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Evaluation of Lactate Dehydrogenase and Gamma Glutamyl Transferase Among Pregnant Women with Hypertensive Disorders and Their Association with Disease Severity in Jimma Medical Center, Ethiopia

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ABSTRACT

Background & Objective: Pregnancy-induced hypertensive disorders (PIHD) are the main reasons for maternal and perinatal mortality, as they complicate 10% of pregnancies worldwide. Serum lactic acid dehydrogenase (LDH) and gamma-glutamyl transferase (GGT) are possible markers reflecting the occurrence of pregnancy-associated complications like preeclampsia and eclampsia. There is a paucity of data with conflicting results showing serum LDH and GGT on PIHD in Ethiopia. This investigation aimed to assess the serum LDH and GGT levels in pregnant women with PIHD along with their correlation with the severity of the disease at Jimma Medical Center (JMC), Ethiopia.

Materials & Methods: This hospital-based comparative cross-sectional study was undertaken from August 03 to September 27, 2020, in JMC. A total of 97 study participants were recruited. Serum GGT and LDH levels were determined using a fully automated Roche Cobas 6000 chemistry analyzer. The data were analyzed using SPSS 25.0. One-way ANOVA and independent samples t-test were employed to compare serum GGT and LDH levels with categories of PIHD.

Results: The significantly highest mean serum levels of LDH (580.9±193.8 U/L) and GGT (86.1±29.2 U/L) were observed in eclamptic women compared to gestational hypertensive (276.7±60.7 and 38.3±16.9 U/L) and preeclamptic patients (353±132.8 and 48.8±29.9 U/L), respectively. Both serum GGT and LDH levels were found to correlate with the severity of preeclampsia, respectively significantly.

Conclusion: Serum LDH and GGT were found to be at the highest levels in eclamptic than preeclamptic and gestational hypertensive women. Blood pressure, gestational age, and severity of hypertensive disorders of pregnancy were predictor variables associated with serum GGT and LDH.

Keywords: Eclampsia, Ethiopia, GGT, LDH, Preëclampsia

Introduction

Pregnancy-induced hypertensive disorders (PIHD) or hypertensive disorders of pregnancy(HDP) are a set of usual medical complications in pregnancy that are the leading reasons for maternal and perinatal illness and mortality globally **(1, 2)**. HDP is described as new onset of hypertension (Blood Pressure (BP) ≥ 140 and/ or ≥ 90 mmHg recorded while the woman is made comfortable via being at rest and her arm held at the extent of heart) after 20 weeks of gestation **(3, 4)**. There are four categories of HDP, namely, chronic hypertension, gestational hypertension, preeclampsia and eclampsia **(4-6)**. Gestational hypertension is defined as new onset of hypertension after 20 weeks of gestation in pregnant women who were previously normotensive and is characterized by elevated BP (≥ 140/90mmHg), measured on two occasions at least 4-6hours apart, without proteinuria **(1)**. Preeclampsia is defined as the emergence of new-onset hypertension (BP 140/90 mmHg) accompanied by new-onset proteinuria (300 mg/ 24 hours), which can occur as late as 4-6 weeks after delivery **(5, 7, 8)**. Eclampsia is defined as preeclampsia with sudden onset of seizure or coma during the gestational or postpartum period that is not due to other neurological illnesses that would excuse the convulsive condition **(9)**. Chronic hypertension is defined as a new-onset of hypertension before 20 weeks of gestation or its persistence beyond 12 weeks postpartum period. It is characterized by elevated BP (≥ 140/90 mmHg) taken on two occasions at least 4-6 hours apart and is associated with preeclampsia (22–25% of women with chronic hypertension will develop preeclampsia during

pregnancy), intrauterine growth restriction, and placental abruption **(10, 11)**.

