Non-invasive Self-Care Anemia Detection during Pregnancy Using a Smartphone Camera

M D Anggraeni*, A Fatoni

1Department of Nursing, Faculty of Health Sciences, Universitas Jenderal Soedirman, Purwokerto, Indonesia
2Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Jenderal Soedirman, Purwokerto, Indonesia.

*E-mail: mekar.dwi@gmail.com

Abstract. Indonesian maternal mortality rate is the highest in South East Asia. Postpartum hemorrhage is the major causes of maternal mortality in Indonesia. Anemia during pregnancy contributes significantly to postpartum hemorrhage. Early detection of anemia during pregnancy may save mothers from maternal death. This research aim to develop a non-invasive self-care anemia detection based on the palpebral color observation and using a smartphone camera. The color intensity (Red, Green, and Blue) was then measured using a Colorgrab software (Loomatix) and analyzed compared to the hemoglobin concentration of the samples, measured using standard Spectrophotometer method. The result showed that the red color intensity had a high correlation ($R^2=0.814$) with a linear regression of $y=14.486x + 50.228$. This preliminary study may be used as anemia early detection which more objective compared to visual assessment usually performed.

1. Introduction
The maternal mortality rate (MMR) among Indonesian mothers is the highest in ASEAN country[1]. The MMR in Indonesia was 228 per 100,000 live births in 2007 and it increased up to 359 per 100,000 live births in 2012 [2, 3]. The MMR in Indonesia is still far from the Millennium Development Goal's target which stated that the MMR should be 102 per 100,000 live births in 2015 [4]. Several factors contribute to the high MMR in Indonesia. According to Khan [5], the principal cause of MMR in Asia was a hemorrhage. The Indonesian Ministry of Health [4] also reported that the major cause of MMR during 2010-2013 remained the same, it was a hemorrhage. In 2013, 30.3% of Indonesian mothers died due to hemorrhage during the perinatal period. There was a significant association between perinatal hemorrhage with anemia status [5, 6]. The lower hemoglobin level during pregnancy caused the higher risk of postpartum hemorrhage [7]. The combination between low hemoglobin level during pregnancy and postpartum hemorrhage contributed significantly to 40 - 43% of maternal death in Africa and Asia [8].

Anemia during pregnancy is a public health problem in developing countries. More than 50% of pregnant mothers in developing countries were anemic [9]. In addition, Indonesia Basic Health Research [4] reported that 37.1% of Indonesian women suffered from anemia during pregnancy. Anemia early detection may prevent Indonesian mothers from postpartum hemorrhage [10]. Several strategies are conducted by the Indonesian government to reduce anemia during pregnancy. It includes anemia early detection which is conducted during trimester 1 and 3 of pregnancy at the health care facilities. Then,
the pregnant mothers are categorized into certain anemia status. The anemia cut-offs among pregnant mothers are divided into normal: >11g/dL, mild: 10 - 10.9g/dL, moderate: 7 - 9.9g/dL, and severe: < 7g/dL [11]. The Indonesian health care providers use several methods to detect anemia among pregnant mothers.

Several methods have been developed to detect hemoglobin levels, such as immunoassay, electrochemical, chemiluminescence, high performance liquid chromatography and mass spectroscopy. Those methods require expensive equipment, complicated sample preparation, and trained analysts. In the other hand, a physical examination has long been used to detect anemia status among pregnant mothers by health care providers. The anemia status is evaluated by looking at the reddish color of the inside lower eyelid. A pale red color shows an anemia status but a pink to clear red color shows a non-anemia status [12]. This method has long been used by health care providers, particularly who have limitation to access modern testing instruments. However, this method requires examiner's experience and has a high subjectivity. Develop a simple instrument to detect the anemia status by using the reddish color of the lower eyelid may increase the result's objectivity. Pregnant mothers also may use the simple instrument to detect the anemia status by themselves.

The use of simple equipment for colorimetric analysis (color comparison) pioneered by Liebhafsky and Winslow in 1950 that using a light bulb and a cylindrical graded to determine the levels of iron and copper in the water[13]. Furthermore, various studies has been reported in the use of simple equipment as an analytical tool, such as using a scanner to determine iron (III) [14], camera to detect complex starch-iodine and biological markers (biomarkers)[15] and chromium - iron [16]. Nowadays, almost everyone has a mobile phone with camera-equipped. This phone camera could be an opportunity as a self-tool for camera-based detection. We reported the use of a mobile phone application to detect anemia among pregnant women, which would replace the conventional method of anemia early detection by visual observation of palpebral conjunctiva color. The method was based on the capturing of a digital image of the inferior palpebral conjunctiva using a mobile phone. The color of the palpebral conjunctiva was then correlated with the participant's hemoglobin levels obtained by the standard method performed in the hospital. In this way, the evaluation of the inferior palpebral conjunctiva would more objective compared to the visual assessment. Another factor which may affect the hemoglobin level to predict the anemia were also collected, including the parity status, age, body mass index, blood type and geographical altitude of the participants. This self-care early anemia prediction would easy, fast, accurate as an important anemia monitoring status among pregnant women. Furthermore, the application will be used widely by the health professionals and the society as a self-care method as early detection of anemia during pregnancy especially in the location which the absence of modern instruments to detect hemoglobin.

