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Automatic Platelets Counter for Supporting Dengue Case Detection in Primary Health Care in Indonesia

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Abstract

Dengue fever is a major problem in many developing countries, including Indonesia. Laboratory examination is used to diagnose dengue infection and to monitor disease progression. Hematology tests, such as platelet count, are also used for timely recognition of the development of severe dengue. In primary health care centers platelet counting is typically performed manually, which is labor intensive and requires an experienced laboratory technician. To address this challenge, we have developed an automatic platelet counter for primary health care and resource-poor settings. The technology is based on a conventional microscope equipped with a digital camera linked to a personal computer, which can capture and analyze microscope images of blood samples. To evaluate the accuracy of the technology, it was compared to platelet counts performed manual by an experienced laboratory technician. Statistical analysis shows no difference between the techniques with a kappa coefficient of 0.6. This method is judged to have great potential as a tool to help primary health centers and other facilities with limited resources to deal with the burden of dengue.

Keywords:
Dengue, Platelet Count, Computer-Assisted Image Analysis.

Introduction

Dengue fever is a major threat to people's health in many low and middle-income countries, including Indonesia. Dengue is a viral infection transmitted by mosquitoes of the genus aedes, such as *Aedes aegypti* and *A. albopictus*. The infection causes a spectrum of illness, ranging from no symptoms or mild fever to severe and fatal hemorrhage, depending on the patient's age and immunologic condition. The global burden of dengue is large with potential for further spread due to globalization of trade [1], change in travel behaviors [2] and climate change [3]. Early and correct diagnosis of dengue infection in primary care settings has potential to reduce the risk of complications if applied wisely. Platelets count and hematocrit values are important laboratory tests to perform [4] since thrombocytopenia, i.e., low platelet count, is often relied upon as an important criterion for the diagnosis of dengue. Furthermore, these tests are recommended to be repeated frequently to allow prompt recognition of the development of dengue hemorrhagic fever, which can be fatal. Unfortunately, many primary healthcare facilities in dengue endemic areas are lacking laboratory support and access to tools that can provide a reliable diagnosis. Consequently, many primary health centers rely on manual techniques for hematology examination, which is a subjective and labor-intensive strategy. To address this challenge, we have developed a new method for automatic platelet count based on a personal computer and a standard microscope equipped with a digital web camera. The new technology aims to be low-cost, easy to use and will add value to the effort of improving dengue diagnosis and management in Indonesia.

Methods

This project has used an action research methodology to address the challenge of developing an automatic platelet counter for primary health care settings in Indonesia. The platelet counter is based on a standard microscope Olympus CX series equipped with a 5-megapixel web camera that can capture and transfer images to a personal computer with dual core CPU 1,66 GHz and 1 GB of RAM. The software was developed using C#.net and Matlab was applied to develop the algorithm to enable automatic detection and count of platelet in the microscope images.

A blood sample is applied to the microscope film and the camera is mounted on the microscope, capturing an image of the sample. The image is transferred to the computer and converted into gray scale with a resolution of 1024 x 768 pixels. The grayscale image is subsequently inverted to increase contrast and minimize the background noise. The next step of the image processing is to analyze the size and morphology of each blood cell. Platelets are usually less than 30 pixels in size and this operation will differentiate platelet from other blood cells. Thereafter, the Otsu algorithm [5] is applied to enhance the image differentiation and produce binary maps. This map is thereafter used to automatically count the number of platelets (Figure 1).

To evaluate the performance of the software in identifying and counting platelets from microscope images, the method was compared with the standard manual procedure as performed by an experienced laboratory technician. The expert has been working for more than five years in a clinical pathology laboratory and has additionally received a certificate in Good Clinical Laboratory Practice (GCLP).

19 different microscope slides with blood samples from healthy donors were assessed in this primary evaluation. Each blood sample was analyzed by the expert and by the new software independently, but at the same time to prevent miscalcu-

lations due to sample handling and cell degradation. Kappa coefficient was calculated to measure inter-rater agreement.

Results

We have developed a software that can be used to detect and count platelet automatically. The software works based on image processing technology and applying an algorithm proposed by Otsu [5]. The detailed illustration of the image processing, from original image derived from the microscope to the image visualizing the platelets, is shown if Figure 1.

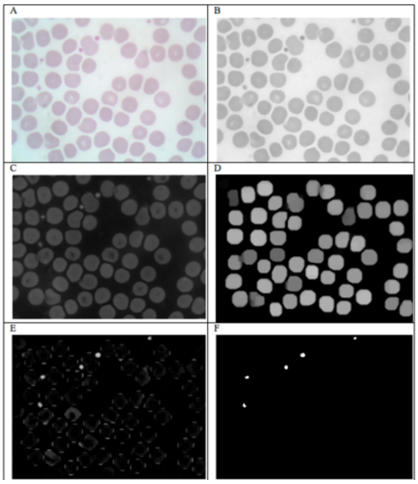

Figure 1 – Illustration of the different image processing steps. A) original image, B) original image converted to grayscale, C) inverted grayscale image, D) grouping of sizes and morphologies E) application of the Otsu algorithm F) final image showing the platelets in binary format

To make a first assessment of the method, results from automated platelet counts were compared with manual platelet counts performed by a laboratory expert. Each slide was coded with a number from 1-19. The results are summarized in Table 1.

