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Correlation between Hematologic Parameters and Asymptomatic Bacteriuria in the Full-Term Pregnant Patients in Dr. Kariadi Hospital, Semarang, Indonesia

Muhammad Syukri[1], Ratnasari Dwi Cahyanti[1], Besari Adi Pramono[1*]

[1] Obstetrics and Gynecology Department, Diponegoro University, Indonesia – Kariadi General Hospital Semarang

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*) Correspondence to:
babas1504@yahoo.com

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ABSTRACT

Background: Asymptomatic bacteriuria is the presence of bacteria in the properly collected urine of a patient without signs or symptoms of a urinary tract infection. possible. Hematological parameters are easily measured at low cost using modern hematological analyzers. These parameters are widely used for risk stratification, diagnosis, and determination of prognosis

Objective: We investigated the role of hematologic parameter such as hemoglobin, white blood cells, platelet, hemoglobin platelet ratio (HPR), hemoglobin white blood cells ratio (HWR) in full-term pregnant patients and correlate the result with their urine culture following delivery.

Methods: Between 2019-2020, a total number of 95 pregnant patients were retrospectively evaluated at the maternal ward.

Results: The average age of the subjects was 29.15 (SD ± 5.95), median of parity of 2 (range 1- 4) and mean of gestational age was 37.5 (SD ± 1.67). There is no difference between groups on the surgery types and comorbidities condition. Among the patients, 14 urine cultures produced growth of 105 CFU/ml bacteria. Pearson's correlation test showed that leukocyte inversely correlated with bacteriuria, meanwhile hemoglobin white blood cell ratio (HWR) is positively correlated with urinary culture result. In the diagnostic performance, HWR had AUC of 0.765 with sensitivity and specificity of 78.6% and 64.2% respectively at the cut off of 11.92.

Conclusion: Prediction of asymptomatic bacteriuria in pregnant patient by simple calculation of HWR might be helpful in significantly reducing workload and costs of urine culture. It is a great advantage that the parameters we use in our work are easily accessible and can be performed in emergency conditions

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1. Introduction

Asymptomatic bacteriuria is the presence of bacteria in the properly collected urine of a patient without signs or symptoms of a urinary tract infection. This condition is very common in daily clinical practice.[1] Pregnant women are specific population with higher risk of asymptomatic bacteriuria as well as urinary tract infection.[2] The prevalence of asymptomatic bacteriuria in pregnant women is approximately 2%–10%.[3] Their reduced immunity appears to encourage the growth of both commensal and noncommensal microorganisms. Asymptomatic bacteriuria in pregnancy poses a significant risk because untreated cases have a high likelihood (up to 40%) of progressing to acute pyelonephritis that can cause morbidity and even death of the mother and fetus. Treatment should be provided immediately to prevent perinatal complications such as bacteremia, premature birth, and low birth weight.[3–5] Besides pregnancy, route of delivery especially cesarean section has been suggested to increase the risk of urinary tract infection and bacteriuria up to 2.5 times compared to vaginal delivery. [6]

The gold standard for the diagnosis of a urinary tract infection is the detection of the pathogen in the presence of clinical symptoms. The pathogen is detected and identified by urine culture (using midstream urine). This also allows an estimate of the level of the bacteriuria. Asymptomatic bacteriuria (ASBU) is present if a patient does not exhibit the clinical signs of UTI and the upper limit of ≥ 105cfu/mL is exceeded in two consecutive properly collected samples of midstream urine on women.[7,8]

Although the conventional method of urine culture is time-consuming, about 70–80% of urine culture results are negative. Due to the lack of other reliable diagnostic indicators, clinicians often obtain urine cultures in patients without localizing urinary symptoms or positive culture results.[7] To address the shortcomings of urine culture, several researchers are trying to find a rapid screening method that can reduce the necessity of urine

culture, which will have a significant impact on the overall turnover time and laboratory economy.[9,10] Frequently used screening items such as microscopy analysis for WBCs and bacteria as well as dipstick testing and nitrite in urine are fast but with low sensitivity yet still costly.[7,10–12] Therefore, rapid screening, accurate prediction yet affordable of culture results are needed for clinicians shorten the diagnosis time, improve the efficiency and accomplish the treatment opportunity for patients as early as possible. Hematological parameters are easily measured at low cost using modern hematological analyzers. These parameters are widely used for risk stratification, diagnosis, and determination of prognosis.[13–15]

