

## Neutrophil to Lymphocyte ratio *versus* Monocyte to Lymphocyte ratio in predicting hypertensive diseases of pregnancy

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**Background:** The neutrophil to lymphocyte ratio (NLR) and the monocyte to lymphocyte ratio (MLR) are two systemic inflammatory indices with promising prognostic and predictive abilities for HDP. The study aimed to determine the abilities of the NLR and MLR in predicting HDP among pregnant women in Ghana.

**Methods:** This was a case-control study that was carried out between September 2015 and May 2016 at the Bolgatanga regional hospital. The study involved 50 pregnant women of whom 60% (30/50) had normotensive pregnancies (controls) and 40% (20/50) were confirmed to have HDP (cases). The cases were compared with the controls in terms of their socio-demographic characteristics, full blood count parameters, NLR and MLR. Probability value <0.05 was considered statistically significant.

**Results:** The chances of developing HDP is more likely when lymphocyte count is increased [OR:1.126(95%CI:1.028-1.233)] but less likely with increased NLR [OR: 0.776(95%CI:0.651-0.926)] and MLR [OR: 0.039(95%CI: 0.003-0.469)]. There was no significant difference in the area under the curve (AUC) between NLR and MLR (0.77 vs 0.76, p>0.05). The sensitivities of NLR and MLR were 95.0% and 70.0%, while their specificities were 56.7% and 73.3%, respectively. The positive likelihood ratio (+LR) of MLR was higher than that of NLR (2.6 vs. 2.2).

**Conclusion:** Both the NLR and MLR have moderate predictive ability for hypertensive diseases of pregnancy (HDP). However, the MLR will be a better predictor for HDP than the NLR. We recommend the addition of NLR and MLR when reporting full blood count results for pregnant women.

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**Keywords:** neutrophil, monocyte, lymphocyte, ratio, hypertensive diseases of pregnancy, Ghana

### INTRODUCTION

Hypertensive diseases of pregnancy (HDP) are characterized by a new onset of hypertension (systolic  $\geq 140$ mmHg and/or diastolic  $\geq 90$ mmHg) after 20 weeks of pregnancy with or without proteinuria or haematological or biochemical abnormalities as stated by International Society for the Study of Hypertension in Pregnancy (ISSHP) (Brown *et al.*, 2018). Hypertensive diseases of preg-

nancy is a syndrome of multi-system disorder of unknown aetiology which includes gestational hypertension (GH), pre-eclampsia (PE) and eclampsia (EC). Globally, HDP complicates about 5-11% of all pregnancies and PE alone contributes about 3-5% of the total cases (Aouache *et al.*, 2018; Gogoi *et al.*, 2019).

Hypertensive diseases of pregnancy are usually characterized by hyperactivation of inflammatory

and immunologic responses leading to leukocytosis. The modulation of neutrophil function in HDP favours the production of superoxides as opposed to nitric oxide, which may be responsible for the observed inflammation, oxidative stress, and endothelial dysfunction in HDP (Gogoi *et al.*, 2019). Various studies have examined the usefulness of changes in haematological parameters in the prediction of HDPs and its severity. The systemic inflammatory indices, the neutrophil to lymphocyte ratio (NLR) and the monocyte to lymphocyte ratio (MLR), have proved useful as possible prognostic and predictive tools in the investigation of HDP. Although some studies have found the NLR and MLR useful in predicting HDP (Oylumlu *et al.*, 2014; Kurt *et al.*, 2015; Kurtoglu *et al.*, 2015; Serin *et al.*, 2016; Gogoi *et al.*, 2019; Wang *et al.*, 2019), others have not (Kirbas *et al.*, 2015; Yücel and Ustun, 2017).

The pathogenesis of HDP varies among populations due to genetic and environmental variabilities (Phipps *et al.*, 2019). There has always been a need for newer models for the early detection of HDPs among pregnant women to reduce the perinatal and maternal morbidity and mortality associated with HDPs. Many studies have been conducted elsewhere among ethnic populations to evaluate the predictive abilities of the NLR and MLR for HDP (Kurtoglu *et al.*, 2015; Gezer *et al.*, 2016). However, there is a paucity of research data in Ghana in this regard. The aim of this study, therefore, was to investigate the abilities of the NLR and MLR in the prediction of hypertensive diseases of pregnancy among pregnant women in Ghana.

