Non-Invasive Detection of Anemia (NIDA)

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ACRONYMS

LR Likelihood Ratio. 2

NPV Negative Predictive Value. 2

PPV Positive Predictive Value. 2

Non-Invasive Detection of Anemia (NIDA)

***Abstract*—NIDA, an open-source software that noninvasively detects hemoglobin concentration using raw image from a consumer camera and a color calibration card.The patient pull lower conjunctiva downwards with one hand while holding a color calibration card in the other hand. Photographs are then taken and analyzed using the software. Hemoglobin measurement is a standard clinical tool commonly used for screening anemia and assessing a patient's response to iron supplement treatments. Anemia is a major health burden worldwide. Although the finding of conjunctival pallor on clinical examination is associated with anemia, inter-observer variability is high, and definitive diagnosis of anemia requires a blood sample. My goal was to develop a low cost and non-invasive screening test for anemia .**

I. Introduction

The advancement of computing technologies have revolutionized the health care facilities providing cost effective and remote health care platform. A number of research has been conducted for the detection of anemia using digital photographs, however no dedicated software was developed [1], [2]. Smartphone application such as HemaApp can non-invasively monitors blood hemoglobin concentration using the smartphone's camera and various lighting sources but is limited to the devices for which it has been calibrated [3]. In this paper I present NIDA an open-source software that can noninvasively detect hemoglobin concentration using raw image.

Anemia is considered as a proxy indicator of iron deficiency [4] because it is defined as an abnormal iron biochemistry with or without anemia [5]. Iron deficiency reduces the learning capacity of the children aged below five years, decreases attentiveness, and causes low intelligence [6]. The consequences of anemia for women include increased risk of low birth weight or prematurity, perinatal and neonatal mortality, inadequate iron stores for the newborn, increased risk of maternal morbidity and mortality, and lowered physical activity, mental concentration, and productivity. Women with even mild anemia may experience fatigue and have reduced work capacity [7].Thus, anemia leads to decrease of the actual economic productivity of human resources and ultimately impacts on the development of the country [6], [7].

The gold standard for anemia diagnosis is ex-vivo measurement of hemoglobin concentration in whole blood. This method requires venepuncture and specialized equipment, which may introduce delays or be unavailable in resource-poor settings [2].

Hemoglobin predominantly absorbs green light and reflects red light, and as a result hemoglobin concentration affects tissue color [8]. An "erythema index" (EI) has been developed to objectively quantify the degree of erythema of skin lesions, using digital photography followed by analysis of the red and green components of images [2], [8], [9].

II. Problem Definition

About 58% children between the age 6–59 months are anemic with Hb level less than 11.0 g/dl.Non-pregnant women between age 15–49 years having Hb level less than 12 g/dl is 53.1% and pregnant women between age 15–49 years who are anemic($<$ 11.0 g/dl) is 50.3%. Among men, anemia is less with about 23% men being anemic with Hb level less than 13.0 g/dl [10].

Although nutritional problem is very common in all states, it is more prevalent and severe in the particular states, whose performances are very poor in respect of the other important demographic and socioeconomic indicators. The Government of India (GOI) has named these states as Empowered Action Groups (EAG) states, which consist of Uttarakhand, Uttar Pradesh, Madhya Pradesh, Bihar, Odisha, Jharkhand, Chhattisgarh, and Rajasthan. The EAG states comprise almost 45% of Indian population [6].

There is currently no health services being provided by the government or private organizations which is cost-effective , convenient and reaches people across all rural and urban areas. Also, no medical history is maintained of the people which can be accessed digitally across the globe.

III. Proposed Solutions

A quick and convenient delivery of health services which can reach distant areas, this will reduce footfall in government hospitals, with service delivery closer-to-home. To use the best of what we have we could use the basic services already provided to the consumer through eMitra (G2C and B2C services provided by the government of Rajasthan). Government of Rajasthan have set up the eMitra platform of eGovernance way back in the year 2004. Currently, covering all rural and urban areas in 33 districts of Rajasthan. EMitra platforms already have the access to computers, cameras and printers. So, a technology which could use these already available facilities to provide health services would be beneficial for the people.

The solution provided in this paper aimed to detect anemia by quantifying conjunctival pallor using digital photographs taken with a consumer camera. Before it could be used, refinement of the image standardization technique to reduce the impact of device and lighting characteristics is required [2]. Following techniques could be used for the refinement of the image standardization.

A. White calibration card

Conjunctiva of patients are photographed in ambient lightning using a digital camera alongside an in-frame calibration card. Mean brightness of the color calibration card's white square is used for standardization.

