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LEVELS OF SERUM ALANINE/ASPARTATE AMINOTRANSFERASE AND UREA IN APPARENTLY HEALTHY RURAL COMMUNITY IN GHANA: A CASE STUDY IN SABIN-AKROFROM AND TREDE IN THE ASHANTI REGION

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ABSTRACT

Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST) and urea levels were assessed in 27 males (mean age 32.33 yrs) and in 34 females (mean age 27.85yrs) Ghanaian rural dwellers to determine the functional status of their liver (ALT/AST) and kidney (Urea). No significant (P≥0.05) differences were observed between the sexes in all the assessed parameters. Mean values of 28.92 U/L, 31.64 U/L, 9.04 mmol/L for males and 30.09 U/L, 33.92 U/L, 8.72 mmol/L for females were obtained respectively for ALT, AST and Urea. The serum levels of ALT, AST and AST to ALT ratio indicated that both groups had normal functioning liver but the urea levels for both sexes appear to suggest renal impairment. Further investigations are needed to establish the underlying pathology.

INTRODUCTION

Levels of certain enzymes and metabolites are used as biomarkers in routine biochemical investigations which form an important component of diagnosis, prognosis and treatment of disease (Tietz *et al.*, 1992; Beld *et al.*, 1998; Pratt and Kaplan, 2000; Al-Quaiz *et al.*, 2003; Mateescu *et al.*, 2006). Also, the levels of these biomarkers give information on the physiological state of the organs that produce them (Goldie and McConnell, 1990; Kanai, 2005). For instance, liver function can be assessed by measuring the activities of enzymes such as alanine aminotransferases (ALT), aspartate aminotransferase and gamma glutamyltransferase (Goldie and McConnell, 1990; Valentine *et al*., 1990; Pratt and Kaplan, 2000; Kanai, 2005; Kariv *et al*., 2006). On the other hand, the function of the kidney can be monitored by using urea and creatinine levels as biomarkers.

The levels of these biomarkers are influenced by conditions such as hepatitis, cirrhosis, muscle injury and drugs (Kamath, 1996; Green and Flamm, 2002). A lot of factors including physical activity, high alcohol consumption, viral infection and drugs like paracetamol create the above conditions (Kamath, 1996; Green and Flamm, 2002). Such conditions damage the liver parenchymal cells and release the aminotransferases into the blood to increase the levels of these enzymes in the bloodstream (Akkaya *et al.*, 2007).

In the Ghanaian society in general and the rural communities in particular, self-medication with paracetamol, high intake of hard liquor

(akpeteshie) and increased farm-related physical activity are common. To investigate the effect of these rural lifestyles on the functional status of the liver and kidney, the AST, ALT and urea levels were measured in apparently healthy members of rural communities in the Ashanti Region of Ghana.

MATERIALS AND METHODS

The study was conducted from November, 2007 to May, 2008, at Sabin- Akrofrom and Trede, which are villages in the Bosomtwe-Atwima Kwanwoma District in the Ashanti Region. Bosomtwe-Atwima-Kwanwoma District is located at the central portion of the Ashanti Region. It lies within latitude 6º 43' North and longitude 1º 46' West. The District is bounded on the North by Atwima Nwabiagya and Kumasi Metropolis and on the East by Ejisu- Juaben District. The southern section is bounded by Amansie West and East Districts. Sabin- Akrofrom and Trede are found in the southern section of the district and about 17 kilometers from Kumasi. The two communities were chosen because the lifestyle of the inhabitants is representative of rural communities in Ghana. The main occupation is farming and alcohol consumption pattern is a reflection of the situation in most rural areas of Ghana. Paracetamol consumption has been their lot, as a result of the pain they experienced due to the exertion during farming activities. Excessive alcohol and paracetamol consumptions could have negative impact on the functional status of vital organs like the liver.

Sample Collection and Preparation

Numbers were assigned to the houses in the two villages. About 100 of the houses numbered were selected at random and respondents from such houses who consented and met the inclusion criteria were recruited. Questionnaires were administered to collect information on demography, alcohol consumption pattern, self-medication with paracetamol, general health status and other lifestyle activities. Those found to be taking liver enzyme inducer drugs like barbiturates were excluded. In all, sixty-one respondents participated in the study. Blood samples were taken from respondents by an experienced medical laboratory technician using the disposable syringes in a standard venipuncture technique. The blood samples were placed in labeled plastic tubes with gel barriers and taken to the laboratory at St. Michael's Hospital, Pramso, also in the Asanti Region of Ghana.