## **MATERIALS AND METHODS**

### **Study design and setting**

This was a case-control study that was conducted among pregnant women who visited the ante-natal unit of the Bolgatanga Regional Hospital (BRH) in Ghana from September 2015 to May 2016. The BRH is the largest hospital in the Upper East Region of Ghana. It serves as the main referral hospital in the region.

### **Study population**

The study involved 50 pregnant women of whom 30

(60.0%) had normotensive pregnancies and 20 (40.0%) had hypertensive diseases of pregnancy. Pregnant women without any medical complications were regarded to have normotensive pregnancies. HDP was defined according to the International Society for the Study of Hypertension in Pregnancy (ISSHP) criteria as a new onset of hypertension in which the systolic blood pressure was  $\geq 140$  mmHg together with or without a diastolic blood pressure  $\geq 90$  mmHg at or after 20 weeks of gestation in the presence or absence of proteinuria and abnormal biochemical and haematological parameters, (Brown *et al.*, 2018).

### **Data collection**

A structured interview and medical records were used to collect socio-demographic data (age, parity, gravidity, gestational age, and adherence to anti-malarial prophylaxis) as well as the clinical history of the participants.

### **Anthropometric measurements**

A stadiometer and a bathroom scale were used to measure the standing height and body weight, respectively, of the women following standard guidelines (Best and Shepherd, 2020). The maternal Body Mass Index (BMI) was calculated by dividing the weight (kg) by the square of the height in meters.

### **Blood pressure measurement**

Blood pressure was measured using a mercury sphygmomanometer and a stethoscope. The reading/measurement was repeated 10 minutes and the average was calculated and used in the study.

### **Laboratory investigations**

#### **Venous blood collection**

A 4ml venous blood sample was collected from the antecubital vein of the women into an EDTA vacutainer tube. The blood was thoroughly mixed with the anticoagulant by inverting the tube about 5-8 times. Each tube was then labelled with the study identifier before analysis.

#### **Full blood count analysis**

The anticoagulated venous blood samples were

mixed thoroughly before they were analysed using an XN-450 5-part haematology autoanalyzer (Sysmex, Hamburg, Germany). The NLR was derived as the ratio of the neutrophil count and the lymphocyte count. Similarly, the MLR was derived as the ratio of the monocyte count and lymphocyte count.

### **Sickling test**

The sickling slide test was done following the recommendation of Cheesbrough (1984). A drop of freshly mixed anticoagulated blood was placed on a clean glass slide. A drop of an equal amount of freshly prepared 2% sodium metabisulphite solution was added, mixed to achieve homogeneity before the mixture was covered with a glass cover slide, carefully excluding air bubbles. Positive and negative controls were also prepared. The slides were then placed in a slide box with a damp piece of tissue paper to prevent drying. The slides were examined after 10-20 minutes, firstly, under 10x objective followed by 40x objective. The presence of sickle-shaped red cells was reported as sickle cell positive and negative if absent.

### **Peripheral malaria**

Thick and thin blood films were prepared on a clean microscope slide following international best practices (WHO, 2010). The blood films were allowed to air dry before the thin film was fixed with absolute methanol. The slides were then stained with filtered, freshly prepared, quality controlled 1 in 10 diluted Giemsa Stain for 10 minutes. The slides were washed with a buffer (pH:7.2) and then air-dried. The slides were examined by 2 experienced microscopists for the presence of malarial parasites, firstly under 40x objective followed by 100x objective under oil immersion.

### **Data analysis**

The analysis of differences between controls and cases was performed using the unpaired t-test. Odds and adjusted odds ratios were determined using logistic regression analysis in IBM SPSS v23 (SPSS Inc., Chicago, IL, USA). Receiver operator characteristics (ROC) graph was constructed for predictor variables by plotting the sensitivity against

100-specificity and the area under the curve (AUC) was determined using the Hanley and McNeil method in MedCalc v. 14.8.1.0 (MedCalc Software LTD, Belgium). A  $p < 0.05$  was considered as statistically significant.

### **Ethical considerations**

The study was approved by the Navrongo Health Research Centre Institutional Review Board (RN#: NHRCIRB216). Written informed consent was gotten from each enrolled participant. Participants were assured of confidentiality and anonymity.