HDP complicates 5-10 % of all pregnancies worldwide, with consequent maternal and perinatal mortality **(1, 12)**. Globally, around 76,000 pregnant women and 500,000 babies die as of preeclampsia and associated hypertensive disorders per annum **(13)**. Every day, 830 women die due to pregnancy-related problems, of which 14% are due to HDP. Though HDP is preventable and treatable, maternal and fetal morbidity and mortality rates related to HDP have been increasing recently due to the lack of diagnostic biochemical markers to be used in clinical areas **(4, 12, 14)**. The triads of high BP, edema, and albuminuria have long been used as diagnostic criteria, but they are neither specific nor sensitive. Hence, reliable biomarkers have to be searched for and evaluated to be used as diagnostic tools. Several biochemical markers for assessing HDP during pregnancy have been proposed **(8, 14, 15)**. Lactate dehydrogenase (LDH) and gamma-glutamyl transferase (GGT) are useful indicators of pregnancy-related problems such as preeclampsia and eclampsia.

LDH is a tetrameric ubiquitous intracellular enzyme that catalyzes the interconversion of lactate and pyruvate, and its increased level in serum signifies cellular death and enzyme leakage from the cell **(15)**. GGT is a 68KDa heterodimeric glycoprotein with a 46-kilodalton heavy chain and a 22-kilodalton light chain joined by a non-covalent bond **(16, 17)**. This enzyme catalyzes the transfer of the gamma-glutamyl group from peptides containing gamma-glutamyl groups, such as glutathione, to acceptors like peptides and L-amino acids. Hence, it takes part in amino acids transport across the cellular membrane as well as in glutathione metabolism **(18)**. It also plays a vital role in the homeostasis of glutathione and the detoxification of xenobiotics in mammals **(19)**. Endothelial cell dysfunction within the uteroplacental circulation associated with HDP causes the systemic release of GGT since its considerable activity occurs both in the endothelium and epithelium at the cellular level **(20)**.

Despite many international studies related to HDP, the exact association between serum LDH and GGT levels and with the degree of HDP severity remains enigmatic **(21-23)**. Besides, there is a scarcity of data in Ethiopia showing the role of GGT and LDH as potential biomarkers of HDP. Hence, this study was primarily aimed to compare serum LDH and GGT levels between gestational hypertension, preeclampsia, and eclampsia and their association with disease severity among pregnant women at JMC, Southwest Ethiopia.

Methods

The investigation was conducted at Jimma Medical Center (JMC) in Jimma Town, which is located 352 kilometers southwest of Addis Ababa, the capital city of Ethiopia, from August 3 to September 27, 2020, using a facility-based comparative cross-sectional study design. JMC is the largest public hospital in Southwestern Ethiopia, providing teaching, diagnostic, and referral services for 15 million people. This research was carried out primarily at JMC's obstetrics and gynecology wards.

We enrolled 97 pregnant women with HDP (33 preeclampsia, 32 eclampsia, and 32 gestational hypertension) diagnosed by physicians in obstetrics and gynecology wards of JMC and came for medical and other services at these wards during the study period. Women diagnosed with eclampsia in their immediate postpartum period and those recorded as new cases of gestational hypertension and preeclampsia during the data collection period were included via the purposive non-probability sampling technique. However, pregnant women with chronic hypertension, gestational or pre-existing diabetes mellitus, thyroid disorder, hemolytic anemia, epilepsy, renal or liver diseases, and those with a history of alcoholism and/ or smoking were excluded from the study.

Study Variables

Serum GGT and LDH level were considered as dependent variables, whereas family or previous history of HDP, gestational and maternal age, disease duration, anthropometric parameters, and clinical parameters (blood pressure, severity of HDP, and antihypertensive therapy) were taken as independent variables.

Data Collection method and Procedure

After each study participant signed a written informed permission form, all necessary information regarding sociodemographic factors, participants' medical history, and related data were collected using a structured questionnaire through face-to-face interviews and by reviewing participants' medical records. Data were collected by three trained midwives working in the obstetrics and gynecology ward of JMC.

Anthropometric Measurement

All study participants' anthropometric measurements (height and weight) were taken with a conventional weight scale, and their height was measured with a height measuring scale and light clothing.

