

A Methodological Literature Review on Non-Invasive Blood Group Detection

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Abstract— Blood grouping is the method of determining the type of blood inherent in an organism's body based on the unique types of molecules present in their body- namely antigens and antibodies. Blood groups are differentiated based on the general ABO classification system. Identification of the blood group is a key factor, specifically in the field of healthcare. Organ transplantation and blood transfusion require the blood groups of the individuals to be determined rapidly, in case of diseases or accidents. The standard method of blood grouping requires samples of blood to be extracted from the person, which is then directed for further chemical processing. This conventional method is painful and time-consuming; thus, the introduction of a novel non-invasive method would bring convenience to most humans. The proposed systems have generally used visible light for voltage detection, image processing and deep learning algorithms, NIR spectroscopy, and methods of molecular detection in order to yield results. But limited literature based on this subject exists. Hence, this methodological literature review focuses on the existing peer reviewed literature that explores methods related to non-invasive blood grouping. Out of the methods reviewed, voltage detection using visible light and NIR spectroscopy proved to have the highest rates of success.

Keywords: *ABO blood grouping, non-invasive, methodological review*

I. INTRODUCTION

Accurate blood grouping is a mandatory process in the medical field, since mismatches in blood typing can lead to hemolysis which could be fatal (Rudlof *et al.*, 2011). Blood grouping is a prime factor to be considered during blood transfusions, identification of suspects or victims using blood

samples in crime scenes and organ transplantations. During critical conditions like diseases and accidents, where the medical practitioners do not have access to the patient's blood group, but urgent blood transfusions are required, the patient's blood type must be detected rapidly and accurately. Apart from this, people with certain blood groups are more prone to contract certain diseases. This is backed up by the results of a study conducted using 454 patients with gastric ulcers, in which 217 people had the blood group O (Mentis *et al.*, 2014). So, it's of utmost importance that the blood group is determined accurately.

The conventional ABO and Rh detection tests are performed to determine the type of blood. Humans can have the blood groups A, B, AB or O and the Rhesus (Rh) factor can be positive or negative. The genes inherited from one's parents will determine the antigens on the surface of the Red Blood cells and the antibodies in plasma, which in turn will determine the blood group of a person. To perform a traditional blood typing test, a blood sample must be withdrawn from a vein of the patient using a syringe. The blood samples are reacted with monoclonal antibodies and any occurrence of agglutination will be inspected. Commonly used tests are slide tests, tube tests, microplate method and column or gel centrifugation.

This conventional process takes from 10-20 minutes and modern detectors can minimize this time to achieve results within 5 minutes. But devices that minimize the time taken will be expensive (prices ranging above 7000USD) (Zhang *et al.*, 2017). Apart from the added cost, withdrawal of blood samples from a patient under a clinical setting causes discomfort to the patient. This might lead to symptoms like nausea, fainting and in rare conditions, even anxiety attacks can be observed in hemophobic patients. According to statistical data, 2.5% of the human population tends to faint after or during the withdrawal of

blood. ('How Blood Collection Errors Impact Patients', 2021) Moreover, needles can cause bruising at the site of puncture and cause excessive loss of blood in patients with high blood pressure and other blood related diseases, such as hemophilia. Additionally, lacerations and arterial damages can occur, and poorly sanitized needles can increase the risk of pathogens entering the body. The spread of bloodborne pathogen diseases like HIV, malaria and syphilis can escalate when using poorly disinfected syringes.

Given the profusion of the health and safety risks, the cost effectiveness and the length of the detection period, it is comprehensible that non-invasive blood grouping methods will indeed reduce the risk of disease spread. It's a real time

prototype has yet been output to the market. However, existing methods do reveal a promising future in developing this model. This literature review aims to discuss an advanced yet economical method of blood typing, which will elevate the quality of the existing healthcare systems. Furthermore, the limitations of the existing research that have been performed in this field will be identified in order to assist future research.

II. METHODOLOGY

Health based research benefits from methodological literature reviews, mainly because they highlight the methods utilized in their research, their potential benefits and drawbacks. This enables the researchers to reduce the time utilized in scanning the resources.

