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Comparative Evaluation of Some Liver Enzymes in Preeclamptic and Non-Preeclamptic Patients in the Enugu Metropolis South East Nigeria

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Abstract

Preeclampsia (PE) is one of the most common causes of maternal mortality and morbidity. It complicates 3-6% of all pregnancies globally and up to 15% of pregnancies in the Sub-Saharan Africa. The present study was designed to determine the level of liver enzymes in preeclamptic patients compared to control in the Enugu metropolis. A total of 70 subjects comprising 35 preeclamptic patients and 35 non-preeclamptic controls aged 18-40years were recruited for the study. Blood samples (10ml) were collected from subjects for estimation of liver enzymes involving the Alanine Transaminase (ALT), Aspartate Transaminase (AST) and Alkaline Phosphatase (ALP) levels using Randox Kit, UK.The data was analyzed using T-test and Pearson correlation. The level of significance was set at $p<0.05$. The result revealed significant increase in ALT (57.70$\pm$28.72 vs14.19$\pm$2.96Iu/L), AST (42.54$\pm$8.66 vs 10.5$\pm$3.801u/L) and ALP (380.12$\pm$15$\pm$62 vs 174.14$\pm$46.531u/L) between the preeclamptic and non-preeclamptic subjects. There was a significant positive association of the ALT (p=0.031 vs 0.700) and AST (p=0.02 vs 0.222) with the systolic blood pressure between the preeclamptic and non-preeclamptic subjects as well as the ALT(p=0.011 vs 0.106) and AST(p=0.003 vs 0.225) with the diastolic blood pressure between the preeclamptic and non-preeclamptic subjects. These findings provides scientific evidence for the management of the adverse outcomes of preeclampsia in our population.

Keywords: Preeclampsia, Liver enzymes, Enugu Metropolis

I. Introduction

Preeclampsia (PE) is one of the most common causes of maternal mortality and morbidity (1). It complicates 5-6% of all pregnancies as well as 25% in women with pre-existing hypertension (2). It is a multi-system disorder observed as gestational hypertension usually after 20th week of gestation with systolic blood pressure $\geq$ 140mmHg and diastolic blood pressure $\geq$ 90mmHg accompanied by significant proteinuria (>300 mg/L or 500mg/24 hours urine or 2+ or more proteinuria on dipstick) with or without oedema (1,2). According to the

classification of American College of Obstetrics and Gynecology (ACOG), preeclampsia can be categorized into mild (140-159/90-109mmHg) and severe (≥ 160/110mmHg)(2).Mild preeclampsia occurs in approximately 15% of pregnancies while severe preeclampsia occurs in about 1% to 2% (3). The liver plays a pivotal role in normal physiologic function, aiding in metabolism, detoxification, immune function, bile production, synthesis of albumin and clotting factors, storage of glycogen and minerals (4). Given the complex role of the liver, assessment of its function is important particularly in special conditions such as pregnancy. Changes in liver enzymes may indicate an intrinsic or systemic disease affecting the liver and can have significant adverse effect to both the fetus and the mother (4.5). There is currently a paucity of data on the liver enzyme status of preeclampsia patients in the Enugu metropolis. The present study was therefore designed to determine changes in liver enzymes involving the Aspartate Transaminase, Alanine Transferase and Alkaline Phosphatase in preeclampsia patients and non-preeclampsia controls in the Enugu Metropolis.

II. Materials and Method

Study Area

This study was carried out in Enugu State, South east, Nigeria. Enugu State is made up of three senatorial zones namely Enugu East, Enugu West and Enugu North. The senatorial zones are divided into seventeen Local Government Areas comprising 450 communities. The state takes its name from its capital and largest city, Enugu. It has an area of 7,161km^2 with a population of 3,267,837 comprising mainly the Igbo tribe of the South Eastern Nigeria; about 50% of which lives in rural areas. It lies between longitudes $6^0 30^1$E and $6^0 55^1$E and latitude $5^0 15^1$N and $7^0 15^0$E (6).

Study Design

This was a case control study carried out on patients attending antenatal clinic and/or admitted in the maternity wards in four different hospitals in the Enugu metropolis namely the Enugu State University of Science and Technology Teaching Hospital Parklane, University of Nigeria Teaching Hospital Ituku-Ozalla, Mother of Christ Specialist Hospital and the Annunciation Specialist Hospital. The subjects were divided into two groups. Group A comprised 35 cases of preeclampsia patients defined by blood pressure ≥140/90mmHg and proteinuria in 24 hours ≥300mg and edema after 20 weeks of gestation while group B involved 35 normal pregnant women after their 20 weeks of gestation.

