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Liver Protein and Enzymes in HIV Infected Pregnant and Non-pregnant Women on Antiretroviral Therapy

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Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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ABSTRACT

This in vivo study was carried out to investigate alterations in the levels of proteins and enzymes produced by the liver of HIV infected pregnant women and HIV infected non pregnant women under different antiretroviral therapy. Forty six human patients (Pregnant patient, n=21, Non pregnant patient, n=25) were recruited during this study from the PEPFAR (President Bush Emergency Plan for Aids Research) clinic in LUTH (Lagos University teaching Hospital), Lagos. The patients were between the ages of 29 – 34 years. All samples were analyzed for Albumin, Transferrin, Urea, Total protein, Total bilirubin, Creatinine and Cholinesterase. Along with it, liver enzymes – Alkaline phosphate, Alanine aminotransferases and Aspartate aminotransferases were also analyzed to confirm proper liver function for each patient. Result showed that total bilirubin and transferrin were statistically higher in the pregnant group while other liver proteins (Albumin, Urea and Total protein) were statistically lower in the pregnant group. Two liver enzymes,

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Creatinine and Cholinesterase, were statistically lower in the pregnant group. Though, other liver enzymes; aspartate aminotransferases and alanine aminotransferases were also lower in the pregnant group. No significant difference were noted when statistics were applied. Only alkaline phosphatase showed a non significant increase in the pregnant group. Findings in this study suggest that effective antiretroviral therapy stabilizes proteins and enzymes production in both HIV groups, however, slight alterations which were observed in the pregnant HIV group were due to physiological changes during pregnancy.

Keywords: HIV; liver proteins; liver enzymes; antiretroviral therapy.

1. INTRODUCTION

The liver is a large organ located in the upper right portion of the abdomen. It serves as the body's chemical factory. The liver is a very important organ of the body because many organs in the body depend on the liver's products to support their activities. Dysfunctions in the liver are frequent causes of illness and death in people with HIV infection, even in those previously considered healthy [1]. Illnesses that affect the liver are hepatitis (inflammation of the liver), fatty liver cirrhosis, cancer, and gallstones. These broad categories reflect changes in the liver, as opposed to what is actually causing the symptoms or changes. The origin of these changes can be viral hepatitis, alcohol, toxic exposures or medications. These infections and substances can damage the liver and may lead to changes that ultimately compromise its ability to function normally [2].

Most proteins and enzymes in the body are manufactured in the liver. The level of these proteins when measured can be used to tell if there are abnormalities in the liver or if a physiologic change has occurred in the body due to pregnancy, intake of drugs or disease condition.

Hence, the present study was designed to determine if there are alterations in the levels of liver proteins and enzymes, for both group of HIV patients, and to ascertain the possible causes of such alterations.

2. MATERIALS AND METHODS

All human patients (n=46) that participated in the research were recruited after ethical consent from the PEPFAR Clinic of the Lagos University Teaching Hospital, Lagos. Patients were eligible because they all showed no liver disorder after undergoing the Liver Function Test. The study population were divided into two groups; the pregnant group and non pregnant group. The pregnant group (n=21: Age= 30±3) were all HIV positive women in their second trimester of pregnancy. They were administered one of the group of the following antiretroviral drugs, (i) Zidorudine (AZT) [2] Combivir (CBV), Retonavir (RTV) and Saquinavir (SQR) [3] Trurada and Nevirapine [4] Fixed Dose (FDC). For the purpose of research no personal identifier were used on the blood samples of the participants, instead their LUTH identification number were used to ensure anonymity of the patients to facilitate laboratory procedures and minimize the chances of error during the handling of the blood specimens.

Venous blood was collected into a plane tube for each patient. The samples in the plane tube were allowed to clot, centrifuged at 1.6 RCF for 10 minutes. Serum for biochemical analyses were separated into cryogenic vial and stored at 20^{o}C and they were analyzed within one week. Analysis of the liver proteins and enzymes were done colometrically with the Roche/Hitachi 902 Automated Analyzer. Viral load values were analyzed using the HIV-1- Amplicor kit.