## **RESULTS**

### **General maternal characteristics**

Table 1 shows a summary of the general characteristics of the study population. The study population was made up of 60.0% (30/50) controls and 40.0% (20/50) HDP. The mean age of the study population was  $27.8 \pm 6.55$  years. Most of the pregnant women were characterized by multiparity (48.0%) and multigravida (66.0%). A larger proportion of pregnant women delivered vaginally (72.0%) and more than half (94.0%) were taking anti-malarial prophylaxis.

### **Comparison of maternal characteristics**

From Table 2, the chance of developing HDP was less likely when the gestational age was increased [OR:0.722 (95%CI: 0.533-0.977),  $p=0.035$ ]. However, the odds of developing HDP increased with increasing maternal BMI [OR: 1.134 (95%CI: 1.005 -1.280),  $p=0.027$ ] and also, increased by about 53 times with every caesarean delivery [OR:53.857 (95%CI:5.997- 483.656),  $p<0.001$ ].

### **Comparison of maternal full blood count results**

The total maternal WBC, neutrophil count, NLR, and MLR were all significantly reduced in HDP ( $p < 0.05$ ). The likelihood of HDP decreased with increased neutrophil count [OR: 0.916 (95%CI: 0.854-0.982),  $p=0.014$ ], NLR [OR: 0.776(95%CI: 0.651-0.926),  $p=0.005$ ] and MLR [OR: 0.039(95% CI: 0.003-0.469),  $p=0.011$ ]. However, the lymphocyte count was significantly increased in HDP

Table 1. General characteristics of the study population

Variable	Statistic
Age (years.)	27.8±6.55*
Gestational age (weeks.)	38.0±3.05*
BMI (Kg/m <sup>2</sup> )	26.4±5.67*
<b>Participants</b>	
Normotensive Pregnancy (NP)	30(60.0)
HDP	20(40.0)
<b>Parity</b>	
Nulliparous	17(34.0)
Primiparous	9(18.0)
Multiparous	24(48.0)
<b>Gravidity</b>	
Primigravida	17(34.0)
Multigravida	33(66.0)
<b>Mode of delivery</b>	
Vaginal	36(72.0)
Caesarian	14(28.0)
<b>Sickle cell phenotype</b>	
Negative	46(92.0)
Positive	4(8.0)
<b>Peripheral malaria</b>	
No	48(96.0)
Yes	2(4.0)
<b>Anti-malarial prophylaxis</b>	
No	3(6.0)
Yes	47(94.0)

Asterisks (\*) presented as mean ± SD for parametric data; all others were presented as frequency (percent).

(p=0.003) and the chances of a pregnant woman developing HDP increased with increased lymphocyte count as compared to controls [OR: 1.126 (95%CI: 1.028-1.233), p=0.011] (Table 3).

### Receiver operator characteristics of independent variables

From figure 1, mode of delivery had the largest AUC at 0.81 (p<0.001), and the smallest was observed in gestational age which was not significant (AUC:0.66, p=0.057). There was no significant difference in AUC between NLR (AUC:0.77, p<0.001) and MLR (AUC:0.76, p<0.001). The lymphocyte count and the NLR showed the highest sensitivity (95.0%, both). However, the highest specificity was observed in the mode of delivery (96.7%) and the specificity of MLR (70.0%) was higher than that of NLR (56.7%). Although the highest PPV was observed in the mode of delivery (92.9%), the PPV of MLR (63.6%) was higher than NLR (59.4%). Additionally, the highest NPV was observed in both lymphocyte count and NLR (94.4%, both), while that of MLR was 78.6%. Gestational age recorded the highest +LR (5.3) followed by MLR (2.6) before the NLR (2.2). The lowest -LR was observed in both lymphocyte percentage count and NLR

Table 2. Crude and adjusted odds ratios of maternal characteristics in predicting HDP

