* 8(4): 12-19.
- [13] El-Masry, H., Hassan, A.A., Hashim, A.M., Aladawy, M.A.A., Abdelwahab, A.A.A. (2020): Evaluation of Serum Endothelin-1 (ET-1) and Nitric Oxide (NO) Levels in Unconjugated Hyperbilirubinemic Neonates. – *The Egyptian Journal of Hospital Medicine* 81(4): 1858-1865.
- [14] Fathi, A., Barak, M., Damandan, M., Amani, F., Moradpour, R., Khalilova, I., Valizadeh, M. (2021): Neonatal Screening for Glucose-6-phosphate dehydrogenase Deficiency in Ardabil Province, Iran, 2018-2019. – *Cellular, Molecular and Biomedical Reports* 1(1): 1-6.
- [15] Feldman, A.G., Sokol, R.J. (2020): Recent developments in diagnostics and treatment of neonatal cholestasis. – In *Seminars in Pediatric Surgery*, WB Saunders 29(4): 12p.
- [16] Gaafar, M.M., Rasheed, E.M., Abdel Halim, S.M., El Gendi, M.M.A.M. (2020): Effect of phototherapy on serum level of calcium and magnesium in term and preterm neonates with hyperbilirubinemia. – *The Egyptian Journal of Hospital Medicine* 80(1): 743-747.

- [17] Gani, M.S., Ahmad, M.M. (2021): Pre-experimental study to assess the effectiveness of self-instructional module on knowledge regarding phototherapy among staff nurses working in a selected hospital of Srinagar Kashmir. – *IOSR Journal of Nursing and Health Science* 10(1): 36-42.
- [18] Ifeanyi, O.E. (2019): Physiological jaundice: a threat to the newborns. – *CPQ Medicine* 6(1): 1-4.
- [19] Grossman, M.R., Berkwitt, A.K., Osborn, R.R. (2022): Questioning Our Approach to Hyperbilirubinemia. – *Hospital Pediatrics* 12(4): e137-e139.
- [20] Huda, W.M., Sharma, P., Aggarwa, J., Agrawal, A. (2021): A comparative study of cord blood bilirubin and albumin as a predictor for neonatal jaundice in term newborns. – *Journal of Datta Meghe Institute of Medical Sciences University* 16(2): 295-302.
- [21] Kaplan, M., Hammerman, C. (2004): Understanding and preventing severe neonatal hyperbilirubinemia: is bilirubin neurotoxicity really a concern in the developed world? – *Clinics in Perinatology* 31(3): 555-575.
- [22] Karabulut, B., Şimşek, A. (2019): Effect of Neonatal Hyperbilirubinemia on Ventricular Functions. – *E-Journal of Cardiovascular Medicine* 7(3): 142-146.
- [23] Long, S., Nash, J., Young, M.A. (2022): Newborn Challenges: Hyperbilirubinemia and Hypoglycemia. – *Core Curriculum for Interdisciplinary Lactation Care* 457p.
- [24] Miah, M.M.M., Tazim, R.J., Johora, F.T., Al Imran, M.I., Surma, S.S., Islam, F., Shabab, R., Shahnaz, C., Subhana, A. (2019): Non-invasive bilirubin level quantification and jaundice detection by sclera image processing. In 2019 IEEE Global Humanitarian Technology Conference (GHTC), IEEE 7p.
- [25] Moghadam, M.B., Esmaeili, M., Khosravan, S., Mojtavavi, S.J. (2020): Effects of foot reflexology on neonatal jaundice: A randomized sham-controlled trial. – *European Journal of Integrative Medicine* 38: 7p.
- [26] Mustafa, F.I., Al-Ammri, A.S., Ahmad, F.F. (2017): Direct and indirect sensing two-axis solar tracking system. – In 2017 8th International Renewable Energy Congress (IREC), IEEE 4p.
- [27] Nokhsorova, M., Borisova, N., Ammosova, A. (2022): The Results of Laboratory Studies of Connective Tissue Dysplasia in Children Living in Yakutia. – In Conference on Health and Wellbeing in Modern Society (CHW 2021), Atlantis Press 5p.
- [28] Pace, E.J., Brown, C.M., DeGeorge, K.C. (2019): Neonatal hyperbilirubinemia: an evidence-based approach. – *Journal of Family Practice* 68(1): E4-E11.
- [29] Petterson, M., Eriksson, M., Blomberg, K. (2022): Parental experiences of home phototherapy for neonatal hyperbilirubinemia. – *Journal of Child Health Care* 12p.
- [30] Pranty, A.I., Shumka, S., Adjaye, J. (2022): Bilirubin-Induced Neurological Damage: Current and Emerging iPSC-Derived Brain Organoid Models. – *Cells* 11(17): 24p.
- [31] Qattee, I., Farghaly, M.A., Elgendy, M., Mohamed, M.A., Aly, H. (2022): Neonatal hyperbilirubinemia and bilirubin neurotoxicity in hospitalized neonates: analysis of the US Database. – *Pediatric Research* 91(7): 1662-1668.
- [32] Rai, S., Sood, M., Kaur, A. (2022): Is perinatal asphyxia associated with an increase in serum bilirubin in neonates? A case-control study. – *Journal of Family Medicine and Primary Care* 11(7): 3840-3843.
- [33] Rashwan, N.I., Ahmed, A., Hassan, M., Taqi, F., Mohamed Ahmed, M., Helmi Bakri, A. (2021): Assessments of Serum 25-Hydroxy Cholecalciferol Levels in Neonates with Physiological Jaundice Candidate for Phototherapy. – *International Journal of Pediatrics* 9(5): 13445-13454.
- [34] Seneadza, N.A.H., Insaidoo, G., Boye, H., Ani-Amponsah, M., Leung, T., Meek, J., Enweronu-Laryea, C. (2022): Neonatal jaundice in Ghanaian children: Assessing maternal knowledge, attitude, and perceptions. – *Plos One* 17(3): 13p.
- [35] Slaughter, J.L., Kemper, A.R., Newman, T.B. (2022): Technical report: Diagnosis and management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. – *Pediatrics* 150(3): 42p.

- [36] Turkmen, D. (2020): Serum bilirubin and uric acid antioxidant levels in rosacea patients. – *Journal of Cosmetic Dermatology* 19(10): 2717-2720.
- [37] Wang, Q., Huang, B., Shen, G., Zeng, Y., Chen, Z., Lu, C., Lerner, A., Gao, B. (2019): Blood–Brain Barrier Disruption as a Potential Target for Therapy in Posterior Reversible Encephalopathy Syndrome: Evidence From Multimodal MRI in Rats. – *Frontiers in Neurology* 10: 8p.