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Original Research Article

Assessment of Hematological Parameters, Hematological Ratios and Serum Lactate Dehydrogenase Levels in Patients with Preeclampsia

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Abstract

Aim: To study haematological parameters, haematological ratios and serum total lactate dehydrogenase (LDH) levels in normal pregnant women and in women with preeclampsia. ***Materials & Methods:*** 30 women with preeclampsia and 30 normotensive pregnant women admitted to the Department of OBG were recruited for the study. Blood samples were collected and analysed for CBC, serum LDH and ALP in the Clinical Biochemistry & Pathology Laboratory of MVJ Medical College. Statistical tests were employed to evaluate the significance of the differences obtained between the groups. ***Results:*** Serum LDH and Neutrophil – Lymphocyte ratio (NLR) showed a significant difference between control group and preeclampsia group. Platelet count showed a negative correlation with systolic blood pressure and serum LDH levels and serum ALP showed a positive correlation with serum LDH levels in the patient group. ***Conclusion:*** These simple markers might be used as predictors of preeclampsia if analysed routinely in the third trimester of pregnancy. The study needs to be replicated with a larger sample size and prospective study design to validate the findings and implement these in clinical practice.

Keywords: Preeclampsia, CBC, LDH, ALP, NLR, PLR.

INTRODUCTION

Preeclampsia is a pregnancy specific syndrome that can affect every organ system. It is a rapidly progressive condition characterised by increased blood pressure (140/90 mm Hg), with fluid retention and proteinuria that occurs after 20 weeks of gestation [1]. Globally, preeclampsia leads to approximately 76,000 maternal and 5,00,000 infant deaths per year and is the prime cause of maternal and infant mortality [2]. India has an incidence rate of 8% to 10% [3].

Preeclampsia becomes a challenging condition due to absence of early warning signals and its sudden and acute onset. Hence, the delayed diagnosis contributes to serious complications causing maternal and neonatal morbidity and mortality. This warrants the need for markers which could help in early and cost-effective risk prediction and diagnosis of the developing condition and hence lead to its effective management improving maternal and foetal outcomes.

Normal pregnancy is characterised by many physiologic haematological changes which are principally induced by changes in the hormonal milieu. It is characterised by a localised and controlled innocuous inflammatory state during the early stages and generalised in the last trimester of pregnancy [4, 5]. Preeclampsia is characterised by all the inflammatory changes of normal pregnancy, albeit to a much higher and intense degree [4]. Placental under perfusion in preeclampsia initiates systemic endothelial dysfunction, coagulation system is activated by interaction of platelets with the injured endothelium [6, 7]. The inflammatory milieu triggers platelet-leukocyte cross talk and stimulates the migration of neutrophils to the site of inflammation, the formation of platelet-leukocyte aggregates and the peripheral consumption of platelets [6]. Therefore, it would be worth evaluating the degree of haematological changes in preeclampsia when compared to normal pregnancy and investigate its possible role to serve as a warning signal of impending preeclampsia.

The central theme of preeclampsia revolves around uteroplacental hypoxia and hence markers of hypoxia also arouses interest. Lactate Dehydrogenase (LDH), a predominantly intracellular cytoplasmic

enzyme of anaerobic glycolysis catalyses the inter conversion of pyruvate to lactate. It is composed of 'H' and 'M' chains coded by two different genes (LDH – A coding M chain & LDH – B coding H chain) that combine in different combinations to form five isoenzymes [8, 9]. It is usually released from its tissue of origin to the general circulation during cellular death and may be increased in preeclampsia due to vigorous glycolysis and chronic anoxemia as a result of placental ischemia. Thus, an evaluation of serum LDH levels might also serve to explore the possibility of its use as a cost-effective marker and predictor of preeclampsia.

AIM

To study haematological parameters and serum total Lactate dehydrogenase (LDH) levels in normal pregnant women and in women with preeclampsia.