Variable	Control (30)	HDP (20)	cOR (95%CI)	P-value	aOR(95%CI)	P-value
Age (years.)	26.8±6.39	29.4±6.63	1.066(0.97-1.17)	0.171	1.034(0.917-1.166)	0.586
Gestational age (weeks.)	38.9±1.52	36.8±4.20	0.722(0.53-0.98)	0.035	0.715(0.475-1.077)	0.109
BMI (kg/m <sup>2</sup> )	25.0±4.48	28.6±6.64	1.134(1.01-1.28)	0.041	1.043(0.889-1.224)	0.606
<b>Parity</b>						
Nulliparous	12(70.6)	5(29.4)	1		1	
Primiparous	6(66.7)	3(33.3)	1.200(0.21-6.801)	0.837	0.0	0.998
Multiparous	12(50.0)	12(50.0)	2.400(0.64-8.937)	0.192	2.500(0.403-15.501)	0.325
<b>Gravidity</b>						
Primigravida	12(60.6)	5(29.4)	1		1	
Multigravida	18(54.50)	15(45.5)	2.000(0.57-6.968)	0.276	1.412(0.276-7.232)	0.679
<b>Mode of delivery</b>						
Vaginal	29(80.6)	7(19.4)	1		1	1
Caesarian	1(7.1)	13(92.9)	53.857 (5.99- 483.66)	<0.001	1	1
<b>Sickle cell phenotype</b>						
Negative	29(63.0)	17(37.0)	1		1	
Positive	1(25.0)	3(75.0)	5.118(0.49-53.18)	0.172	1.066(0.031-36.168)	0.972
<b>Peripheral malaria</b>						
No	29(60.4)	19(39.6)	1		1	
Yes	1(50.0)	1(50.0)	1.526(0.09-25.90)	0.770	0.545(0.006-46.571)	0.789

**Table 3. Full blood count profile of the study population stratified by the presence or absence of HDP**

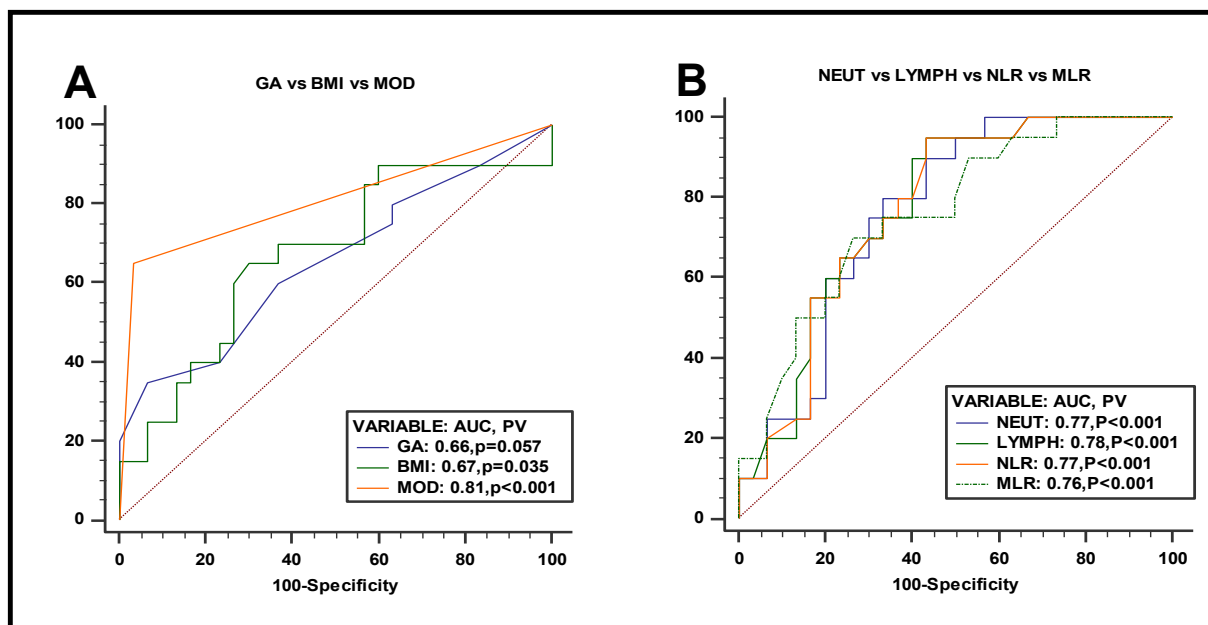
Variable	Control (30)	HDP (20)	P-value	cOR (95%CI)	P-value	aOR(95%CI)	P-value
RBC (x 10 <sup>6</sup> /μl)	3.9±0.52	3.67±0.60	0.103	0.404(1.33-1.232)	0.111	0.464(0.136-1.591)	0.222
Hb (g/dl)	10.7±0.93	9.9±1.93	0.050	0.655(0.419-1.023)	0.063	0.659(0.414-1.050)	0.079
HCT (%)	31.8±2.93	30.2±5.64	0.192	0.911(0.790-1.050)	0.197	0.915(0.787-1.066)	0.254
MCV (fl)	81.8±8.59	82.3±7.0	0.813	1.009(0.939-1.085)	0.809	0.986(0.909-1.070)	0.740
MCH (pg)	27.7±3.23	26.9±2.63	0.395	0.918(0.757-1.114)	0.387	0.855(0.685-1.065)	0.165
MCHC (g/dl)	33.6±1.65	32.7±2.39	0.154	0.806(0.598-1.086)	0.157	0.774(0.555-1.078)	0.130
PLT (x 10 <sup>3</sup> /μl)	204.2±67.0	204.5±82.8	0.991	1.000(0.992-1.008)	0.992	1.001(0.993-1.010)	0.782
WBC (x 10 <sup>3</sup> /μl)	15.1±6.23	11.4±5.78	0.041	0.896(0.803-1.000)	0.050	0.921(0.821-1.034)	0.162
Neutrophil (%)	82.12±9.46	73.7±10.83	0.005	0.916(0.854-0.982)	0.014	1.090(0.820-1.449)	0.551
Lymphocytes (%)	10.7±7.22	18.1±9.62	0.003	1.126(1.028-1.233)	0.011	1	
Monocytes (%)	6.4±2.78	6.3±2.42	0.893	0.985(0.791-1.226)	0.890	0.776(0.563-1.070)	0.122
NLR	11.7±7.73	5.3±2.98	0.001	0.776(0.651-0.926)	0.005	0.745(0.542-1.024)	0.070
MLR	0.77±0.46	0.43±0.23	0.003	0.039(0.003-0.469)	0.011	0.107(0.006-1.824)	0.122