B. Medical history and color-scale combined

Clinical history with the use of a color-scale while assessing for conjunctival pallor. Disintermediation and robustness are more important for this use case than confidentiality and performance, hence a blockchain database maybe preferred over regular databases.

IV. Research Methodology

There was a cross-sectional observational study of hospital inpatients and outpatients attending Wellington Blood and Cancer Centre, a regional haemato-oncology service [2]. De-identified participant data are available from the Dataverse which contains hemoglobin results, erythema index values, reproducibility data, and clinician consistency values [11]. Proposed solution A ("White calibration card") [2], [12] is used as case study in the following analysis and result is compared with prior studies done using proposed solution B [13]. Photographs of the case study were taken at a distance of approximately 40 cm, and framed to include the eye and color calibration card within the same image and the same coronal plane. Automatic focus was used throughout. Photographs were taken without flash and saved using the RW2 file format . The internal white balancing feature was utilized, using a white sheet of paper as a reference.

Images were loaded in OpenCV and were standardized using a previously established method [14]. Each images was split into its 8-bit red, green and blue channels using the OpenCV $cv :: split()$ function. From the image white square was selected and its mean brightness was calculated. Each channel's brightness was adjusted by multiplying its brightness by $200/M_B$, where M_B is the mean brightness of the color calibration card's white square. Then each channels were merged to produce 24-bit white-balanced image and saved for future assessment. The other set of the standardized color channels was then used for EI analysis.

The EI was determined using the equation reported by Yamamoto et al [9], [15].

$$EI = \log S_{red} - \log S_{green} \tag{1}$$

where, S is the brightness of the conjunctiva in the relevant color channel. Since, these were 8-bit color channels, the $\log$ value has to be scaled for results within the pixel scale of 0–255. The scaling $\log$ function used was:

$$f(p) = 255 * \log p / \log 255 \tag{2}$$

The function was applied to all three color channels. Following this the log green channel was subtracted from the log red channel using the OpenCV $cv :: subtract()$ function. Palpebral portions of the conjunctiva was selected individually using a polygon tool made in QML and OpenCV. The intensity of the pixel brightness of the selection is the EI. In the appendix code used for this process is provided.

V. Analysis and Interpretation

Digital EI analysis using the data [11] showed that it identified 70% of images as anemic or not anemic whereas clinician assessment showed that clinicians were less accurate with images, scoring mean 60.33%. Digital EI analysis resulted in a higher positive likelihood ratio and stronger statistical association between conjunctival pallor and proven anemia than assessment by clinicians. Table I shows test characteristics of conjunctival pallor assessment by three clinicians compared with digital EI analysis for detection of anemia (hemoglobin < 11.0 g/dl). Threshold of < 18.14 for anemia detection used for conjunctival EI values from photographs [2].

	Digital Image EI	Clinician 1	Clinician 2	Clinician 3
PPV	0.76	0.59	0.62	0.71
NPV	0.67	0.63	0.52	0.58
Positive LR	3.39	1.16	1.29	2.02
Sensitivity	0.57	0.88	0.62	0.58
Specificity	0.83	0.24	0.52	0.71

TABLE I
Comparison of palpebral conjunctival EI with clinician assessment

	(I) Clinical pallor	(II) I + Medical history	(III) II + Color scale
Sensitivity	0.74	0.78	0.83
Specificity	0.76	0.85	0.91

TABLE II
Sensitivity, specificity for detecting anemia at three sequential phases of assessment

Prior studies shows that solution B have improved test characteristics by combining a clinical history with the use of a color-scale while assessing for conjunctival pallor, increasing sensitivity from 74% for pallor alone to 83% when medical history and color-scale were combined. However sensitivity remained low for milder degrees of anemia [13]. Sensitivities (Hb < 11 g/dl)and specificities (Hb > 11 g/dl) improved consistently over the three sequential phases of clinical assessment based on pallor, medical history and the color scale in each category of anemia as seen in Table II.

Although the method of image standardization used by solution A is cost effective and less complex it was not able to eliminate the effect of ambient lightning on EI. Using the color scale in assessing conjunctival pallor improved both sensitivity and specificity although an important point to note is that in each subsequence phase of clinical assessment relatively, greater improvement occurred in specificity than in sensitivity. Perhaps the evidence indicates the improved ability to correctly diagnose non-anemic subjects who were inaccurately diagnosed in the preceding solution. In real situations the accuracy of clinical assessment by the paramedics may decrease over time, especially in the absence of regular examination of patients; thus, occasional training may be necessary to maintain their level of skills. On the other hand, implementation of solution B would require larger database and online access to it, which would increase its complexity. A blockchain database would be preferable here so that the transactions would be shared on a peer-to-peer basis across the densely connected nodes across different locations. End users generating the transactions connect to (say) 5 of these nodes, so it doesn't matter if a few communication links go down.