OBJECTIVES

- To assess haematological parameters and total LDH in serum in all subjects.
- To evaluate the diagnostic accuracy of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in preeclampsia.
- To assess the relationship between altered haematological parameters and LDH in preeclampsia.
- To estimate the serum alkaline phosphatase levels in patients with preeclampsia and to assess its correlation with LDH and other haematological parameters and ratios.

MATERIAL AND METHODS

The present study was carried out in 30 women with preeclampsia admitted to the Department of Obstetrics and Gynaecology in MVJ Medical College and Research Hospital. 30 normotensive pregnant women (after 20 weeks of gestation) attending antenatal clinic in OBG Department of MVJ MC & RH served as controls. The study was ethically approved by the Institutional Ethical Committee and an informed consent was obtained from all the participants.

Inclusion Criteria

Blood pressure (>/=140/90 mmHg) on at least 2 occasions, six hours apart and/or proteinuria (>/=300mg/24 hours or >/=1+ dipstick) after 20 weeks of gestation.

Exclusion Criteria

Known cases of chronic hypertension, any renal disease, hypothyroidism, hyperthyroidism, any metabolic disorder or medication known to affect thyroid function.

Procedure

The study participants were divided into 2 groups:

Group A: Normotensive pregnant women

Group B: Preeclamptic women

Group B patients were further divided into mild and severe group. Severity of preeclampsia was based on systolic and diastolic blood pressure. Mild preeclampsia was defined as systolic BP = 140 mm Hg-159 mm hg or diastolic BP = 90 mm Hg- 109 mm hg and proteinuria of 300 mg/day (that is normal, negative by dipstick method). Severe preeclampsia was defined as systolic BP ≥ 160 mm Hg or diastolic BP ≥ 110 mm Hg, with severe proteinuria and/or signs and symptoms of target organ damage [2].

Study samples were separated for assayed for LDH by Deutsche Gesellschaft für klinische Chemie (DGKC) method and the samples from preeclampsia group were assayed for ALP by IFCC method (Kinetic) in the Clinical Biochemistry Laboratory of MVJ Medical College and Research Hospital. The haematological parameters were analysed in the Pathology Laboratory of MVJ Medical College.

RESULTS

Our study included 60 women in their third trimester of pregnancy, out of which 30 belonged to normotensive group (Normal Control) and 30 belonged to our study group (Preeclampsia Group). The mean maternal age in the control group was 23.63 ± 2.65 years with a gestational age of 34.7 ± 5.62 weeks while in the patient group was 24.4 ± 4.47 years with a gestational age of 34.9 ± 6.34 weeks.

Table-1: Observations in Control & Preeclampsia Group

	Control Group	Preeclampsia Group
Maternal Age (Years)	23.63 ± 2.65	24.4 ± 4.47
Gestational Age (weeks)	34.7 ± 5.62	34.9 ± 6.34
Systolic BP (mm Hg)	113.07 ± 7.71	158.5 ± 19.85
Diastolic BP (mm Hg)	70.87 ± 6.80	100.0 ± 9.83

The comparison of the various analytes and their p values are represented in Table-2. NLR ratio and serum LDH showed significant difference between normotensive controls and preeclampsia group (p value < 0.05).

Table-2: Comparison of results between Control and Preeclampsia Group

	Control Group	Preeclampsia Group	P value
Heamoglobin (gm %)	11.32 ± 1.42	10.97 ± 2.24	0.477
WBC Count (cumm)	11145 ± 3339	12472 ± 3465	0.136
Neutrophil Count (cumm)	83555 ± 2900	9879 ± 3432	0.068
Lymphocyte Count (cumm)	2625 ± 1065	2357 ± 1030	0.421
Platelet Count (lakhs)	2.46 ± 0.70	2.31 ± 0.72	0.404
Neutrophil Lymphocyte Ratio (NLR)	**3.61 ± 1.58**	**6.77 ± 10.21**	**0.040**
Platelet Lymphocyte Ratio (PLR)	105.56 ± 40.29	113.85 ± 56.79	0.517
Lactate Dehydrogenase (U/L)	**400.50 ± 148.87**	**702.73 ± 415.44**	**0.0006**
Alkaline Phosphatase (IU/L)		178.57 ± 108.88	

Figure-1 shows the difference in the NLR between the controls and preeclampsia group.