In this study, we investigated the new parameter using routine blood testing on the the full-term pregnant patients admitted to our maternal ward and correlated the results of blood parameter with bacteriuria confirmed by urinary culture following cesarean delivery. We evaluated the hemoglobin, white blood cell (WBC), platelet, hemoglobin to white blood cell ratio (HWR), hemoglobin to platelet ratio (HPR), platelet to white blood cell (PWR) to predict the asymptomatic bacteriuria on the selected population. To the best of our knowledge, this is the first time that these markers have been investigated in predicting asymptomatic bacteriuria in full-term pregnant women.

2. Methods

This study is done in Kariadi teaching hospital in Semarang, Indonesia in the period of July 2019 to August 2020. The study population consists of 95 full-term pregnant women. Blood sample was taken prior to delivery and sent for routine blood count consists of hemoglobin, leukocytes, platelet, RDW, and MPV. Urine sample is then collected following delivery and submitted to urine culture

Data were analyzed using the IBM Statistical Package for Social Sciences v25 (SPSS, Inc., Chicago, IL, USA). Descriptive statistics, such as frequencies or percentages for categorical variables and mean (± standard deviation) and median for continuous variables, were used to describe baseline demographic data and clinical characteristics. The variables were investigated using analytic methods (Kolmogorov Smirnov test) to determine whether or not they are normally distributed. The Mann-Whitney U test or Student's t-test were applied to compare continuous variables, depending on the normality of the data distribution. The p-values <0.05 were considered to be statistically significant for all analysis. Correlations between variables were examined using Spearman's correlation analysis. Receiver operating characteristics (ROC) curve used to assess the validity of the studied indices in bacteriuria from urinary culture result. The interpretation of AUC depends on the standard cut off points as followed: Significance was considered when P value equal to 0.05 or below.

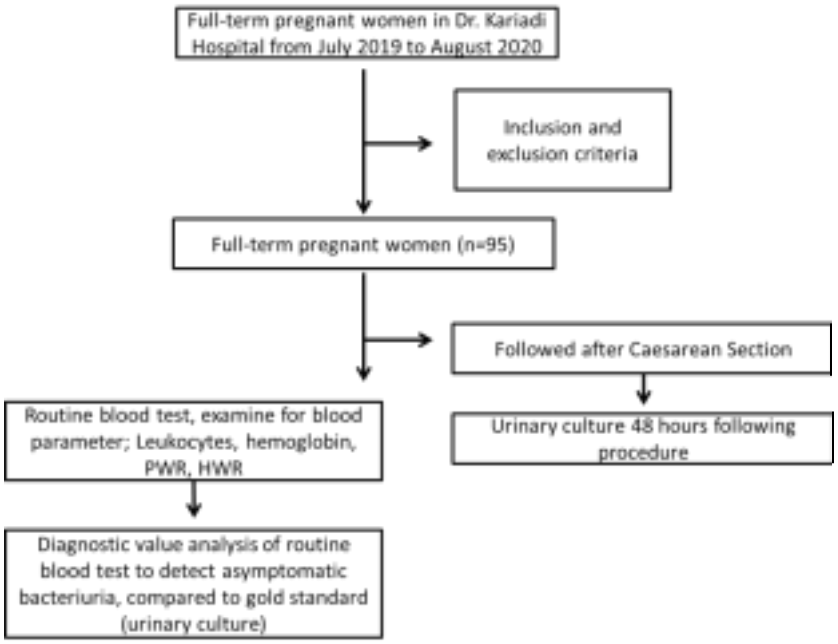

Figure 1. Schematic flow of the study.