Table 1. Comparison Methods

Method	Invasive	Time taken	Mean Sample size	References
Visible light- (Voltage Detection, Image processing , Deep learning)	No	Low	103 for voltage detection, undefined for image processing, deep learning	(Patel, Joshi and Khambhati, 2019) (Kumar, Soundariya, Yuvasree and Balasundaram, 2019) (Gayathri, Rekha, Aksha and Nithyakalyani, 2018) (NON-INVASIVE BLOOD GROUP DETECTION, 2016) (Sornalatha, Yamuna, Vasanthi and Yuvarani, 2021) ('Blood Group Measurement using Light Emitting Diode', 2019) (Mehare et al., 2014) (Agarwal et al., 2020)
Maternal samples	Partially invasive	High	400	(Mari et al., 1995; Daniels et al., 2009; Hyland et al., 2009; Clausen, 2014; Rieneck, Clausen and Dziegiel, 2016; <i>Noninvasive fetal blood group genotyping of rhesus D, c, E and of K in alloimmunised pregnant women: evaluation of a 7-year clinical experience - Scheffer - 2011 - BJOG: An International Journal of Obstetrics & Gynaecology - Wiley Online Library</i> , 2015) (Scheffer et al., 2011)
Body fluids	No	High	60	(Metgud et al., 2016) (KAUR and SHARMA, 1988; Motghare et al., 2011; BoKhedher et al., 2020; <i>Effects Of Fabric Materials On Abo Blood Grouping Of Blood Group A And B From Blood</i> , 2018)
Antibodies	No	High	120	(Boettcher and Kay, 1973)
Spectroscopy	No	Low	70	(Sultan et al., 2018)

procedure, meaning that the time delay in displaying the results will be minimal and it does not pose any of the side effects that invasive methods do. Thus, developing a non-invasive blood group detection method will be beneficial to society. Existing research has used detection methods like optical signaling and spectroscopy, which will be discussed in detail throughout this review. The feasibility of these procedures cannot be accurately guaranteed since a limited amount of literature is available and no successful device or

Thus, to perform this literature review an effective, methodological approach was used. To compile the literature review, a meta-ethnography was conducted- following the Noblit and Hare's seven stepped technique. (Cunningham et al., 2019)

A. Step 1-Focus of the Review

The research scope was initially established; in this case, it was the feasibility of several non-

invasive blood grouping approaches. Methods which were partially invasive were also examined due to the limitation of resources.

B. Step 2-Area of Relevance

To study the area of interest, peer reviewed articles and scientific journals that explore blood grouping and non-invasive methods were explored. Initially the keywords were noted down and their synonyms were listed. The keywords were chosen to be 'blood-grouping', 'non-invasive', 'spectroscopy' and 'ABO classification'. The listed synonyms were 'blood typing', 'spectrometry', 'spectroscopic analysis', 'spectrographic analysis', 'non-intrusive', and 'minimally intrusive'. To narrow down the search results, Boolean operators including 'and' and 'or' were employed.

This resulted in keyword combinations such as "Blood grouping and non-invasive methods", "Blood Types and spectroscopy", "Non - invasive ABO classification", "Minimally intrusive or non-invasive detection methods" and "Spectrographic analysis and blood grouping". The titles and abstracts of recently written and published (most were peer-reviewed) research articles were skimmed and scanned, to obtain the latest literature. To obtain the relevant research articles, databases including google scholar, PubMed, Science Direct and ResearchGate were used.

C. Step 3- Examining the Studies

Out of the 50 results that were obtained, the articles of controlled studies that were frequently cited were chosen. To compose the literature review, the articles were ordered based on the relevance after scanning the abstracts of all articles. The number of citations were also considered. Only 22 research articles were chosen based on these criteria.

D. Step 4-Relationship Between Studies

The recurrent methods of blood grouping were identified along with their properties. A table was set up to compare the identified approaches (Table 1).

E. Step 5- Translating Between Studies

The data were critically analyzed and tabulated based on methods used, increasing frequency of occurrence of the method, time taken for detection and sample sizes.