Results presented as Mean ±SD, and odds ratios. RBC; red blood cells, Hb; haemoglobin, HCT; haematocrit, MCV; mean cell volume, MCH, mean cell haemoglobin, MCHC, mean cell haemoglobin concentration, PLT; platelets, WBC; white cell count, NP; normotensive pregnancies, HDP; hypertensive diseases of pregnancy, cOR; crude odds ratio.

**Table 4. Receiver operating characteristics of predictors of hypertensive diseases of pregnancy**

Variable	C u t - o f f value	Sensitivity (95%CI)	Specificity (95%CI)	PPV (95%CI)	NPV (95%CI)	+LR (95%CI)	-LR (95%CI)
Gestational age (weeks)	≤36.0	35.0 (15.4 - 59.2)	93.3 (77.9 - 99.2)	77.8 (40.0-97.2)	68.3 (51.9-81.9)	5.3 (1.2 - 22.7)	0.7 (0.5 - 1.0)
BMI (kg/m <sup>2</sup> )	>26.4	65.0 (40.8 - 84.6)	70.0 (50.6 - 85.3)	59.1 (36.4-79.3)	75.0 (55.1-89.3)	2.2 (1.1 - 4.1)	0.5 (0.3 - 0.9)
Mode of delivery	N/A	65.0 (40.8-84.6)	96.7 (82.8-99.9)	92.9 (66.1-99.8)	80.6 (64.0-91.8)	19.5 (2.8-137.6)	0.36 (0.2-0.7)
Neutrophil (%)	≤80.9	80.0 (56.3 - 94.3)	66.7 (47.2 - 82.7)	61.5 (40.6-79.8)	83.3 (62.6-95.3)	2.4 (1.4 - 4.2)	0.3 (0.1 - 0.7)
Lymphocyte (%)	>8.9	95.0 (75.1 - 99.9)	56.7 (37.4 - 74.5)	59.4 (40.6-76.3)	94.4 (72.7-99.9)	2.2 (1.4 - 3.3)	0.1 (0.0-0.6)
NLR	≤9.4	95.0 (75.1 - 99.9)	56.7 (37.4 - 74.5)	59.4 (40.6-76.3)	94.4 (72.7-99.9)	2.2 (1.4 - 3.3)	0.1 (0.0-0.6)
MLR	≤0.44	70.0 (45.7 - 88.1)	73.3 (54.1 - 87.7)	63.6 (40.7-82.8)	78.6 (59.0-91.7)	2.6 (1.4 - 5.1)	0.4 (0.2 - 0.8)

Results of ROC analysis. GA; gestational age, BMI; body mass index, NLR; neutrophil-lymphocyte ratio, MLR; monocyte-lymphocyte ratio, PPV; positive predictive value, NPV; negative predictive value, +LR; positive likelihood ratio, -LR; negative likelihood ratio



**Figure 1: Receiver operator characteristics plots of the sensitivity of predictor variables against 100-specificity. Diagram A [gestational age (GA), body mass index (BMI), and mode of delivery (MOD)]. Diagram B [neutrophil count (NEUT), lymphocyte count (LYMPH), the neutrophil to lymphocyte ratio (NLR), and the monocyte to lymphocyte ratio (MLR)]. Differences between AUCs were not significant ( $p>0.05$  for all).**

(0.1 both) which was better compared to that of MLR (0.4) as shown in Table 4.