3. Results

Between July 2019 to August 2020, a total number of 95 full-term pregnant patients were admitted to maternal ward for delivery. The average age of the subjects was 29.15 (SD ± 5.95), median of parity of 2 (range 1-4) and mean of gestational age was 37.5 (SD ± 1.67). There is no difference between groups on the surgery types and comorbidities condition. Among the patients, 14 urine cultures produced growth of 105 CFU/ml bacteria. The comparison of hematological parameters revealed that hemoglobin, platelet, hemoglobin platelet ratio (HPR),

and platelet white blood cell ratio (PWR) level was not significantly different between bacteriuria and non bacteriuria groups. Meanwhile, leukocytes and hemoglobin-white cell ratio were significantly different between the groups (Table 1)

Table 1. Data distribution was tested using Kolmogorov Smirnov. Differences between patients with bacteriuria and non-bacteriuria based on urinary culture result were assessed using the independent sample t test

Characteristics	All patients n=95 (100%)	Bacteriuria n=14 (14.73%)	No Bacteriuria n=81 (85.26%)	P-value
Age, mean (SD)	29.15 ± 5.95	29.07 ± 6.03	29.17 ± 5.98	.953
Parity, median (range)	2 (1-4)	2 (1-3)	2 (1-4)	
Gestational age, mean ± SD	37.5 ± 1.67	37.07 ± 1.49	37.59 ± 1.71	.292
Laboratory				
Hemoglobin	11.22 ± 1.39	11.64 ± 1.22	11.15 ± 1.41	.231
Leukosit	10.89 ± 3.43	9.21 ± 2.93	11.18 ± 3.45	.047*
Platelet	267.69 ± 67.73	258.35 ± 67.7	269.30 ± 68.03	.579
HPR	0.45 ± 0.18	0.48 ± 0.16	0.45 ± 0.19	.541
HWR	11.13 ± 3.03	13.52 ± 3.15	10.71 ± 2.83	.001*
PWR	26.89 ± 10.22	30.65 ±12.55	26.24 ± 9.71	.137
Surgery type				
Cito, n (%)	21 (22.1)	4 (28.6)	17 (21)	-
Elective, n (%)	74 (77.9)	10 (71.4)	64 (79)	-
Comorbid				
HIV, n (%)	16 (16.8)	1 (7.1)	14 (17.3)	-
SLE, n (%)	1 (1.1)	1 (7.1)	0 (0)	-
Obesity, n (%)	3 (3.2)	0 (0)	2 (2.5)	-

Pearson's correlation test showed that leukocyte inversely correlated with bacteriuria, meanwhile hemoglobin white blood cell ratio (HWR) is positively correlated with urinary culture result. There was no correlation on the other parameters such as hemoglobin, platelet, HPR and PWR to bacteriuria (Table 2). Diagnostic performance of HWR for asymptomatic bacteriuria was assessed using ROC curve analysis and AUC as shown in figure 1. HWR had AUC of 0.765 with sensitivity and specificity of 78.6% and 64.2% respectively at the cut off of 11.92.

ROC curves showing the relative diagnostic performance of Hemoglobin to White Blood Cell Ratio (HWR) for prediction of bacteriuria in patients with asymptomatic bacteriuria following cesarean section.

Table 2. Results of Pearson correlation test between research variables

No.	Research Variable	Coefficient Correlation (r)	Direction of correlation	P-value
1	Hemoglobin	0.124 (weak)	Positive	.231
2	Leukocytes	0.205 (weak)	Negative	.047**
3	Platelet	0.058 (weak)	Negative	.579
4	Hemoglobin White Blood Cell Ratio (HWR)	0.329 (moderate)	Positive	.001**
5	Hemoglobin Platelet Ratio (HPR)	0.064 (weak)	Positive	.541
6	Platelet White Blood Cell Ratio (PWR)	0.154 (weak)	Positive	.137

4. Discussions

Asymptomatic bacteriuria (ASBU) is a common problem in pregnant women as different complications could be seriously progressing to acute pyelonephritis that can cause morbidity and mortality to both mother and fetus. However, diagnosis is difficult because of the asymptomatic nature of the condition. Besides, urine culture as the gold standard in determining ASBU is not routinely performed in the clinic as it is time consuming and is not cost effective. [1,9,16] Therefore, it is important to have a more rapid and affordable screening diagnostic tool of asymptomatic bacteriuria in pregnant women.