Ethical Considerations

Ethical approval was obtained from the respective institutions Ethical Management Committee as well as signed informed consent from the subjects.

Sample Size

The sample size for the study was calculated using the Leslie Kish formula (7)

$$n = \frac{z^{\alpha 2} PQ}{D^2}$$

Where n = minimum required sample size when the population is greater than 10,000

z^{α} = the α level of the coefficient internal or the standard normal deviate set at 1.96 corresponding to the 95% confidence interval.

P = the proportion in the target population estimated to have preeclampsia

D = The width of the confidence internal set at 0.05

Q = (1-p); the proportion of non-occurrence

Substituting into the formula

$$n = \frac{1.96 \times 1.96 \times 0.033\ (1.033)}{0.05 \times 0.05} = 49$$

But an estimate of 68 registered preeclampsia patients attended the four different clinics in the last one year. Since this is less than 10,000, the sample size was adjusted using the formula.

$$nf = \frac{n + (n)}{1 \quad N} = \frac{49}{1+49/68} = 28$$

Considering a response rate of 90%, the sample size was further adjusted to accommodate attrition using the formula

$$Ns = nf/r$$

Where Ns = adjusted sample size for response rate

nf= calculated sample size

r = the anticipated response rate of 90% (0.9)

Substituting $Ns = \frac{28}{0.9} = 31$

Therefore, a total of 70 subjects involving 35 cases of preeclampsia and 35 non-preeclampsia control were recruited for the study.

Subject Recruitment

Subjects were recruited for the study by convenient sampling.

Inclusion Criteria: Both the cases and controls were in the age group of 18-40years.

Exclusion Criteria: Those with a major systemic disease which may elevate the patient's blood pressure or which may change the liver enzyme values e.g liver disease, hepatitis infection, diabetes mellitus and cardiovascular disease were excluded. Patients using any drug that affect liver function were also excluded.

Sample Collection

About 10 milliliters of clean catch urine were collected in clean dry containers for the determination of proteinuria and 6 milliliters of blood were draw aseptically by venipuncture and dispensed into plain bottle for estimation of liver enzyme levels.

Determination of Proteinuria

Proteinuria was determined using the dipstick method for urinalysis (2).

This is a semi-quantitative test aimed at detecting abnormal levels of chemical substances (in this case, protein) in urine. The combi-9 test strips impregnated with tetrabromophenol blue for protein detection was used.

Principle: Tetrabromophenol blue is yellow at pH 3.0, but changes to bluish green in the presence of protein at the same pH. The intensity of the color change is roughly proportional to the amount of protein present in the urine.

Procedure: The test end of the strip was dipped into freshly voided urine for about 1 second, the excess urine was drained along the container and the color on the strip was compared with the color chart on the test strip container. Presence and/or absence of protein was noted and the degree of proteinuria scored subjectively as Nil, 1+ (30mmg/dl),2+(100mg/dl), 3+(300mg/dl) and 4+(more than 300mg/dl).

Determination of Liver enzymes

Estimation of liver enzymes involving Aspartate Transaminase (AST), Alanine transaminase (ALT) and Alkaline Phosphatase (ALP) were done using commercial kits obtained from Randox Ltd, UK.

Aspartate Transaminase

Principle: Aspartate transaminase catalyses the reversible transfer of an amino group from aspartate to ketoglutarate forming glutamate and oxalacetate. The oxalacetate produced is reduced to malate by malate dehydrogenase and reduced nicotinamide adenine dinucleotide. The rate of decrease in the concentration of nicotinamide adenine dinucleotide measured photometrically is proportional to the catalytic concentration of aspartate transaminase present in the sample.

Procedure: 1ml of the working reagent was mixed with 0.1ml of the sample in a cuvette and a stop watch started. The initial absorbance (A) of the mixture was red at 1 minute. The delta absorbance (ΔA) was read after 1,2,3 and 4minutes.

ΔA/min x 1746 = Iu/L of AST

Alanine Transaminase

Principles: Alanine aminotransferase catalyzes the transfer of the amino group from alanine to oxaloglutarate with the formation of glutamate and pyruvate. The latter is reduced to lactate by lactate dehydrogenase in the presence of reduced nicotinamide adenine dinucleotide. The reaction is monitored kinetically at 340nm by the rate of decrease in absorbance resulting from the oxidation of reduced nicotinamide adenine dinucleotide to oxidized nicotinamide dinucleotide proportional to the activity of ALT present in the sample. The absorbance of the color produced is measured in a colorimeter at 505mm (blue-green filter).