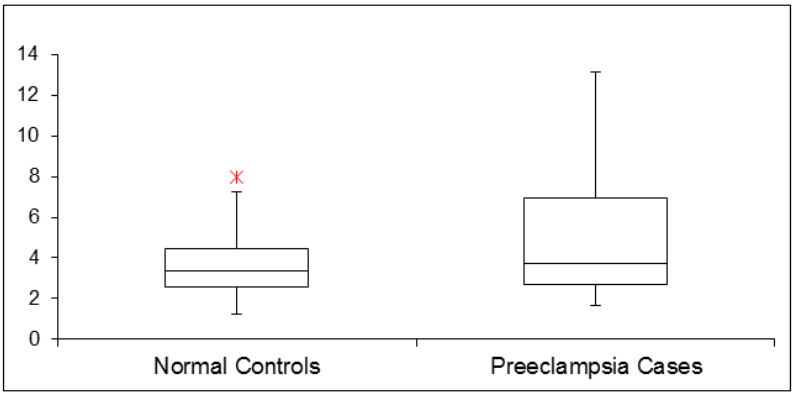

Fig-1: Neutrophil Lymphocyte Ratio in Healthy Controls and in Preeclampsia Patients

The preeclampsia group was further classified into mild and severe preeclampsia based on their blood pressure recording at the time of admission. 16 women of the case group had mild preeclampsia while 14 women had severe preeclampsia. The systolic BP had a mean of 144.13 ± 4.92 mm Hg and the diastolic BP had a mean of 93.75 ± 4.67 mm Hg in the mild preeclampsia group compared to the severe preeclampsia group which had a mean systolic BP of 173.57 ± 13.93 mm Hg and a mean diastolic BP of 107.14 ± 8.25 mm Hg.

The haematological parameters, NLR, PLR, LDH and ALP were compared between the two groups. The observed results and the corresponding p values are represented in Table-3.

Table-3: Comparison of results between Mild Preeclampsia and Severe Preeclampsia Group

	Mild PE Group	Severe PE Group	P value
Heamoglobin (gm %)	10.48 ± 2.00	11.53 ± 2.43	0.206
WBC Count (cumm)	11920 ± 2839	13102 ± 4085	0.360
Neutrophil Count (cumm)	9401 ± 2895	10425 ± 4000	0.424
Lymphocyte Count (cumm)	2168 ± 1029	2563 ± 1042	0.306
Platelet Count (lakhs)	2.42 ± 0.65	2.17 ± 0.79	0.340
Neutrophil Lymphocyte Ratio (NLR)	8.27 ± 13.60	5.17 ± 3.88	0.416
Platelet Lymphocyte Ratio (PLR)	207.58 ± 353.73	106.09 ± 62.70	0.299
Lactate Dehydrogenase (U/L)	520.38 ± 209.09	911.14 ± 496.85	0.007
Alkaline Phosphatase (IU/L)	154.81 ± 34.23	205.71 ± 153.64	0.206

Only LDH levels showed significant difference between the mild and severe preeclampsia groups.

Further, a negative correlation between observed haematological values and the blood pressure for all 60 patients was estimated. Total platelet count showed a moderate negative correlation with r = - 0.247 and a p value of 0.05 (Kendall's Tau = - 0.187, p = 0.03).