Blood Pressure Measurement

A mercury Sphygmomanometer was used to measure blood pressure once the woman was comfortable in a sitting position, her arm set at the heart level, and at least 10 minutes of rest was given from her right arm in a quiet room. As per the guideline of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy, gestational hypertension was then subcategorized based on its clinical stages (BP level) to mild and

severe hypertension. Mild gestational hypertension: if blood pressure is between 140/90 and 159/109 mmHg taken on two separate occasions at least 4-6 hours apart, without substantial proteinuria (≥0.3g/d), and is diagnosed after 20 weeks of pregnancy. Severe gestational hypertension: if BP ≥ 160/110 mmHg measured on two separate occasions at least 4-6 hours apart without significant proteinuria **(1)**. Preeclampsia can be mild preeclampsia: if elevated BP (Systolic BP is between 140 and 159 mmHg, while diastolic BP ranges from 90 to 109 mmHg), normal platelet count, normal level of liver transaminases, significant proteinuria (0.3-0.5g/24 hour) and no maternal symptoms, severe preeclampsia: if BP is elevated (≥160/110 mm Hg), thrombocytopenia ($<1\times10^5$/μL), two times the normal upper limit of liver transaminases, a doubling of serum creatinine level (>2 mg/dL), proteinuria (>0.5 g/24hr), pulmonary edema, severe chronic right upper quadrant pain, or new-onset cerebral or visual problems **(10)**.

Blood sample collection and Laboratory analysis

Three milliliters (ml) blood sample from each study subject was taken via venipuncture from the medial antecubital vein and tipped into a serum separator tube (SST), followed by its transportation to the clinical chemistry laboratory unit of JMC and centrifuged for 10 minutes at 3000 rpm and room temperature within two hours of blood collection to obtain the cell-free serum. The serum was then analyzed for measurement of serum GGT and LDH by an enzymatic colorimetric assay using a fully automated, highly-sensitive, quantitative Roche/Hitachi Cobas© 6000 chemistry analyzer at the clinical chemistry unit of JMC laboratory. The normal range for serum LDH and GGT levels taken were 135-214 U/L and 5-36 U/L, respectively.

Data Quality Management

The questionnaire prepared in the English language was translated into local languages (Amharic and Afaan-Oromo language), and then back to English to keep it consistent. At Shenen Gibe hospital in Jimma zone, Southwest Ethiopia, 5% of the study subjects were given a pre-test. Furthermore, training was given to the data collectors before the commencement of data collection concerning the objective of the study, the data collection process, and the inclusion and exclusion criteria of study participants to prevent the data's quality from being hampered. In addition, standard aseptic operational procedures were strictly followed by data collectors during blood sample collection. The kits were maintained clean, and laboratory analysis of the blood sample was done according to the manufacturer's instructions. Qualified laboratory personnel undertook laboratory procedures, and the supervisor double-checked the results daily for accuracy.

Data Processing and Statistical Analysis

The data was entered into EPI Info version 7.2.0.1, exported to, and statistically analyzed using Statistical Package for Social Sciences (SPSS) software version 25.0 once it was gathered, coded, and validated for completeness. The data was presented using tables and graphs. Proportions and summary statistics such as mean and standard deviation (SD) were calculated for variables as appropriate. One-way analysis of variance (ANOVA) with the Games-Howell post hoc test was employed to compare differences in the mean levels of serum GGT and LDH among the three study groups: gestational hypertension, preeclampsia and eclampsia. The difference in the mean values of LDH and GGT between subgroups of gestational hypertensive and preeclamptic patients was assessed using an independent sample t-test. A P-value below 0.05 was considered significant.

Results

Sociodemographic Characteristics

A total of 97 study participants with HDP took part in this study. The study participants ranged in age from 16 to 40 years. Concerning occupation, more than one-third (39.2%) of the total study participants were housewives, followed by government employees, accounting for 26 (26.8%). Regarding the place of residence of the study participants, 72 (74.2%) of the total study subjects were urban dwellers, and the remaining 25 (25.8%) were rural residents (Table 1).

Clinical and Anthropometrical Profiles of Study Participants

Most of the preeclamptics, 22(66.7%), were found to have one or more complication/s (HELLP syndrome, Acute renal failure, Disseminated Intravascular Coagulation, and/or Abruptio placenta) attributed to HDP followed by gestational hypertensives 14 (43.7) and Eclamptic 13(40.6%) study subjects. Out of the total study subjects, 51 (52.7%) participants did not use any antihypertensive/anticonvulsant medication, and 22 (43.1%) accounted for the eclamptic group. The clinical and anthropometric profiles of our study participants are summarized in Table 2.