Procedure: 1ml of the working reagent was mixed with 0.ml of the sample in a cavette and a stop watch started. The initial absorbance was read and the timer started simultaneously. The delta absorbance (ΔA) was read after 1,2 and 3 minutes.

ΔA/min x 1746 = Iu/L of ALT

Alkaline Phosphatase

Principle: In the presence of magnesium ions, p-nitrophenyl phosphate is cleaved by phosphatases into phosphate and p-nitrophenol. The p-nitrophenol released is directly proportional to the catalytic ALP activity. It is determined by measuring the increase in absorbance at 405nm.

Procedure: 0.01ml of sample and 0.05ml of working reagent were mixed in a cuvette. The initial absorbance was read and the timer started simultaneously. The delta absorbance (ΔA) was read again after 1,2 and 3 minutes.

ΔA/min x 2760 =Iu/L of ALP.

Statistical Analysis

Statistical analysis was done using the statistical package for Social Sciences Version 22 (SPSS Inc,Chicago).Differences of mean among two groups was compared by unpaired T-test. Determinations of correlation between variables were done by Pearson correlation test. The level of significance for all the inferential statistics was set at $p<0.05$.

III. Result

There was a significant ($p<0.05$) increase in both the systolic and diastolic blood pressure as well as the liver enzymes involving the alanine transaminase, aspartate transaminase and alkaline phosphatase among the

preeclamptic group (Table 1). There was a significant positive association between the systolic pressure and the AST and ALT among the preeclamptic group with the exception of the alkaline phosphatase which had a positive but non-significant correlation. There was also a positive but non-significant association between the systolic blood pressure and the liver enzymes among the non-preeclamptic group (Table 2). There was a significant positive association between the diastolic blood pressure and the alanine transaminase and aspartate transaminase enzymes among the preeclamptic group but a non-significant positive association was observed in the alkaline phosphatase. There was also a non-significant positive association between the ALT,AST and ALP among the non-preeclamptic group (Table 3).

Table 1: Liver enzymes in cases and controls

Parameter (mean ± SD)	Preeclampsia (n=35)	Non-preeclampsia (n=35)	P-value
Systolic BP (mmHg)	169.56±20.02	117.42±6.01	0.006
Diastolic BP(mmHg)	107.45±8.14	75.36±8.20	0.002
ALT (Iu/L)	57.70±8.14	14.19±2.96	0.004
AST (Iu/L)	42.54±8.66	10.5±3.80	0.001
ALP (Iu/L)	380.12±151.62	1740.14±46.53	0.002

ALT – Alanine transaminase, AST = Aspartate Transaminase, ALP = Alkaline Phosphatase, Data expressed as mean ± SD, significant at p value $p<0.05$.

Table 2: Correlation of Systolic blood pressure with liver enzymes

Parameter	Preeclampsia		Non-preeclampsia	
	r value	p value	r value	p value
ALT	0.136	0.031	0.019	0.700
AST	0.189	0.002	0.047	0.222
ALP	0.211	0.141	0.123	0.516

ALT = Alanine Transaminase, AST = Aspartate Transaminase, ALP = Alkaline Phosphatase, r = coefficient of correlation, significant at p value $p<0.05$.

Table 3: Correlation of diastolic blood pressure with liver enzymes

Parameter	Preeclampsia		Non-preeclampsia	
Liver enzymes	r value	p value	r value	p value
ALT	0.178	0.011	0.057	0.106
AST	0.124	0.003	0.133	0.225
ALP	0.230	0.109	0.091	0.538

ALT = Alanine Transaminase, AST = Aspartate Transaminase, ALP = Alkaline Phosphatase, r = coefficient of correlation, significant at p value $p<0.05$

IV. Discussion

Abnormal liver function in pregnancy has been recognized as a biomarker for preeclampsia (9). However, there is a paucity of data on the values of liver enzymes in preeclamptic patients in the Enugu Metropolis. In the present study, we recorded significant increase in the liver enzymes involving the Alanine Transaminase(ALT), Aspartate Transaminase(AST) and Alkaline Phosphatase(ALP) levels in the preeclamptic patients compared to the non-preeclamptic controls. This is consistent with the findings of many studies which had reported increased

level of the ALT, AST and ALP in preeclamptic patients compared to non-preeclamptic controls (10,11,12,13). It is thought that elevated liver enzymes among preeclamptic patients are due to hypoxic effect of preeclampsia on the liver, since hypoxia results in necrosis with a resultant alteration of membrane permeability, degeneration of hepatocytes and release of liver enzymes into the circulation (14). Hazariet al (12) had described an abnormal prevalence of 40% in AST, 45% in ALT and 87.50% in ALP for preeclamptic subjects. Our assessment of the relationship of the liver enzymes with the blood pressure of preeclamptic patients in the present study revealed that increase in blood pressure is associated with increase in the liver enzymes. This positive association is consistent with the findings of Ekunet al (14) and Patraet al (15) which suggests that preeclampsia predisposes to increased risk of hepatic pathology with severe preeclampsia a higher risk factor to hepatic pathology. These findingsprovides scientific evidence which may be very useful to prevent and manage the adverse outcomes of preeclampsia in our population.