The blood samples were allowed to clot in sterile centrifuge tubes at room temperature for 30-60 minutes and centrifuged at 4000 rpm for 10 minutes using a Hitachi 20PR- 52D centrifuge. The sera were separated and transferred into labeled 15ml centrifuge tubes. The sera were then transferred into dry and well-labeled eppendorf tubes and stored at a temperature of -20^{o}C for less than 24 hours prior to laboratory analysis.

Ethical Approval

The study was approved by the Ethics Committee of the University of Cape Coast, Cape Coast, Ghana. Informed consent was obtained from all the study participants. All protocols followed were in line with the ethical standards of the Ghanaian Ministry of Health.

Biochemical Analyses

The Microlab 300 Semi-automated Clinical Chemistry Analyzer (Vital Scientific, N.V. Netherlands) was used for all the analyses following the manufacturer's instructions. All measurements were made at a wavelength of 340 nm. The operation of the analyzer for the enzyme assay is based on the coupled assay principle described by Phillip and Graham, (1995). All the enzymes and reagents used for the analyses were obtained from Cypress Diagnostics, Belgium.

Assay of ALT

A reconstituted reagent was prepared by dissolving one tablet of a reagent containing 0.18 mmol/L NADH, 1200 U/L LDH and 15 mmol/L α-ketoglutarate in 15 ml of 100 mmol/L TRIS buffer (pH 7.8) and 500 mmol/L L-alanine. Exactly 0.1 ml of serum sample was

pipetted into 1.0 ml of the reconstituted reagent, mixed thoroughly and transferred into a 1cm cuvette for analysis.

Assay of AST

A reconstituted reagent was prepared by dissolving one tablet of a substrate containing 0.18 mmol/L NADH, 800 U/L LDH, 600 U/L MDH and 12 mmol/L α-ketoglutarate in 15 ml 80 mmol/L TRIS buffer (pH 7.8) containing 200 mmol/L L-aspartate. A 0.1 ml serum sample was pipetted into 1.0 ml reconstituted reagent, mixed thoroughly and transferred into a 1 cm cuvette for analysis.

Urea Assay

A reconstituted reagent was prepared by mixing 30000 U/L urease with 140 mmol/L Sodium hypochlorite, 150 mmol/L Sodium hydroxide and 50 mmol/L phosphate buffer (pH 6.7) containing 2 mmol/L EDTA, 60 mmol/L Sodium Salicylate and 10 mmol/L Sodium Nitroprusside. A 10 µl serum sample was pipetted into a 1ml reconstituted reagent and mixed with 10 µl of 50 mg/dl standard aqueous urea. The mixture was then transferred into a 1 cm cuvette for analysis.

Statistical Analysis

The data obtained were analyzed with the SPSS 16.0 statistical software. The means and standard deviations (SD) were determined and reported as mean ± SD. Mean values were compared using the independent sample t-test and a p-value of <0.05 was considered significant.

RESULTS

Sixty-one participants consisting of 34 (56.73%) females and 27 (44.26%) males consented to donate blood for the analyses. Their ages ranged from 13 to 75 years. The males were 13 to 75 years old with mean age and standard deviation of 32.33±16.30 while the females were 15 to 65 years old with mean age and standard deviation of 27.85±13.78 years. The mean age of males and female did not differ significantly (P = 0.25). The age and serum biochemical profile of donors are shown in Table 1.

The ALT values ranged from 7.53 U/L to 117.41 U/L and 10.33 U/L to 110.60 U/L (Table 1b) for males and females respectively. The mean and standard deviation for males and females were 28.91±24.48 U/L and 30.08± 19.50 U/L respectively. The mean ALT levels in the males and females did not differ significantly (P = 0.84).

The AST levels ranged from 7.02 to 78.43 U/L and 14.25 to 84.83 U/L for males and females respectively (Table 1c). The means and standard deviations were 31.64±16.16 U/L and 33.95±13.23 U/L respectively for male and female participants. There was no significant (P = 0.53) difference observed between the mean AST levels of males and females.

The results of the serum urea analysis (Table 1d) show that the values ranged from 4.90 to 28.60 mmol/L and 4.70 to 47.30 mmol/L for males and females respectively. The means and standard deviations were respectively 9.04±4.89 mmol/L and 8.72±8.44 mmol/L for males and females. The mean values for the sexes did not differ significantly (P = 0.87).

AST/ALT ratios for both sexes (Table 1e) ranged from 0.38 to 4.07 and 0.53 to 2.62 for males and females respectively. The mean AST/ALT ratios and standard deviations were 1.38 ± 0.70 and 1.36 ± 0.60 for male and female donors respectively. About 30%, 33% and 37% of male donors had AST/ALT ratios of less than 1, between 1 and 1.5 and greater than 1.5, respectively. With respect to female donors, approximately 38%, 29% and 32% had AST/ALT ratios of less than 1, between 1 and 1.5 and more than 1.5, respectively.