3. RESULTS

The student t-test was used to assess significant mean differences in both HIV group while ANOVA (Analysis of Variance) were used to check the effect of the different antiretroviral therapy on the various liver enzymes and proteins.

Apart from Total bilirubin (1.90±0.25) and Transferrin (2.49±0.19) which were statistically higher in the pregnant HIV group ($p<0.05$), other serum proteins: Albumen (29.22±0.27), Urea (2.81±0.01) and Total protein (53.47± 2.38) were statistically lower in the pregnant group (see Table 1).

Liver enzymes, Cholinesterase (3959.33±336.34) and Creatinine (76.74±3.41) were statistically lower in the pregnant HIV group (P<0.05). Aspartate aminotransferase (20.05±2.02) and alanine aminotransferase (8.83±1.59) of the pregnant HIV group were non-significantly different from the non- pregnant HIV group (see Table 2).

Using ANOVA, no particular ART showed a higher effect on the level of enzyme production (see Table 3).

Also, with ANOVA all ART had equal effect on the protein level production (see Table 4).

The results in Tables 6a and 6b showed that there is no statistical linear relationship between viral load and the various serum proteins for both group of patients.

4. DISCUSSION

The present study reveals that the mean value of the serum proteins; albumin, urea, total protein and enzymes; cholinesterase and creatinine showed a significant decrease in the HIV positive pregnant group when compared with those of the HIV positive non pregnant group. Other serum proteins; total bilirubin and transferrin levels were significantly higher in the pregnant group. However, all increase and decrease were within the normal range. Serum albumin, total protein, urea, creatinine and cholinesterase level were reduced in the HIV positive pregnant group

Table 1. Statistical comparison on some serum parameters of both groups

Parameters	Non-pregnant patient group	Pregnant patient group	T-test at 75% CI	Inference
(g/l)				Significant
Transferrin	1.93±0.08	2.49±0.19	2.76 > 1.96	difference
(mg/dl)				Significant
Total bilirubin	22.67±2.30	1.90±0.23	1.98 > 1.96	difference
(g/l)				Significant
Albumin	38.20±1.13	29.22±0.27	5.34 > 1.96	difference
(mmol/l)				Significant
Urea	3.67±0.24	2.81±0.01	3.64 > 1.96	difference
(g/l)				Significant
Total protein	72.85±5.90	53.47±2.38	3.04 > 1.96	difference

Values were expressed are mean and standard error of meanCI: Confidence Interval

Table 2. Statistical comparison on enzyme levels of both groups

Parameter	Non-pregnant patient group	Pregnant patient group	T-test at 95%CI	Inference
(Iu/l)				Significant
Cholinesterase	6110.92±353	3959.33±336	4.41 > 1.96	difference
(mmol/l)				Significant
Creatinine	108.56±4.57	76.74±3.41	5.56 > 1.96	different
(Iu/l)				No significant
AST	25.73±2.87	20.05±2.02	1.61 <1.96	difference
(mmol/l)				No significant
ALT	10.48±1.12	8.83±1.59	0.84 < 1.96	difference
(Iu/l)				No significant
ALP	76.70±8.51	94.22±13.84	1.07 < 1.96	difference

Values were expressed as mean and standard error of mean CI: Confidence Interval

Table 3. Effect of ART on the level of enzyme production

Group	Calculated F-value	Tabulated F-value	Inference
Pregnant group	0.87	4.46	Equal effect
Non pregnant group	1.00	3.01	Equal effect

Table 4. Effect of ART on the level of protein production

Group	Calculated F-value	Tabulated F-value	Inference
Pregnant group	1.09	3.89	Equal effect
Non pregnant group	1.01	2.76	Equal effect