And if one or two nodes fail completely on any given day, nobody feels a thing, because there are still more than enough copies to go round. As it happens, this would combine low cost systems and high redundancy.

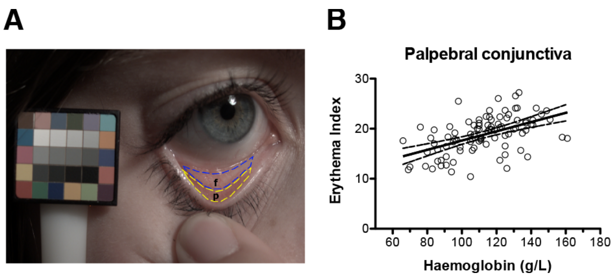

Fig. 1. Relationship between erythema index and hemoglobin for palpebral

Fig.1 (A) Representative calibrated image from a non-anaemic participant showing the palpebral (p) of the conjunctiva. The in-frame color calibration target is shown. (B) Relationship between palpebral conjunctival EI derived from images and measured hemoglobin. Solid line represents best fit by linear regression.

VI. Usage

A. Data input

Before any analysis can be done, an input image file that focuses conjunctiva and a color calibration card must be read, processed and loaded in NIDA. For this click on $File->Open$ and select the image. The image will be loaded in the window as follows

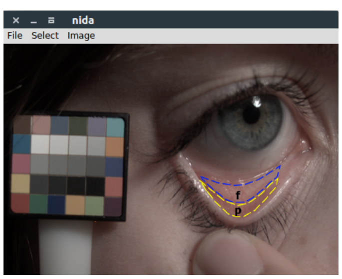

Fig. 2. Main window with image loaded

B. Standardization technique

Before the image could be used,refinement of the image to reduce the impact of device and lighting characteristics is required. Click $Select->Rectangle$ and select the white square in the calibration card.

C. Image analysis

Since the image has been loaded successfully, it's time to do the analysis. Click $Image->Split$ and then $Image->ROI$. The image with be loaded in $OpenCV$; standardization algorithms will be performed.

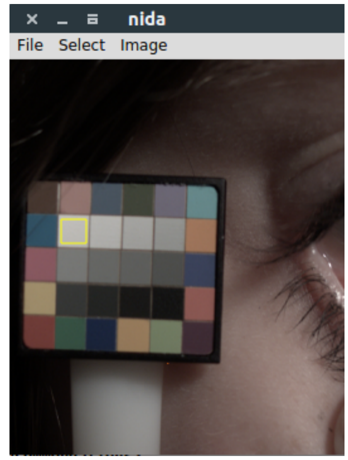

Fig. 3. White square of calibration card selected

D. Getting the EI

Palpebral portions of the conjunctiva will be selected using the 'polygon' tool to maximise sampling area and measured on the EI image. Click $Select->Polygon$ and select the conjunctiva, the yellow portion in the image shown below is the palpebral conjunctiva. Click $Image->Palpebral$ and a dialog box will be opened giving the EI.

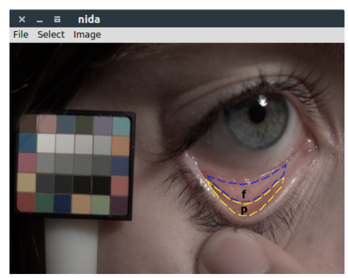

Fig. 4. Yellow portion of the image is conjunctiva

VII. Conclusions and Recommendations

NIDA is an open-source software that noninvasively monitors the hemoglobin concentration using digital photographs. In this study two image standardization technique was analyzed and reported method of quantifying erythema of skin lesions (the erythema index, EI) to quantify conjunctival pallor from digital images. White calibration card image standardization technique proved to be the most cost effective of the alternatives. Medical history and color-scale combined image standardization technique, though a viable option in other contexts, was shown to lack adaptability.

Non-invasive screening for anemia could have numerous applications, particularly in resource-poor settings. A dedicated open-source software to automate image analysis and to predict risk of severe anemia was developed. This study suggest that NIDA has potentials for noninvasive detection of anemia and provide a means of health services to wider audience particularly poor districts in India especially EAG states. To validate the results, a larger national and international study that includes more demographic will need to be deployed.

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