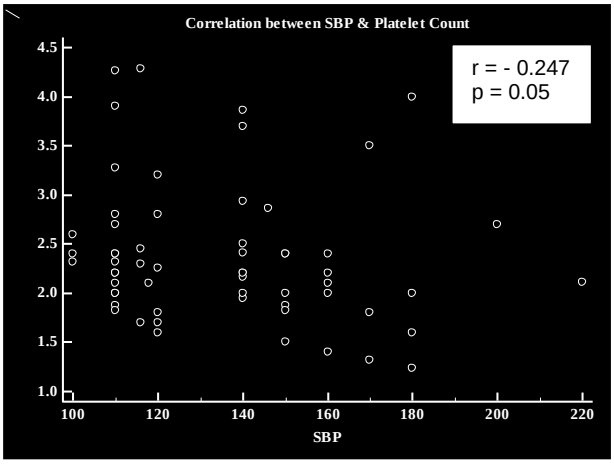

Fig-2: Correlation between Platelet Count & Systolic Blood Pressure

A negative correlation was observed between platelet count and serum LDH with r = - 0.262 and a p value of 0.04 was obtained (Kendall's Tau = - 0.194, p = 0.02).

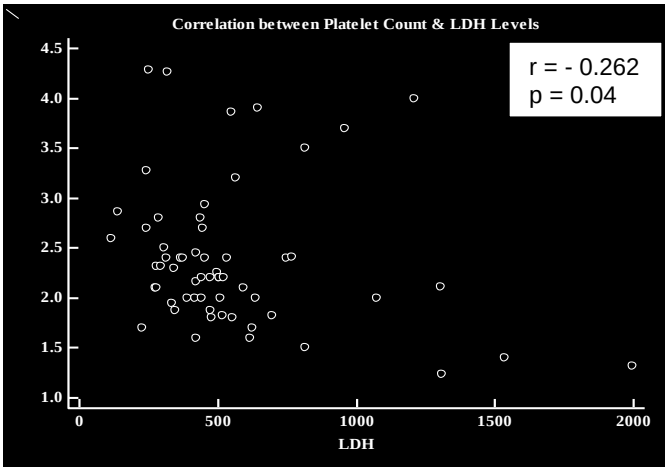

Fig-3: Correlation between Platelet Count & serum Lactate Dehydrogenase Levels

Lastly, the correlation between serum ALP levels and serum LDH showed a moderate positive correlation with r = 0.473 and a p value of 0.008 (Kendall's Tau = 0.349, p = 0.007).

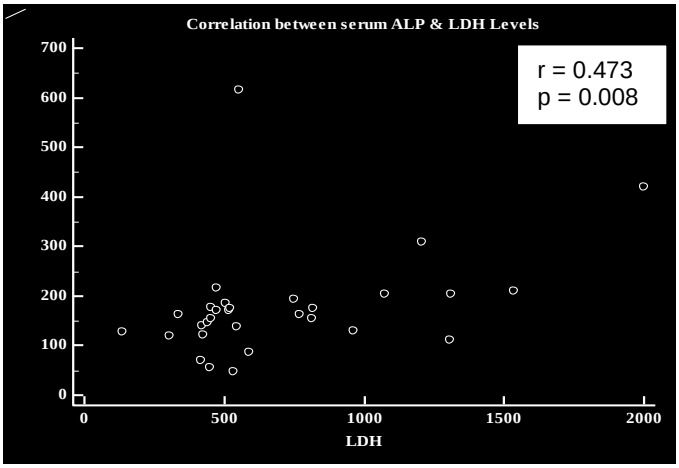

Fig-4: Correlation between serum Alkaline Phosphatase & Lactate Dehydrogenase Levels

DISCUSSION

Research revolving around causes, mechanisms, early diagnosis and effective management of preeclampsia is being revitalised and we are definitely moving closer to the historically elusive answers with the current advances.

The initial event of placentation involves formation of proliferative, non – invasive, extravillous spheroidal trophoblastic shell which excludes oxygenated maternal blood during early embryonic development. This switches into a non – proliferative, invasive phenotype, as the development progresses, causing an exponential rise in the entry of oxygenated maternal blood [10]. The etiology of preeclampsia is thought to be characterised by insufficient and disturbed trophoblastic migration of maternal spiral arteries resulting in reduced intervillous blood flow, oxygen and nutrient deprivation to the fetus [11]. This insufficient nutrient delivery results in increased frequencies of placental infarcts, IUGR and fetal deaths. This ischemic circulation may also be related to an altered and exaggerated inflammatory response in preeclampsia [12].