Table 1. Sociodemographic profile of study participants in JMC, Jimma, Southwest Ethiopia, 2020

Variables*		A study group with a total number(n)		
		Gestational hypertensive (32)	Preeclamptic (33)	Eclamptic (32)
Age (years)		28.2 ± 5.6	26.8 ± 6.7	26.7 ± 5.3
Educational status	Primary school	8 (25)	11(33.3)	10 (31.3)
	Secondary school	10 (31.3)	12 (36.4)	7 (21.9)
	College/university	9 (28.1)	7 (21.2)	9 (28.1)
	Illiterate	5 (15.6)	3 (9.1)	6 (18.8)
Occupation	Government employee	8 (25)	10 (30.3)	8 (25)
	Self-employed	9 (28.1)	3 (9.1)	8 (25)
	Housewife	13 (40.6)	16 (48.5)	9 (28.1)
	Merchant	2 (6.3)	3 (9.1)	3 (9.4)
	Student	0	1 (3 %)	4 (12.5)
Place of residence	Urban	25(78.1)	23(69.7)	24(75%)
	Rural	7(21.9)	10(30.3)	8(25)

*Continuous variables expressed in mean ±SD, while categorical variables are expressed in frequency and percentage (in parenthesis).

Table 2. Clinical and anthropometrical profiles of study participants at JMC, Jimma, Southwest Ethiopia, 2020

A study group with a total number(N)				
Variables*		Ecla mpsia (32)	Gestational hypertension (32)	Preeclampsia (33)
SBP (mmHg)		150.0 ± 11.6	150.6 ± 10.4	149.9 ± 10.3
DBP (mmHg)		100.7± 8.8	102.5 ± 9.3	101.0 ± 7.1
Disease duration (Days)		19.2± 12.8	38.0 ± 21.7	17.9 ± 4.8
Weight (Kg)		68.1±7.4	68.9 ± 8.6	65.8 ±9.5
Height (m)		1.63 ± 0.08	1.66 ± 0.08	1.64 ±0.11
Complication**	Yes	13 (40.6)	14(43.7)	22(66.7)
	No	19 (59.4)	18 (56.3)	11 (33.3)
Antihypertensive/anticonvulsant drug use	Yes	10 (31.2)	18 (56.3)	18 (54.5)
	No	22 (68.8)	14 (43.7)	15 (45.5)
Number of drug therapy	Monotherapy	8(25)	17(53.1)	16(48.5)
	Dual therapy	2 (6.2)	1 (3.1)	2 (6.1)

*Continuous variables expressed in mean ±SD, while categorical variables are expressed in frequency and percentage (in parenthesis); **involves HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet count), acute renal failure, Disseminated Intravascular Coagulation, and/or Abruptio placenta.

Serum GGT and LDH levels among pregnant women with HDP

Serum levels of both GGT and LDH were examined in all three study groups. The normal range for serum GGT and LDH levels are 5-36 U/L and 135-214 U/L, respectively. Our study showed elevation of these parameters from their acceptable upper limit (36 U/L and 214 U/L for GGT and LDH, respectively) in a majority of the study participants. Specifically, serum level of LDH was elevated in 86 (88.7%) of the total study subjects, while serum level of GGT did show an elevation in 60 (61.9%) of them. In addition, the present investigation found a statistically significant difference (P<0.05) in mean serum LDH levels between each pair of study groups; namely, gestational

hypertensive and preeclamptic, gestational hypertensive and eclamptic, and preeclamptic and eclamptic. The mean levels of both LDH and GGT in the eclamptic group (580.9 ±193.8 and 86.1 ± 29.2, respectively) were significantly higher than their mean levels in the preeclamptic groups. Preeclamptic patients had higher mean serum GGT and LDH (48.8±29.9 and 353±132.8, respectively) than gestational hypertensive groups (Table 3).