Table 1 – Platelet counts using two methods: manual counts performed by laboratory expert and computer-generated counts using the new system

Images	Manual	Computer based	Difference
Sample 1	3	3	0
Sample 2	2	2	0
Sample 3	5	6	1
Sample 4	1	3	2
Sample 5	3	3	0
Sample 6	2	2	0
Sample 7	3	1	2
Sample 8	2	2	0
Sample 9	1	1	0
Sample 10	5	5	0
Sample 11	1	1	0
Sample 12	4	4	0
Sample 13	3	3	0
Sample 14	3	2	1
Sample 15	1	2	1
Sample 16	2	1	1
Sample 17	2	3	1
Sample 18	4	6	2
Sample 19	1	1	0

For 11 of the 19 samples, i.e., in 59% of the cases, the agreement of the two methods was 100%. For the remaining 8 samples, the difference in counts was 1-2 platelets. The variation is fairly random and when compared to the manual counts, the computer software overestimated the number of platelets in five cases and underestimated the number of platelets in three cases. Statistical analysis shows no significant difference between the two methods of examination (p=0.48). The kappa coefficient is 0.6 which can be interpreted as 'moderate agreement".

Discussions

The lack of infrastructure, financial as well as human resources in primary health care settings causes ineffectiveness in the dengue control programs in Indonesia. In addition, it is relatively common that patients experiencing fever for more than a few days visit the hospitals directly instead of consulting the primary health centers. The primary health center, however, is the institution responsible for the health of the community and it is important to equip these centers with useful and appropriate technology to support the national dengue control programs. The use of a low cost webcam technology connected to a conventional microscope and desktop computer could become instrumental in this work.

Although this study was of limited scope, the method of counting platelets using image processing shows great promise. The kappa coefficient is currently 0.6 indicating moderate agreement between the computer-based and the manual method. With further development of the software this is expected to increase further by allowing identification of aggregated cells and identification of platelets on the boundaries of the image. Currently only single platelets are identified and counted. In addition, judging by the rapid growth of the information society and access to affordable camera technology, the technical performance of the system can be improved despite the limited resources available.

To assess the future potential of this technology fairly, it should be kept in mind that expensive commercially available instruments for hematology tests and cell counts are known to have certain limitations. In a recent study, 23 different hematology analyzer models based on, e.g., impedance, optical scatter, optical fluorescence, and immunologic flow cytometry, were assessed and compared to the international reference method (IRM) [6]. The platelet counts were overestimated in 66.3% of specimens and significantly overestimated in 16.5% of specimens according to this study. Another study has reported inaccuracy in platelet detection in cases of acute leukemia and disseminated intravascular coagulation (DIC) [7]. Moreover, the morphology of platelets in activation stage or a micro-angiopathy in patients with cancer caused inaccuracy in platelet detection [7]. Hence, we agree with Sutor et al., who suggest that automatic platelet detections should be used with care, particularly in cases of thrombocytopenia [8]. Visual evaluation with phase-contrast microscope can be applied to differentiate platelet from non-platelet particles and was previously considered as the gold standard [9,10], despite being time-consuming and considered imprecise at low counts [11]. Quality control should thus be prioritized [12] and clinical condition should always be used when interpreting the results from platelet counts [13–15].

One important aspect that we wish to emphasize is that the system has been developed using minimal resources and with resource-poor settings in mind. Microscopes are standard equipment that is available in all primary health centers in Indonesia, while PCs now are becoming common. Latest survey from the ministry of health reported that 78,4% of primary health centers already has at least one computer [16]. The only additional investment needed for implementing the system is a camera. A high-resolution camera can still be considered too expensive for health centers with limited budget. We have therefore chosen a low-resolution web-camera, which has proven sufficient for this application although it also leaves room for improvement. Many web-cameras cost less than 50 USD depending on the manufacturer.

This work additionally aims to stress the importance of primary health centers to invest in efficient data documentation and management systems, as well as electronic health records. It is still rare for primary health centers in Indonesia to store microscope images. While blood samples cannot be kept after examination, the images derived from this system can be stored together with other important patient information. The digital data format brings many advantages, including the opportunity for engaging dengue experts in the clinical judgment using tele-consultations and adding value to the education of medical students. Furthermore, although this system has been developed with dengue in focus, it is important to note that there are a number of conditions and cases where platelet count is of major importance [6,7].

Beside the positive aspects that we have mentioned, there are a number of challenges left to be addressed that can potentially delay the adoption of this system among other electronic health information systems and methodologies in Indonesia. The first challenge relates to technological infrastructure. Access to a computer and reliable electricity supply are the minimum requirements to implement the system and power failure is still common in many health care facilities across Indonesia. The second challenge is related to the user capacity and receptiveness to new work models. For example, the process of introducing new technology in the health sector should not disregard the importance of proper training to make the users familiar with and confident enough to use the application. The third challenge relates to standards and regulations and is an important national as well as international concern. Since the data is related to patient care and safety, clear regulations regarding, e.g., data access and storage, encryption and file format should be in place when implementing the system.

Conclusion

We have developed an automatic and low-cost platelet counter that can be used to help health practitioner in primary health care centers and resource-poor setting to support dengue case detection and management. Using this technology, it is now possible to capture and store digital images from conventional microscopes, and to calculate the platelets using the newly developed PC-based software. Although the results are promising, further development and evaluation are needed to assess the reproducibility, accuracy and precision of the instrument. There are no data available on the variation in counts between two independent manual assessments, which also has to be assessed to argue for a replacement of these proven methods. Furthermore, large-scale evaluation with blood samples from various conditions and from patients of different ages and sexes would be highly valuable to improve the accuracy of the software.

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