Haematological parameters have been recognised as systemic inflammatory response markers (SIR) and may have predictive and prognostic in inflammatory diseases and preeclampsia [13]. Normal pregnancy is also a state of controlled and localised inflammation and is characterised by leucocytosis. Neutrophils account for the leucocytosis in pregnancy and the observed neutrophilia may be due to decreased phagocytic activity and impaired apoptosis [4]. Preeclampsia being a state of intense systemic inflammation is believed to show exaggerated inflammatory response [5]. Studies have shown that leukocyte activation plays a significant role in preeclampsia. Activated leukocytes lead to increased superoxide generation (leading to oxidative stress) and release of cytokines, IL8, TNF alpha (mediating endothelial function) [12].

Our study does shows increased leukocyte count in both groups when compared to the physiological cut off, the elevation in WBCs are higher in the preeclampsia group than the control, though the difference is not statistically significant. The increase in leukocyte is accounted by increase in neutrophil count (increased in both groups), elevation being more in the preeclampsia group, though the difference was not found to be significant. Whereas, the lymphocyte count was found to be lower in preeclampsia group when compared to controls, but the difference was not significant.

Our findings are contradictory to a few studies. A study by Canzoneri *et al.*, reported significantly elevated leukocyte count in severe preeclampsia when compared to mild preeclampsia and normal pregnancy and associated the increase mainly due to elevations in neutrophil count [12]. Mihu *et al*., concluded that leukocyte and neutrophil counts could be considered as inflammatory markers of preeclampsia and positively correlated with DBP [5]. Belo et al reported that the extent of neutrophil activation correlates with the severity of preeclampsia [14].

Being associated with hypercoagulable state, coagulation being activated by contact of platelets with the injured endothelium, it is believed that platelets also play a major role in its etiopathogenesis and thrombocytopenia (associated with increase platelet consumption and increased production of immature platelets with a shorter life span) has been reported to be associated with preeclampsia in many studies [6, 15].

Our study shows a decreased platelet count in the preeclampsia group than the control, though the difference is not statistically significant. However, the platelet count showed a moderate negative correlation with systolic blood pressure and the serum LDH levels.

Previous studies have showed significantly lower platelet counts in preeclampsia when compared to controls. AlSheeha et al and Sultana R *et al*., claimed that platelet counts were significantly lower in preeclamptic women when compared to controls [6, 15]. Ustun et al found only significant thrombocytopenia in severe preeclampsia when compared to controls and mild preeclampsia [16]. Nazli R *et al*., concluded that a higher frequency of thrombocytopenia was seen in patients with pregnancy associated hypertension and the severity of thrombocytopenia correlated with the severity of the disorder [17].

More recently, haematological ratios have been studied and their diagnostic accuracy to predict preeclampsia has been tested. Our study shows a significantly higher NLR ratio in preeclampsia when compared to controls. The PLR ratio was increased in preeclampsia when compared to controls though the increase was not statistically significant. Our findings are consistent with reports by Sachan *et al*., which showed a significantly higher NLR ratio in preeclampsia when compared to healthy controls even in early pregnancy [18]. Contrast to this; a study by Yucel *et al*., reported a significantly lower PLR ratio in severe preeclampsia when compared to controls but no significant differences in NLR ratios [13].

The present study shows that the control group of normotensive pregnant women had serum LDH well within the recommended cut off of 525 U/L, while women with preeclampsia showed statistically significant elevations in serum LDH levels. The difference of LDH between mild and severe

preeclamptic groups was also found to be statistically significant.

This is in agreement with many of the previous studies. Jaiswar S et al, shows high serum LDH levels correlate well with the severity of the disease and outcomes in patients of preeclampsia [19]. He S *et al*., shows serum LDH levels were significantly increased in preeclamptic women than those in normal pregnancy [20]. Study done by Vinitha Padmini Mary *et al*., Purnima and Sonal and Munde et al also concludes that LDH can be effectively used as biochemical markers as it reflects the severity of preeclampsia and maybe helpful in its effective management [21-23].