III. LITERATURE REVIEW

The following review depicts the final two stages of Noblit and Hare's approach - the synthesis and the expression of the translations. Recent developments in the medical field have introduced non- invasive methods of blood group detection. Limited resources were available in analyzing this approach since it is a novel method. The following will analyze the relevant literature, based on the methods used.

A. Visible Light

Out of the 22 unique research articles that were analyzed, 8 used non-invasive optical methods.

1) *Voltage Detection*: In 5 of the proposed systems, (Patel, Joshi and Khambhati, 2019) (Kumar,Soundariya, Yuvasree and Balasundaram, 2019)(Gayathri , Rekha , Akmha and Nithyakalyani, 2018)(NON-INVASIVE BLOOD GROUP DETECTION, 2016) ('Blood Group Measurement using Light Emitting Diode', 2019) voltage detection techniques were used, with a mean sample size of 103 individuals. Light was passed through the finger and the photodetector at the receiving end detected the transmitted signal. The detected signal was converted into a digital format and the change in voltage was detected. The signals were processed in order to identify the voltage ranges by an Arduino (Uno) board or a Node MCU. Depending on the voltage range, the type of blood was determined. To minimize the scattering of light these methods used LEDs. The voltage ranges that were commonly observed across multiple researches are summarized in Figure 1.

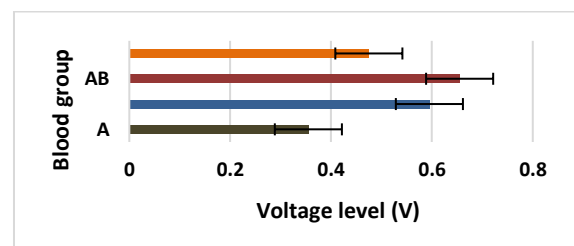


Figure 3. Voltage ranges identified for different blood groups

2) *Image Processing*: Two studies employed image-processing systems (Sornalatha, Yamuna, Vasanthi and Yuvarani, 2021) (Mehare et al., 2014), where the image obtained using a digital camera was converted to a digital format and pre-processed. The image was developed and structured and the noises were eliminated by filtering. The intensity was adjusted, and the image was broken down into pixels to be displayed on a

screen. The pathway of the absorbed light due to hemoglobin and the scattered light due to the antigens was monitored, which represents the unique blood group. The results are depicted in Figure 2. This method is rapid and can be used in any setting due to its non-invasive nature. These apparatuses are lightweight, cheap and do not pose any side effects. But its accuracy is limited due to variation in factors like blood pressure, finger size and colour and the limited sensitivity of the camera used by the image processing technique. The sample size was also undefined. These optical devices are still at the research level and none of these prototypes have yet been manufactured at an industrial scale.

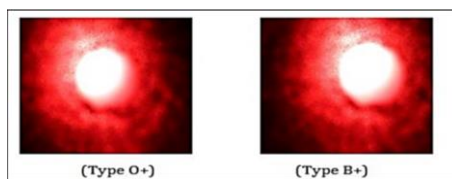


Figure 2. Blood groups identified by image processing
Source: (Mehare *et al.*, 2014)

3) *Deep Learning*: A rare study (Agarwal *et al.*, 2020) used deep learning algorithms to process the data. In this research, a high-resolution camera captures 100-200 images of the fingertip placed over a light source. The dimensions of the image were fixed, and image thresholding was performed. The images were preprocessed by gray scaling, denoising and enhancing the contrast and were converted into binary images. Pixel locations were obtained for the focused area. The model was trained by the input of pre-set values obtained from hospitals. This was used to extract the features using the Gray scale co-occurrence matrix. Depending on the morphological features the output will vary, which can detect the blood group. But the accuracy of this method cannot be validated since only a single study was conducted on this topic and morphological differences can affect the image acquired. The results obtained and sample size were not clearly expressed.