Table 5. Statistical comparison on viral load values of both groups

Parameter	Non-pregnant patient group	Pregnant patient group	T-Test at 95% CI	Inference
Viral Load	58779±49791.74	14352.62±12603.23	0.86 < 1.96	No significant difference

Values were expressed as mean and standard error of mean CI: Confidence Interval

Table 6. Effect of viral load on the level of serum protein production

a. Pregnant subjects

Parameter 1	Parameter 2	Coefficient of correlation	Significant test	Inference
Viral Load	Transferrin	0.39	0.39<0.43	No linear relationship
Viral Load	Total protein	-0.23	-0.23<0.43	No linear relationship
Viral Load	Albumin	0.39	0.39<0.43	No linear relationship

b. Non pregnant subjects

Parameter 1	Parameter 2	Coefficient of correlation	Significant test	Inference
Viral Load	Transferrin	0.32	0.32<0.39	No linear relationship
Viral Load	Total protein	-0.05	-0.05<0.39	No linear relationship
Viral Load	Albumin	-0.25	-0.25<0.39	No linear relationship

because of haemodilution which is an increase in fluid contents of blood resulting in lowered concentration of formed elements; in this case, as a result of the physiological changes that occur normally in pregnant women. Significant increase in serum transferrin in the HIV positive pregnant women was due to increased erythropoiesis, this is as a result of high demand made on the iron stores by the growing foetus and placenta expanding maternal blood volume and red cell mass. Also high blood levels of bilirubin in the HIV positive pregnant group formed by the breakdown of hemoglobin indicates that the liver is not adequately transferring excess bilirubin from the blood stream to the bile. Thus, excess breakdown of hemoglobin occurs to meet the iron demand of the foetus, resulting in a clinical increase. However, the increase is within the normal range and not one that should indicate a liver dysfunction/disease.

Reports from Priscilla et al. [3], Fischbach et al. [4], Satyanranya [5], Cunninghan et al. [6], and Gross et. al. [7] confirmed a significant decrease in albumin, urea, cholinesterase, total protein and creatinine respectively during pregnancy. Also, previous studies by Wells and his colleagues [8] and Schreier [9] showed significant statistical increase in transferrin and total bilirubin levels during pregnancy. These reports were in the line with present study.

Values for all liver function tests (Aspartate aminotransferases, Alanine aminotransferases and Alkaline phosphate) were all within their normal range for both group of HIV positive pregnant and HIV positive non pregnant women indicating proper liver function. These results of proper liver function is also attributed to the effectiveness of the antiretroviral therapy administered. When comparing between both groups, the mean values of Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT) were lower in the pregnant group but the decrease is not statistically significant. Also, the mean value of Alkaline phosphatase for the HIV positive pregnant group was higher than those of the HIV positive non pregnant group, but the increase likewise was not statistically significant ($P<0.05$). This slight increase though not significant is brought about by minute leaks of ALP made by the placenta into the mothers blood stream. The report gotten from Y' Bacq and his colleagues [10] that worked on serum AST and ALT level

were in tandem with present study. Similarly, reports from Y'Bacq et al. [10] and Berk et al. [11] both confirmed that the slight increase in ALP observed in pregnant women is not statistically significant.

Correlation analysis between viral load values and the various serum proteins (transferrin, total protein and albumin) showed no significant linear relationship. Previous studies prove that serum proteins like albumin, transferrin and total bilirubin are lowered with increase in viral load, but this was annulled in present study because of the effective administration of ART.

Analysis on the various antiretroviral types given to both group of HIV patient showed that all the antiretroviral therapy had equal effect on the serum protein and enzymes (Albumin, Total bilirubin, Urea, Total protein, Transferrin, Cholinesterase, Creatine, AST, ALT and ALP) production level.

5. CONCLUSION

The observations in this study showed that effective antiretroviral therapy stabilizes proteins and enzymes production in both HIV groups. Hence, effective antiretroviral therapies could be beneficial to HIV patients.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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