Lastly, we obtained ALP values measured in our patients and observed that ALP levels were increased in cases of severe preeclampsia when compared to mild preeclampsia, though the elevation was not statistically significant. Further, a moderate positive and statistically significant correlation was observed between serum ALP and serum LDH in the preeclampsia group.

Thus, our study clearly shows the association of elevated LDH and NLR with preeclampsia. Platelet count shows a negative correlation with systolic blood pressure and serum LDH levels (a marker of hypoxia). Further, serum LDH and ALP in preeclampsia group showed a statistically significant moderate positive correlation. This is a unique finding which hasn't been reported yet. Thus, these markers together with other biochemical markers could be used as simple risk predictors of SIR and impending preeclampsia, if monitored on a regular basis in the final trimester of pregnancy, though a definite conclusion needs validation of this finding with further studies. A cross sectional study design, a small sample size, absence of additional platelet indices and absence of ALP values for the control group can be seen as the limitations of our present study. The study needs to be replicated with a larger sample size and a prospective study should be taken up with the estimation additional indices like MPV and plateletcrit to obtain a better picture of association and diagnostic efficacy of these parameters with the development and severity of preeclampsia.

CONCLUSION

Our study showed the significant elevation in serum concentration of LDH and NLR in preeclampsia when compared to normotensive healthy pregnant women. Platelet count showed a moderate negative correlation with systolic blood pressure and serum LDH and ALP and serum LDH also showed moderate positive correlation. Thus, routine assessment of these parameters in addition to the routinely assayed markers in the third trimester of pregnancy and evaluation of their combined predictive value might act as robust risk predictors of preeclampsia.

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REFERENCES

1. Cunningham, G. F., Leveno, J. K., Bloom, L. S., Hauth, C. J., Rouse, J. D., & Spong, Y. C. (2010). Pregnancy Hypertension. In: Cunningham G F editor. Williams OBSTETRICS. 23rd Edition. United States of America (USA): The McGraw-Hill Companies, Inc, 706-709
2. Preeclampsia Foundation. About Preeclampsia, Cause of preeclampsia. Canada. 2010 July. Available from: https://www.preeclampsia.org/health-information/about-preeclampsia, https://www.preeclampsia.org/health-information/cause-of-preeclampsia. Accessed on 12th January 2018.
3. National Health Portal of India: Preeclampsia. India. Zahid. 2016 June 1. Available from: https://www.nhp.gov.in/disease/gynaecology-and-obstetrics/preeclampsia. Accessed on 12th January 2018.
4. Chandra, S., Tripathi, A. K., Mishra, S., Amzarul, M., & Vaish, A. K. (2012). Physiological changes in hematological parameters during pregnancy. *Indian Journal of Hematology and Blood Transfusion*, *28*(3), 144-146.
5. Mihu, D., Sabau, L., Costin, N., Ciortea, R., Oancea, M., & Malutan, A. (2010). Evaluation of leukocytes and neutrophils, markers of inflammatory syndrome in preeclampsia. *Applied Medical Informatics*, *27*(3), 15-22.
6. AlSheeha, M. A., Alaboudi, R. S., Alghasham, M. A., Iqbal, J., & Adam, I. (2016). Platelet count and platelet indices in women with preeclampsia. *Vascular health and risk management*, *12*, 477-480.
7. Sahin, S., Ozakpinar, O. B., Eroglu, M., & Tetik, S. (2014). Platelets in preeclampsia: function and role in the inflammation. *Clinical and Experimental Health Sciences*, *4*(2), 111-116.
8. Neal, J. L., Lowe, N. K., & Corwin, E. J. (2013). Serum lactate dehydrogenase profile as a retrospective indicator of uterine preparedness for labor: a prospective, observational study. *BMC pregnancy and childbirth*, *13*(1), 128.
9. Tsoi, S. C. M., Zheng, J., Xu, F., & Kay, H. H. (2001). Differential Expression of Lactate

Dehydrogenase enzyme in human placenta with high expression of LDHA4 isoenzyme in the endothelial cells of preeclampsia villi. *Placenta*, 22(3): 317-322.