B. Maternal/ Fetal DNA

As it was revealed by 7 different studies, it is evident that maternal plasma contains traces of fetal DNA and antigens. Several researchers obtained samples of maternal and sometimes paternal plasma or cord blood, which were then filtered to obtain fetal DNA samples and amplified by PCR techniques. Employing several DNA extraction and identification processes, the fetal components were analyzed. The results were used

to determine the blood group of the fetus, to perform RHD genotyping and to identify any blood related diseases. Methods including genotype testing, next generation sequencing and doppler ultrasound were employed for this process. These methods could only be used for the detection of fetal DNA, to diagnose the blood type and any blood related condition, but postnatal detection cannot be performed by using maternal samples. The level of accuracy was identified as extremely high; in one research where the RHD was determined, out of the 140 samples tested 135 were diagnosed with RHD positive accurately (Mari *et al.*, 1995). This is further substantiated by the large mean sample size that was used, which was 400. But this still requires chemical processing; thus, the time taken to provide the results would not be effectively decreased. Though this method is non-invasive to the fetus, it will be an invasive process for the mother. Another limitation observed through one research (Scheffer *et al.*, 2011) was that the results from genotyping or cord blood serology could be observed in only 59% of the women, thus the feasibility is jeopardized. Also, in early stages of gestation (below 11 weeks) the concentration of fetal DNA is extremely low in the maternal blood, which could lead to false results.

C. Body Fluids

Body fluids can also assist in the detection of blood types. Saliva, urine, vaginal samples and amniotic fluid contain traces of antigens in secretory groups of people. Once the fluid samples were collected by spitting/ excreting, they were isolated by centrifuging and conventional chemical tests were run to isolate the antigens and to detect the blood group. 80% of the human population were proved to be secretors, meaning that they secrete antigens into the body fluids (Motghare *et al.*, 2011). A study involving 80 individuals (Metgud *et al.*, 2016) obtained saliva samples and by using absorption-inhibition/elution methods, it was proven that blood groups A and O were absolute secretors (100%) and 95% of AB and B were secretors. The results of this research are represented in Figure 3. This evidence was backed up by 5 other studies. (KAUR and SHARMA, 1988; Motghare *et al.*, 2011; BoKhedher *et al.*, 2020; *Effects Of Fabric Materials On Abo Blood Grouping Of Blood Group A And B From Blood*, 2018). However, not all individuals are secretors and certain blood types may or may not secrete the antigens. Thus, this method cannot be used for all patients. Furthermore, the sample sizes used in

these researches were inadequate and the validity cannot be assured. Though the method is fully non-invasive, the use of chemical tests would increase the time taken to detect the blood group.

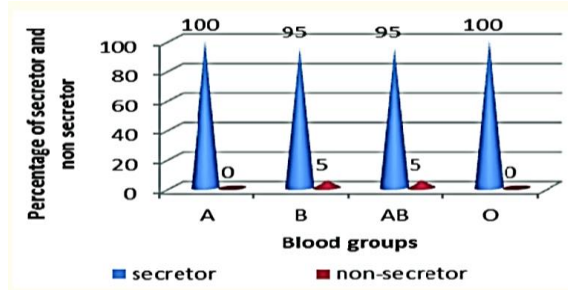


Figure 3. Secretor comparison for each type of blood. Source: (Metgud *et al.*, 2016)

D. Radioactive Antibodies

One interesting research (Boettcher and Kay, 1973) was conducted using Radioactive antibodies from hair samples obtained from humans. The hairs were crushed, radioactively marked and was used to develop x-ray films after adding reagents which are used for blood grouping. The results were compared with standard ABO blood samples (Table 2). However, this research did not produce results for the blood group O and antigen A and insufficient amount of research has been done by using this method. Moreover, preparation of samples took a large amount of time.