## DISCUSSION

The objective of this study was to determine the abilities of the NLR and the MLR in predicting HDP among pregnant women. The maternal WBC, neutrophil count, NLR, and MLR were significantly reduced while the lymphocyte count was significantly increased in HDP. The NLR, compared to the MLR, had better sensitivity but poor specificity.

Leukocytosis occurs in normal pregnancy due to the activation of white cells and this activation increases in HDP due to inflammation. It is thought that the increased number of leukocytes may be responsible for the vascular dysfunction that is associated with some forms of HDP (Kühnert and Schmidt, 2000; Gervasi *et al.*, 2001; Walsh, 2006; Canzoneri *et al.*, 2009; Yavuzcan *et al.*, 2014). Various studies have reported significantly increased numbers of total

WBC, neutrophils, monocytes but reduced lymphocyte count in HDP (Lurie *et al.*, 1998; Abd-Alazim *et al.*, 2018). However, in this study, the total WBC, neutrophil, and monocyte count were reduced in HDP while the lymphocyte count was rather significantly increased (Elgari *et al.*, 2019).

Lymphocytes are early physiological responders to stress and are also involved in the mediation of inflammation in adults (Suppiah *et al.*, 2013). Some studies did not find any significant differences in lymphocyte numbers between HDP and controls (Canzoneri *et al.*, 2009; Ramma *et al.*, 2012; Yavuzcan *et al.*, 2014). The associated leukocytosis in HDP results in a higher NLR and MLR in HDP and this has been reported by some authors to have increased with the severity of PE (Oylumlu *et al.*, 2014; Akil *et al.*, 2015; Kirbas *et al.*, 2015; Serin *et al.*, 2016; Abd-Alazim *et al.*, 2018; Gogoi *et al.*, 2019). However, this study observed a reduced NLR and MLR in HDP as a result of reduced neutrophil and monocyte count accompanied by an increased

lymphocyte count in HDP.

There are various ways of assessing the effectiveness of a diagnostic or screening test in biomedical sciences using various decision theories. One of these is the odds ratio. The change in odds per unit change in NLR (OR:0.776,  $p=0.005$ ) was higher than that of MLR (OR:0.039,  $p=0.11$ ). Higher odds of NLR than MLR may be interpreted as NLR to be a better tool in HDP detection than MLR. However, it has been demonstrated that the odds ratios tend to exaggerate the effect size and may not be an efficient method of assessing the usefulness of a test (Davies *et al.*, 1998).

The AUC is yet another way of comparing two tests. The AUC quantifies the overall ability of a test to discriminate between two outcomes such as disease. An AUC value of 1.0 is considered as perfect, 0.90–0.99 is considered as excellent, 0.80–0.89 as good, 0.70–0.79 as fair, 0.51–0.69 as poor, and 0.50 is considered as non-informative (Brown and Davis, 2006; Antwi *et al.*, 2018). On this score, both NLR and MLR will be considered as fairly good predictors of HDP (AUC:0.77 and 0.76 respectively).

The sensitivity and specificity are another way of assessing the usefulness of a diagnostic test. The intended use of a test may usually determine which level of sensitivity or specificity is desirable. Usually, screening tests tend to have higher sensitivity while the confirmatory test tends to have higher specificity (Brown and Davis, 2006). In this regard, the NLR will be better than MLR for screening, while NLR will be better than NLR in diagnosis. However, even the sensitivity and specificity do not adequately assess the usefulness of a test because they are measures of population characteristics and are also affected by disease prevalence, severity, and risk factors (Attia, 2003; Cook, 2007). The predictive values (PPV and NPV) have been suggested to be better than sensitivity and specificity as they show the probability that a true positive or true negative is positive or negative (Brown and Davis, 2006). However, PPV and NPV are influenced by the prevalence of a disease in the population. In a population where a disease has a higher prevalence,

PPV will be higher while NPV will be lower and vice versa (Chu, 1999; Cook, 2007).