It is generally believed that when UTI occurs, it is often accompanied by inflammation, and the number of red blood cells (RBCs), WBCs and other parameter in the blood will shift. [13,17] We found that some parameters such as hemoglobin, platelet and related ratio are not significantly different between our study groups. Similarly, Tartar et al showed that the laboratory values of patients with pyelonephritis and urosepsis with and without bacteremia were compared and found that hematologic parameters are not significantly different. [18] However, the study has different population to ours, in which we investigated pregnant women that warrant treatment for asymptomatic bacteriuria.

In the present study, HWR in differentiation between bacteriuria and non-bacteriuria groups was assessed using the ROC curve analysis which revealed that lower HWR were significant predictors and were able to differentiate between bacteriuria and non-bacteriuria groups. To the best of our knowledge, HWR has not been described in the hematologic parameter for inflammation marker. We showed that this marker is possible to screen the asymptomatic bacteriuria in pregnant women, therefore speeding the treatment. Bacterial infections typically result in the increase of white blood cell in the circulation which indicates the mechanism of immune system to combat the microorganism.[5,7] In the case of urinary tract infection, white blood cells in the urine are also increasing. Our study found that low white blood cells are associated with higher possibility of asymptomatic bacteriuria in the pregnant women. This might be due to the low inflammation level of asymptomatic bacteriuria as suggested in a study by Kuil et al. The study showed that procalcitonin and C-reactive protein, the inflammation markers are not significantly increase in asymptomatic bacteria.[19] Another study by Jin et al investigated the ability of white blood to hemoglobin ratio in predicting cortical defect in pediatric patient with febrile UTI with satisfactory result. [20]

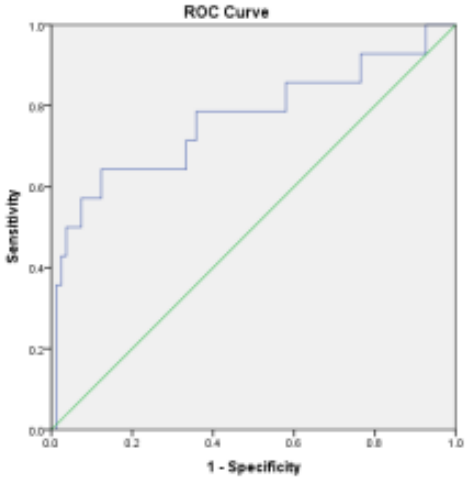

Figure 2. ROC Curve

5. Conclusion

Our study had some limitations that need some considerations. First, this was a single center study with a small sample size and no external validation cohort. Second, hematological parameters were not measured dynamically; thus, it remains unclear whether they exhibit stepwise changes when the patient's condition changes. Is is known that hemoglobin level is decreased in pregnancy due to physiologic dilutional effect.[21] However we did not include other factors influencing hemoglobin levels like nutrition, nutritional supplements, socioeconomic status, or previous hemoglobin levels in the pregnant women.[21] Finally, we did not evaluate other inflammatory markers, such as C-reactive protein and interleukin-6. Evaluation of these markers will help to elucidate the mechanism underlying the findings presented here. In summary, prediction of asymptomatic bacteriuria by simple calculation of HWR might be helpful in significantly reducing workload and costs of urine culture..

Ethical Approval

All procedures have been approved by the issuance of ethical clearance from the Health Research Ethics Commission of The Faculty of Medicine, Diponegoro University, Semarang.

Conflicts of Interest

The authors declare that there was no conflict of interest.

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