10. Caniggia, I., Winter, J., Lye, S. J., & Post, M. (2000). Oxygen and placental development during the first trimester: implications for the pathophysiology of pre-eclampsia. *Placenta*, *21*, S25-S30.
11. Mellembakken, J. R., Aukrust, P., Olafsen, M. K., Ueland, T., Hestdal, K., & Videm, V. (2002). Activation of leukocytes during the uteroplacental passage in preeclampsia. *Hypertension*, *39*(1), 155-160.
12. Canzoneri, B. J., Lewis, D. F., Groome, L., & Wang, Y. (2009). Increased neutrophil numbers account for leukocytosis in women with preeclampsia. *American journal of perinatology*, *26*(10), 729-732.
13. Yücel, B., & Ustun, B. (2017). Neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, mean platelet volume, red cell distribution width and plateletcrit in preeclampsia. *Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health*, *7*, 29-32.
14. Belo, L., Santos- Silva, A., Caslake, M., Cooney, J., Pereira- Leite, L., Quintanilha, A., & Rebelo, I. (2003). Neutrophil activation and C- reactive protein concentration in preeclampsia. *Hypertension in pregnancy*, *22*(2), 129-141.
15. Sultana, R., Karim, S. F., Atia, F., Ferdousi, S., & Ahmed, S. (2012). Platelet count in preeclampsia. *Journal of Dhaka National Medical College & Hospital*, *18*(2), 24-26.
16. Üstün, Y. E., Dogan, K., Türkçüoglu, I., Üstün, Y., Meydanl, M. M., & Kafkasl, A. (2007). Evaluation of hemoglobin and platelet levels in mild, moderate and severe preeclampsia. *Perinatal Journal*, *15*(3), 93-8.
17. Nazli, R., Khan, M. A., Akhtar, T., Mohammad, N. S., Aslam, H., & Haider, J. (2012). Frequency Of Thrombocytopenia In Pregnancy Related Hypertensive Disorders In Patients Presenting At Tertiary Care Hospitals Of Peshawar. *Khyber Medical University Journal*, *4*(3), 101-105.
18. Sachan, R., Patel, M. L., Sachan, P., & Shyam, R. (2017). Diagnostic accuracy of neutrophil to lymphocyte ratio in prediction of nonsevere preeclampsia and severe preeclampsia. *Journal of Current Research in Scientific Medicine*, *3*(2), 79-83.
19. Jaiswar, S. P., Gupta, A., Sachan, R., Natu, S. N., & Shaili, M. (2011). Lactic dehydrogenase: a biochemical marker for preeclampsia–eclampsia. *The Journal of obstetrics and Gynecology of India*, *61*(6), 645-648.
20. He, S., Bremme, K., Kallner, A., & Blombäck, M. (1995). Increased concentrations of lactate dehydrogenase in pregnancy with preeclampsia: a predictor for the birth of small-for-gestational-age infants. *Gynecologic and obstetric investigation*, *39*(4), 234-238.
21. Mary, V. P., Chellatamizh, M., & Padmanaban, S. (2017). Role of serum LDH in preeclampsia as a prognostic factor–a cross sectional case control study in tertiary care hospital. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*, *6*(2), 596-598.
22. Sarkar, P. D., & Sogani, S. (2013). Evaluation of serum lactate dehydrogenase and gamma glutamyl transferase in preeclamptic pregnancy and its comparison with normal pregnancy in third trimester. *Int J Res Med Sci*, *1*(4), 365-8.
23. Munde, S. M., Hazari, N. R., Thorat, A. P., Gaikwad, S. B., & Hatolkar, V. S. (2014). Gamma Glutamyl Transferase and Lactate Dehydrogenase as Biochemical Markers of Severity of Preeclampsia. *International Journal of Medical, Pharmaceutical Science and Engineering*, 8(1): 50-53.