Table 3. Serum LDH and GGT level among different groups of HDP in JMC, Jimma, Southwest Ethiopia, 2020

	A study Group with a total number(N)		
Parameters*	Gestational hypertensive (32)	Preeclamptic (33)	Eclamptic (32)
GGT (U/L)	38.3 ± 16.9	48.8 ± 29.9	86.1 ± 29.2
LDH (U/L)	276.7 ± 60.7	353.0 ±132.8	580.9 ±193.8

*Values of parameters are expressed in mean ± standard deviation (SD)

Games-Howell post hoc test showed statistically significant LDH and GGT mean differences (*P*=0.000) between the eclamptic group and the gestational hypertensive and preeclamptic group (Table 4 and Table 5). Likewise, a significant mean difference for LDH was noted between gestational hypertensive and preeclamptic groups (Table 4).

However, the mean difference in serum GGT between gestational hypertensive and preeclamptic groups was statistically insignificant (*P*=0.20) (Table 5).

Table 4. Multiple pairwise comparison of LDH level among the three groups of HDP using Games-Howell post Hoc test at JMC, Jimma, Southwest Ethiopia, 2020

					95% CI	
Outcome variable	Group (I)	Group (J)	Mean difference (I-J)	P-value*	Lower bound	Upper bound
Serum LDH (U/L)	Eclampsia	Gestational hypertension	304.19	0.000	216.53	391.85
		Preeclampsia	227. 88	0.000	128.3	327.45
	Gestational hypertension	Eclampsia	-304.19	0.000	-391.85	-216.5
		Preeclampsia	-76.31	0.012	-138.08	-14.54
	Preeclampsia	Eclampsia	-227.88	0.000	-327.45	-128.3
		Gestational hypertension	76.31	0.012	14.54	138.08

* P-value less than 0.05 level indicates significant mean difference; CI: Confidence interval; LDH: Lactate dehydrogenase; U/L: Units per liter

Table 5. Multiple pairwise comparison of GGT level among the three groups of HDP using Games-Howell post Hoc test at JMC, Jimma, Southwest Ethiopia, 2020

					95% CI	
Outcome variable	Group (I)	Group (J)	Mean difference (I-J)	P-value*	Lower bound	Upper bound
Serum GGT(U/L)	Eclampsia	Gestational hypertension	47.84	0.000	33.44	62.25
		Preeclampsia	37.37	0.000	19.48	54.96
	Gestational hypertension	Eclampsia	- 47.84	0.000	-62.25	-33.44
		Preeclampsia	-10.48	0.20	-25.00	4.04
	Preeclampsia	Eclampsia	- 37.37	0.000	- 54.96	- 19.78
		Gestational hypertension	10.48	0.2	- 4.04	25.0

*Mean difference less than 0.05 is considered significant. CI: Confidence Interval
GGT: Gamma-glutamyl transferase; U/L: Units per liter

GGT and LDH mean levels were observed to be considerably highest in an eclamptic group (P<0.05) than in preeclamptic and gestational hypertensive subgroups (Figure 1).

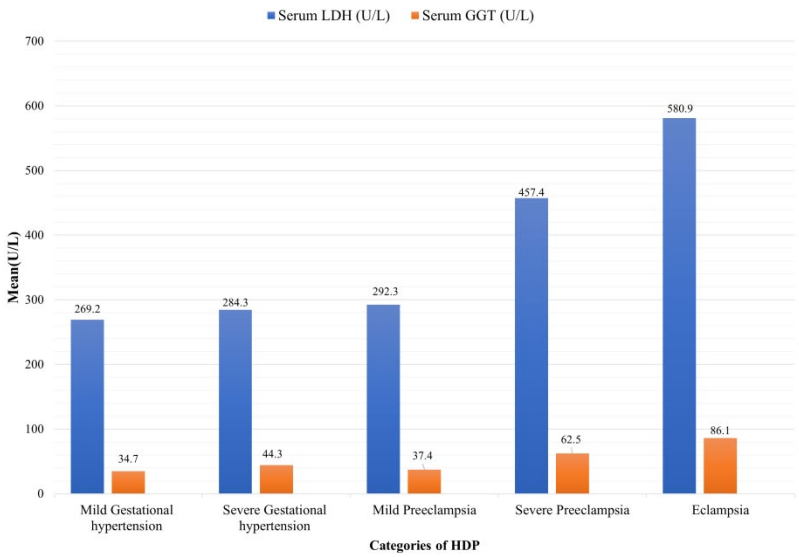

Figure 1. Mean level of GGT and LDH across subgroups of preeclampsia and gestational hypertension, and eclampsia at JMC, Jimma, Southwest Ethiopia, 2020