The likelihood ratios (LR) are better than sensitivity, specificity, and predictive values in the assessment of a biomedical test. Because the LR is a ratio of sensitivity and specificity, they are not affected by population variability and disease prevalence (Chu, 1999; Attia, 2003). It is recommended that a good diagnostic test should have a larger +LR and a smaller -LR. Preferably, an +LR > 10 and -LR ≤ 1 is considered good (Deeks and Altman, 2004; Akobeng, 2007; LeFebvre *et al.*, 2013). Based on these assessment criteria, neither the NLR nor the MLR is a good diagnostic tool for HDP. However, the MLR (+LR:2.6, -LR:0.4) appears to be better than the NLR (+LR:2.2, -LR:0.1) in the prediction of HDP. This means that a pregnant woman who has been diagnosed with HDP using MLR is 2.6 times more likely to be true compared to using the NLR, where the likelihood will only be 2.2 (Brown and Davis, 2006).

Various studies have explored the predictive potential of NLR and MLR in HDP (Kirbas *et al.*, 2014; Gezer *et al.*, 2016; Wang *et al.*, 2019). The cut-off value of NLR was higher compared to the other studies (Oylumlu *et al.*, 2014; Kurtoglu *et al.*, 2015; Abd-Alazim *et al.*, 2018). The study of Gezer *et al.* (2016) was conducted using retrospective first trimester data before the onset of HDP, it was therefore expected to see a reduced cut-off point. It was, however, expected that the cut-off value would have been higher in studies where pregnant women with mild PE were compared to those with severe PE since neutrophilia is expected to have increased (Abd-Alazim *et al.*, 2018; Wang *et al.*, 2019).

Similarly, MLR in this study had the highest cut-off value compared to the findings of Wang *et al.* (2019). The AUC of NLR was fair but was higher than what was reported in studies by Kirbas *et al.* (2014), Gezer *et al.* (2016), and Kurtoglu *et al.* (2015). Cakmak *et al.* (2017) reported an AUC as high as 0.930 for NLR among Turkish women, similar to another Turkish study (Oylumlu *et al.*,

2014). The AUC of MLR was comparable to the NLR and higher than that of Wang *et al.* (2019) when women with mild PE were compared to severe PE but lower than the AUC between normotensive pregnant women and those with PE (Wang *et al.*, 2019).

Despite the smaller AUC of NLR compared to other studies, the sensitivity of NLR was the highest at 95.0% compared to 93% by Cakmak *et al.* (2017) and 84.4% by Mannaerts *et al.* (2019). Just like the NLR, the sensitivity of the MLR (70.0%) was higher than that reported by Wang *et al.* (2019). However, the NLR had the lowest specificity next to what was reported by Kirbas *et al.* (2015). When the sensitivity and specificity of NLR are considered together, the studies of Cakmak *et al.* (2017), and Oylumlu *et al.* (2014) did better than the current study. However, the MLR in this study was better at predicting HDP than what was reported by Wang *et al.* (2019).

The major challenge with the current study was the smaller sample size used compared to the other studies. Despite this limitation, the findings of the current study are comparable to the previous ones. Aside from the variability in sample sizes, the ethnicity, geography, immune, and nutritional status of the study population could also have accounted for some of the variability in results between the studies examined.

## CONCLUSION

There are differences in maternal characteristics and full blood count parameters between normotensive pregnant women and their counterparts with HDP. The gestational age, neutrophil count, NLR, and MLR are negatively associated with HDP, while maternal BMI and lymphocyte count are positively associated with HDP. The NLR and MLR are fairly good predictors of HDP, however, the MLR will be a better screening test for HDP than the NLR. It is recommended that NLR and MLR are reported as part of full blood count results for pregnant women for the early detection of HDP.

## COMPETING INTEREST

Authors declare that they have no competing

interests.

## FUNDING/FINANCIAL DISCLOSURE

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## AUTHOR CONTRIBUTIONS

**MB** conceived and planned the experiments, **YA** and **PPMD** performed the statistical analysis; **GA** contributed to the interpretation of the results. **MAA** carried out the experiments and collected the data. All authors provided critical feedback and approved the final manuscript.

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