2. Materials and Methods

2.1. Study design
Blood samples were collected from a local hospital. The palpebral image was captured using smartphone of Asus Zenfone and the image was analyzed using ImageJ software. Blood hemoglobin was measured using a Shimadzu Biospec 1601 UV-Vis spectrophotometer (Shimadzu, Japan). Blood sample was collected from the participants using standard method used in the hospital, continued by analyzing their hemoglobin level.

2.2. Palpebral conjunctiva imaging
Palpebral conjunctiva digital image was taken using smartphone camera (Asus ZenFone 2 Laser, rear camera, 13 MP, laser autofocus, f/2.0 aperture). Participants asked to hold the lower eyelid with their right hand to easily observe the palpebral conjunctiva, while their right-hand holds a white paper as the white correction (Fig 1). Photograph of palpebral conjunctiva was taken in ambient lighting, without flash, and at a distance about 30-40 cm.
2.3. Image analysis
Images were transferred from the smartphone to a laptop running Windows 8.0 (Microsoft) with a free software image analysis of ImageJ version 1.48v (National Institute of Health, USA). The image was recorded their color intensity of Red, Green, and Blue for both palpebral conjunctiva and white paper as a standard white color. The white color standardized was performed by assuming white paper would have color intensity for both R, G and B of 255. The real color intensity of white when they were less than 255, then added to the sample color intensity.

2.4. Data analysis
Raw data of color intensity (Red, Green, and Blue) of palpebral conjunctiva were collected. In another side, hemoglobin (Hb) level of the participants was analyzed using the standard method of spectrophotometric. Color intensity as the dependent variable was then analyzed using simple regression (Microsoft Excel, Data Analysis) related to Hb level as the independent variable. This regression analysis would result in a regression equation, linear regression chart, and correlation coefficient.

3. Results and Discussion

3.1. Study Participants
Twenty pregnant patients were asked as participants during the research. The age of participants were 22 – 36 years with an average of 28 years. The blood type of participants including A, B, AB and O. Body mass index (BMI) were 19 – 32.5 with an average of 25.6. Geographical altitude based on their address were 25 – 230 with an average of 84.4 m above sea level. All participants have consumed Fe tablet during their pregnancy.

3.2. Palpebral conjunctiva imaging and data processing
All participants were asked to take their palpebral conjunctiva photograph by the research assistant. The image capturing may be repeated in case of low light condition or sufficient view that it should be included the white calibrator paper and palpebral conjunctiva easily observed. The color intensity of palpebral conjunctiva images was corrected their white balance using paper as a reference color. For example, when white paper intensity (R,G,B) was 200,200,200, then the color intensity of palpebral conjunctiva was added their correction based on the maximum color intensity of 255, which was in this
example of 55 (255-200). Many strategies have been reported to correct the digital image color intensity as detection tools, such as software-based white balance [17], red label based white balance [18], standardized color palette [19] and white paper. The use of white paper as the standard white color was simple and easy to apply in wide condition and location, including rural application. The color intensity after correction was then used for further study, analyzing using simple regression related to a hemoglobin level of each participant.

3.3. Regression analysis
The results showed a significant relationship between palpebral conjunctiva image color intensity and hemoglobin concentration of the participants. Among three color intensity (RGB), the red color intensity showed the highest relationship with \( r^2 \) of 0.8139 (Fig. 2). The correlation coefficient (\( r \)) of 0.92 was showed a high correlation [20] between red color intensity and hemoglobin concentration. However, the highest sensitivity of this color intensity versus Hb level was the blue color, with the slope of 17.89 with an \( r^2 \) of 0.568. Therefore, we could conclude the best color intensity to predict the Hb level using palpebral conjunctiva image was the red color intensity, considering the highest coefficient of determination.

The limit of detection (LOD) was calculated based on the regression equation of red color intensity. The calculated LOD was 3.79 g/dL, which was lower than the cut of severe anemia during pregnancy of < 7g/dL. Thus, this imaging based anemia prediction could be used as early detection of anemia during pregnancy.

![Figure 2. Relationship between palpebral conjunctive color intensity and measured hemoglobin (n=20). Dotted line represents best fit by linear regression.](image)

3.4. Factor affecting hemoglobin level
Many factors have been reported to make a variation of the hemoglobin level, such as body mass index (BMI) [21], parity [22] and geographical altitude [23]. We also analyzed this parameter that may would
influence in the proposed anemia prediction. The result showed a weak correlation [24] between BMI and hemoglobin level, with a correlation coefficient of 0.27 which was similar to the previous report [21]. The altitude of the participant was analyzed using online map based on Google map (www.daftlogic.com/sandbox-google-maps-find-altitude.htm) by looking for their address, and mapping on the online altitude map assistant. The result showed no correlation between altitude hemoglobin levels with a correlation coefficient of 0.07 ($P > 0.05$). The similar hemoglobin level may due to the participants were from 25 to 230 m above sea level, with an average of 84.4 m above sea level. The previous study reported that the altitude affected the hemoglobin level in the order of 3000 ft (914 m) above sea level [23], thus, below the 914 m such in this research would not significantly different. The blood type was no correlation between hemoglobin level and blood type with a correlation coefficient of 0.21 ($P > 0.05$). The parity status of the participants was nullipara ($p_0$) of 12%, primipara ($p_1$) of 65% and multipara ($p_2$) of 24%. A previous study [22] reported that the parity was directly related to the prevalence of anemia (low hemoglobin level), however, in this research, the parity was also showed no correlation with the hemoglobin level ($r$ of 0.05, $P > 0.05$), which may due to all participants had consume Fe tablet during their pregnancy.