Correlation of LDH and GGT Level with Severity of Preeclampsia and Gestational Hypertension

A statistically significant positive relationship between serum GGT as well as LDH and the severity of preeclampsia was observed from Spearman's correlation analysis. As the severity of preeclampsia progressed from its mild clinical stage to severe preeclampsia, the level of serum GGT and LDH increased significantly. Unlike LDH, serum GGT showed a significant correlation with the severity of gestational hypertension. (Table 6).

Table 6. Comparison of mean serum GGT and LDH level between preeclamptic subgroups using independent samples t-test at JMC, Jimma, Southwest Ethiopia, 2020

	Preeclamptic subgroup		
Parameter [a]	Mild preeclamptic	Severe preeclamptic	P-value
Serum LDH (U/L)	292.3 ± 105.9	457.4 ± 132.6	0.008
Serum GGT (U/L)	37.4± 14.6	62.5± 32.8	0.009

[a] Values of parameters are expressed in mean ± SD

As it is understood from multiple linear regression analysis, systolic blood pressure(SBP), the severity of HDP, gestational age, and diastolic blood pressure (DBP) had independently considerable association with serum GGT and LDH levels. Systolic BP was found to be a significant positive predictor of both serum GGT and LDH levels among pregnant women. More specifically, for one mmHg increase in SBP, serum GGT and LDH levels increase by 1.078 and 1.034, respectively. Likewise, one mmHg increase in DBP resulted in the elevation of serum GGT by a factor of 0.603 and LDH by 0.632. Moreover, for a one-week increase in gestational age, serum GGT and LDH levels decrease by 0.981 and 5.647, respectively. Lastly, as the severity of HDP progressed from mild to severe clinical stage, serum GGT increased by 5.528 and LDH by 10.155 (Table 7).

Table 7. Spearman's rank correlation analysis of serum GGT and LDH with the severity of preeclampsia and gestational hypertension at JMC, Jimma, Southwest Ethiopia 2020

		Serum LDH	Serum GGT
Severity of preeclampsia	Spearman's rho correlation b coefficient (ρ)	0.519*	0.462*
	P value	0.002	0.007
Severity of gestational hypertension	Spearman's rho correlation coefficient	0.112	0.359*
	P-value	0.543	0.043

* Correlation is significant below 0.05 level (two-tailed)

Discussion

In this study, severe preeclamptic pregnant women had considerably higher mean serum LDH levels than mild preeclamptic patients. The mean serum LDH levels in mild and severe preeclamptic study participants were 292.3±105.9 U/L and 457.4±132.6 U/L, respectively. This result is consistent with a number of similar studies **(13, 24-26)**. In contrast, this result was lower than earlier Iranian research (mean serum LDH levels in mild and severe preeclamptic groups were 337.89 173.15 U/L and 556.41 193.02 U/L, respectively), and in Visakhapatnam mean level of which was 323.3±77.4 U/L in mild preeclamptic and 636.2±132.29 U/L in severe preeclamptic groups **(27, 28)**. In general, an increasing LDH level in severe preeclampsia could imply the progression of cellular damage with the severity of the condition. Furthermore, in severe preeclampsia induced by vascular endothelial injury, multiorgan dysfunction, including maternal liver, kidney, lung, neurological system, hematological, and coagulation system, may contribute to excessive LDH leakage and serum level rise **(29)**.

This study also demonstrated a relatively higher serum LDH in eclamptic subjects (580.9 ± 193.8 U/L) than other categories of HDP. However, it is lower when compared to findings of studies done in India (mean level of LDH was 854.05 ±47.5 U/L, and Visakhapatnam (649.32 ± 153.53 U/L) **(25, 27)**. This observed discrepancy might be due to the lowering effects of anticonvulsants such as magnesium sulfate and diazepam, which were taken by some of our study subjects. Besides, comorbidities, particularly anemia and diabetes mellitus were recorded in the latter studies and might significantly account for raised serum LDH levels.