V. Conclusion

The findings of increased liver enzymes in the present study provides scientific evidence for the management of adverse outcomes for preeclamptic patients in our population.

References

[1] Lisonkova S, Bone JN,Muraca GM, Razaz N, Wang LQ, Sabr Y, Boutin A, Mayer C, Joseph KS,(2021). Incidence and risk factors for severe preeclampsia, hemolysis, elevated liver enzymes, and low platelet count syndrome and eclampsia at preterm and term gestation: a population-based study. American Journal of Obstetrics and Gynecology 538.el: 1-19.

[2] Sonal, Bhojwani P,(2018). Relationship between pregnancy-induced hypertension and liver function test: an observational study. International Journal of Medical Research Professionals. 4(2): 166-171.

[3] Afrox F, Sultana N, Rahman A, Zerin N, Samsuzzaman SM, Chowdhury PP, Andalib MH,Morshed M, Rahman MM, Kamal MM,(2020). A comparative study of hepatic enzymes between preeclampsia and normal pregnant women. Journal of Dhaka Medical College 29(1):18-22.

[4] Johnaon KD,Periselti A, Thandassery R, Inamdar S, Cheryala M, Jecmenica M, Tharian B, Goyal H,(2020). Laboratory evaluation of deranged liver chemistries in pregnancy. Journal of Laboratory and Precision Medicine 5 (4): 1-9.

[5] Naimnai M, Bhargava KK,(2019).A comparison of liver enzymes, bilirubin and uric acid in preeclampsia, eclampsia and normotensive subjects. International Journal of Clinical Obstetrics and Gynacology 3(2): 19-20.

[6] Ogbuabor AO, Ogbuabor GN, Okolo RC,(2022).Significance of some coagulation parameters in women with unexplained recurrent implantation failures.Asian Research Journal of Gyecology and Obstetrics 8(1): 1-6.

[7] Cookey SN,GombaVE,Warriboko CM,(2022).Prevalence of diabetes in rural communities in South South and South East Nigeria, a retrospective cross sectional community based survey. IOSR Journal of Dental and Medical Sciences 2(2): 26-32.

[8] Ugwu EO, Dim CC, Okonkwo CD,Nwankwo TO,(2011). Maternal and perinatal outcome of severe preeclampsia in Enugu, Nigeria after introduction of magnesium sulfate. Nigerian Journal of Clinical Practice 14(4): 418-421.

[9] Zhang Y, Sheng C, Wang D, Chen X, Jiang Y, Dou Y, Wang Y, Li M, Chen H, He W, Yan W, Huang G,(2022). High-normal liver enzyme levels in early pregnancy predispose the risk of gestational hypertension and preeclampsia: a prospective cohort study. Frontiers in Cardiovascular Medicine 9(963957): 1-12.

[10] Asha NS, Varghese A,(2017). Study of liver enzymes in preeclampsia. Journal of Medical Sciences and Clinical Research 5(1): 15169-15172.

[11] Das S, Char D, Sarkar S, Saha TK, Biswas S, Rudra B,(2013). Evaluation of liver function test in normal pregnancy and preeclampsia: a case control. IOSR Journal of Dental and Medical Sciences 12 (1): 30-32.
[12] Hazari NR, Hatolkar US, Munde SM,(2014).Study of serum hepatic enzymes in preeclampsia. International Journal of Current Medical and Applied Sciences 2(1): 1-8.
[13] Dascaj R, Izetbegovic S, Stojkanovic G, Dresha S,(2016). Elevated liver enzymes in cases of preeclampsia and intrauterine growth restriction. Medial Archives 70(1): 44-47.
[14] Ekun AO,Olamumi MO, Makwe CC, Ogidi NO,(2018).Biochemical assessment of renal and liver function among preeclamptics in Lagos metropolis.International Journal of Reproductive Medicine 159 4182: 1-6.
[15] Patra KK,Chattopadhyay S, Biswas S, Hadi A, (2022). A study of abnormal liver function in pregnancy and its correlation with fetomaternal outcome in a teaching hospital of Kolkata in Eastern India. Asian Journal of Medical sciences 13 (8): 1-7.