4. Conclusion

Smartphone camera could be used as non-invasive and self-assessment of anemia prediction, with a high correlation between red color intensity of palpebral conjunctiva and blood hemoglobin concentration and calculated LOD of 3.79 g/dL. The use of digital image would more objective compared to conventional visual assessment usually perform in the rural region as early diagnostic of anemia.

References

[1] Organization W H 2015 *World health statistics 2015*: World Health Organization
[2] Indonesia S 2008 Indonesia demographic and health survey 2007 Jakarta/Calverton: National Family Planning Coordinating Board, Ministry of Health and Macro International
[3] Nasional B K K B 2013 Survey demografi dan kesehatan Indonesia (SDKI) 2012 Jakarta: BKKBN
[4] Indonesia K K 2015 Profil kesehatan Indonesia tahun 2011
[5] Khan K S, Wojdyla D, Say L, Gülmezoglu A M and Van Look P F 2006 WHO analysis of causes of maternal death: a systematic review *The lancet* 367 1066-74
[6] Frass K A 2015 Postpartum hemorrhage is related to the hemoglobin levels at labor: Observational study *Alexandria Journal of Medicine* 51 333-7
[7] Christian P 2008 *Handbook of Nutrition and Pregnancy*: Springer pp 319-36
[8] Sloan N L, Jordan E and Winikoff B 2002 Effects of iron supplementation on maternal hematologic status in pregnancy *American Journal of Public Health* 92 288-93
[9] Candido F and Hofmeyr G 2007 Treatments for iron deficiency anemia in pregnancy: RHL commentary *The WHO Reproductive Health Library. Geneva: World Health Organization*
[10] Risnawati I and SN A H P 2015 Anemia in pregnancy effect on postpartum hemorrhage *Jurnal Ilmu Keperawatan dan Kebidanan* 6 57-67
[11] Organization W H 2011 Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity
[12] McKinney E S, Murray S S, James S R and Nelson K 2013 *Maternal-child nursing*: Elsevier Health Sciences)
[13] Kehoe E and Penn R L 2013 Introducing colorimetric analysis with camera phones and digital cameras: an activity for high school or general chemistry *J. Chem. Educ.* 90 1191-5
[14] Kompany-Zareh M, Mansourian M and Ravaee F 2002 Simple method for colorimetric spot-test quantitative analysis of Fe (III) using a computer controlled hand-scanner *Anal. Chim. Acta* 471 97-104
[15] Oncescu V, O'Dell D and Erickson D 2013 Smartphone based health accessory for colorimetric
detection of biomarkers in sweat and saliva Lab Chip 13 3232-8

[16] Firdaus M L, Alwi W, Trinoveldi F, Rahayu I, Rahmidar L and Warsito K 2014 Determination
of chromium and iron using digital image-based colorimetry Procedia Environmental
Sciences 20 298-304

[17] Seo J-H, Park Y-B and Park Y-J 2014 Reliable facial color analysis using a digital camera and
its relationship with pathological patterns: a pilot study European Journal of Integrative
Medicine 6 322-7

[18] Zhao Y, Tao J and Tu P 2013 Quantitative evaluation of efficacy of photodynamic therapy for
port-wine stains using erythema index image analysis Photodiagnosis and photodynamic
therapy 10 96-102

[19] Collings S, Thompson O, Hirst E, Goossens L, George A and Weinkove R 2016 Non-Invasive
Detection of Anaemia Using Digital Photographs of the Conjunctiva PloS one 11 e0153286

[20] Asuero A, Sayago A and Gonzalez A 2006 The correlation coefficient: An overview Crit. Rev.
Anal. Chem. 36 41-59

[21] Ghadiri-Anari A, Nazemian N and Vahedian-Ardakani H-A 2014 Association of body mass
index with hemoglobin concentration and iron parameters in Iranian population ISRN
hematology 2014

[22] Uche-Nwachi E, Odekunle A, Jacinto S, Burnett M, Clapperton M, David Y, Durga S, Greene
K, Jarvis J and Nixon C 2010 Anaemia in pregnancy: associations with parity, abortions and
child spacing in primary healthcare clinic attendees in Trinidad and Tobago

[23] Ruiz-Argüelles G J 2006 Altitude above sea level as a variable for definition of anemia Blood
108 2131-2

[24] Munro B H 2005 Statistical methods for health care research vol 1: Lippincott Williams &
Wilkins)