Besides, this study showed a significant positive correlation of serum level of GGT with the severity of gestational hypertension, which is in line with the findings of other studies **(28)**. Our study found the mean level of GGT to be 48.8±29.9 U/L in preeclamptic subjects, which was much higher than in a study done in India on similar subjects (22.5±14.1U/L) **(30)**. Concerning the mean level of GGT in preeclamptic subgroups (mild and severe preeclamptics), our study demonstrated a more elevated level (37.4±14.6 and 62.5±32.8 U/L) in mild and severe preeclamptic groups, respectively than studies undertaken in India (18.5±5.9 in mild preeclamptics and 23.9±5.8 in severe preeclamptics) and in Sudan (14.5±7.8 and 16.3±8.3 U/L in mild and severe preeclamptics), respectively **(31, 32)**. These discrepancies might be owing to differences in chemistry analyzers and substrates used. The latter studies employed L-γ-glutamyl-p-nitroanilide as a substrate, which is less soluble and stable than L-γ-glutamyl-3-carboxy-4-nitroanilide (which was used in our study), and semi-automated chemistry analyzer **(8)**.

In this study, significantly higher levels of serum LDH and GGT were noted in eclamptic group than preeclamptic and gestational hypertensive groups (P=0.000), which was in line with several studies **(25, 29, 33, 34)**. This could be due to HDP particularly in eclampsia where local platelet-endothelial interaction is thought to occur as a result of aberrant placentation. As a result, it is likely that endothelial cell death in the uteroplacental circulation causes GGT and LDH to be released into the bloodstream.

Our study also found mean serum LDH level to be considerably greater in preeclamptics than in gestational hypertensive study groups (P=0.012), and another study31 supported it. This could be due to progressive endothelial failure in the maternal vasculature resulting from toxins released from preeclamptic individuals' hypoxic placenta, which leads to severe vasoconstriction in all organ systems, including the liver. Hepatic cells and other organs suffer ischemic damage due to hypoperfusion resulting in increased intracellular LDH release into the circulation **(27, 31)**.

A higher serum GGT has been associated with the severity of preeclampsia in various studies **(27, 29)**. This investigation also showed a statistically significant positive association between serum GGT and the severity of preeclampsia. This is contradictory to findings from previous studies **(32, 35)**. Serum LDH level was also observed to have a significant positive correlation with the severity of preeclampsia, indicating that the more severe the disease, the higher the serum LDH level. This is in agreement with other studies which showed a significant association between

elevated serum LDH levels and the degree of preeclampsia **(24, 36, 37)**. A significant positive moderate correlation has also been demonstrated between LDH and the severity of preeclampsia in previously reported studies **(31, 32, 37)**.

Limitations of the Study

Despite unreserved efforts made for the success of this research work, it was not without limitations. Our findings may not represent the general population because the study was conducted at a single institution with small sample size. Furthermore, because the study was cross-sectional, residual confounding variables may exist. As the exposure and result were measured concurrently, the study did not reveal a causal relationship.

Conclusion

Serum LDH and GGT were more elevated among eclamptic than preeclamptic and gestational hypertensive patients. Blood pressure, gestational age, and severity of HDP were predictor variables associated with serum GGT and LDH.

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Abbreviations

ANOVA: Analysis of Variance; GGT: Gamma Glutamyl Transferase; BP: Blood pressure; HDP: Hypertensive Disorders of Pregnancy; HELLP syndrome: hemolysis, elevated liver enzymes, and low platelet count); JMC: Jimma Medical Center; LDH: Lactate Dehydrogenase; SD: Standard Deviation; SPSS: Statistical Package for Social Sciences; SST: Serum Separator Tube; U/L: Units per Liter;

Ethical Approval and Consent

Ethical clearance and approval letters for data collection were taken from the Institutional Review Board (IRB) of Jimma University. Written informed consent was obtained from each study subject once they were informed about study objectives before data and blood sample collection. Moreover, all the information provided by the study participants was kept confidential and anonymous.

Availability of Data and Materials

The dataset used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Author contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas, took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Conflict of Interest

The authors declare no conflict of interest in this work.

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