Table 2. Accuracy of the results obtained for radioactive antibodies

ABO RBC type	Number of subjects	Number of subjects showing results						
		H	A	B	A+H	B+H	A+B+H	NR
A	5	1						4
AB	3	1				1	1	
B	4			1		3		
O	5	3						2
A ₂	3	1						2
A	8	1	3		4			
B	9			3		6		
O	6	6						
A	3		1					
O	4	4						
O	2	1			1			

Source: (Boettcher and Kay, 1973)

E. Spectroscopy

NIR photon transmission spectroscopy is based on the concept that different antigens have unique interaction of photons, thus creates varying levels of scattering and absorption. (Sultan *et al.*, 2018) In this the 850 nm transmitter was placed as a cuff around the lower arm and the RF absorption levels were measured by using the receiver. Modulation and demodulation is performed by the network analyzer. The changes in wave amplitude and phase were displayed (Insertion and phase losses)

as a spectrogram for each type of blood, in which the Rh factors for each blood type were also considered unlike the optical method. These in vivo values were compared with values from an experiment performed in vitro. The two results had a correlation greater than 0.95, indicating that non-invasive blood typing provided accurate results similar to invasive processes. Among the methods that were explored, this displayed the highest level of accuracy, with least complications and lowest detection time. However, the sample size that was used was relatively low (70).

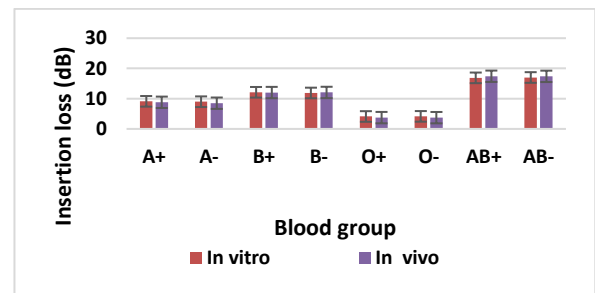


Figure 4. In vivo /In Vitro results from NIR photon transmission. (Sultan *et al.*, 2018)

IV. DISCUSSION

Out of all the literature that were reviewed, it can be deduced that the visible light-voltage detection method of blood grouping had the highest reliability because it was the only method which had 8 research-based evidence out of the non-invasive techniques, and it took less time for detection. However, no prototype has yet been introduced to the society and all models are still at the primary trial levels due to the limitations posed; the sensitivity of the instrument should be very high to obtain an accurate measurement of light that is detected after passing through several layers of the body. This will increase the cost of production and make it undesirable. The variations in morphology will also affect the results. The sample sizes used for image processing and deep learning techniques were undefined. Despite its advantages, the validity of the deep learning method proved to be inconclusive since the results were not displayed. The NIR photon transmission method that was discussed proved to have the highest accuracy and detection speed based on the results, and the Rh factors were also considered, unlike the optical method. Yet its validity is inconclusive due to the shortage of literature and it did not use a considerably large sample size to validate the accuracy. Limited evidence was available to prove

the effectiveness of the detection methods using body fluids and antibodies, they did not yield results for all blood groups, and were time intensive. Maternal fluid testing which was carried out to determine the blood group of the neonate produced successful results, with the highest reported sample size. However, it requires maternal samples; thus, it is not fully non-invasive.

V.CONCLUSIONS

Significant amount of evidence exists to prove that the development of a method to detect blood groups non-invasively is successful. The major problem is the accessibility of the antigens from the external environment, since the human body is composed of several layers. If this barrier could be overcome, more accurate results could be obtained. This would also require cheaper yet highly precise detection instruments that could be used as an alternative to the expensive detectors that are currently proposed. The visible light-voltage detection method had the highest reliability, but NIR spectroscopic analysis proved to have a high accuracy in detection (due to the comparison of in vivo and in vitro samples producing a large correlation value of 0.95), with the least detection time. If more research-based evidence existed and a larger sample size was used to back up the method, it can be concluded that NIR spectroscopy has the highest feasibility out of all the methods considered. The development of a functional NIR spectrometer for blood group detection would be a major breakthrough in the healthcare sector. Thus, my area of research will be based on a low-cost, lightweight, and an accurate wearable NIR spectrometer that can non-invasively detect blood groups in clinical and forensic settings, crime scenes and war zones, using an embedded signal transducer and receiver that can detect the blood type in a small time span with high accuracy. This innovation could contribute to a colossal development in the fields of biomedical engineering, computer science and medicine.

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