The scatter plots (Figs. 1 and 3) show the Pearson's correlation between ALT and AST levels for male and female donors respectively. A significantly positive correlation was observed between the ALT and AST levels for males (P = 0.001, r = 0.593) and females (P = 0.000, r = 0.790).

DISCUSSION

Elevated ALT level is associated with several liver-related pathologies (Anand and Velez,

Table 1: Age and Serum Biochemical Profile of donors

a. Age and sex distribution of donors			
Sex	No. of donors	Mean age ±S.D	Age range
Male	27	32.33±16.30	13-75
Female	34	27.85±13.78	15-65
b. Serum ALT levels in male and female donors			
Sex	Mean ±S.D	Range(U/L)	Ref. range (37^oC)
Male	28.91±24.48	7.53-117.41	10-40
Female	30.08±19.50	10.33-110.60	10-32
c. Serum AST levels in male and female donors\			
Sex	Mean ±S.D	Range(U/L)	Ref. range (37^oC)
Male	31.64±16.16	7.02-78.43	5-38
Female	33.95±13.23	14.25-84.03	5-31
d. Serum UREA levels in male and female donors			
Sex	Mean ±S.D	95% C.I	Ref. range (37^oC)
Male	9.04±4.89	7.11-10.97	2.50-7.50
Female	8.72±8.44	5.77-11.67	5.50-7.50
e. Serum AST/ALT ratios in male and female donors			
Sex	Mean AST/ALT ratio ± S.D	95% C.I.	% < 1.
Male	1.38 ±0.70	1.12-1.645	29.63
Female	1.36 ±0.60	1.34-1.38	38.24

KEY ±S.D = ±Standard deviation, C.I= Confidence Interval Ref. range - normal reference ranges
** represents approximate percentage of individuals with possible abnormality. ALT –alanine aminotransferase, AST- aspartate aminotranferase

2004; Nyblom *et al.*, 2004; Akkaya *et al.*, 2007). In this study, ALT, AST and urea levels of healthy-looking rural dwelling Ghanaians were determined. Compared to established reference values the mean ALT levels for both male and female participants fell within the normal range. Although the established reference values for ALT have been recently challenged (Prati *et al.*, 2002; Mohamadnejad *et al.*, 2003) with country-specific reference cut-offs being suggested (Akkaya *et al.*, 2007), we still compared our findings with the established international reference values because no specific reference values for Ghanaians were available. Our result suggested that in general, the participants had normal functional liver.

Since ALT level alone has been observed to be an inadequate diagnostic marker for determining liver functional status (McCormick *et al.*, 1996; Lazano *et al.*, 1998; Mahl, 1998; Ito *et al.*, 2004; Shiffman *et al.*, 2006) we further investigated the level of AST to see how the two enzymes are related.

Mean AST level of 31.64 U/L for males was within the reference range but the mean AST level of 33.95 U/L for females was a bit higher than the reference cut-off though not clinically significant.

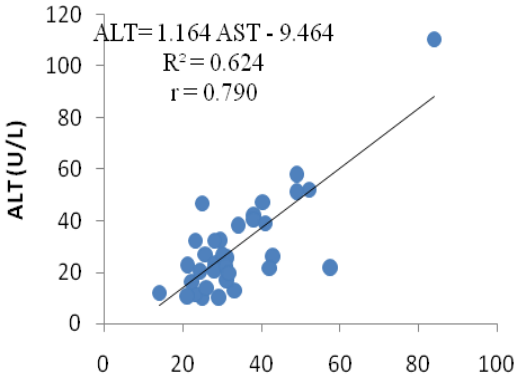

Fig. 1: Relationship between ALT and AST in females

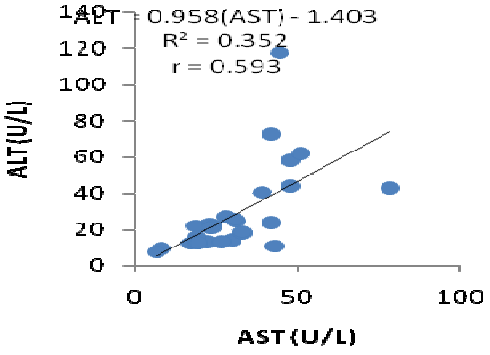

Fig. 2: Relationship between ALT and AST in males

A comparison of levels of AST to ALT is believed to be a reliable diagnostic marker (Nyblom *et al.*, 2004) for liver diseases. It has even been suggested that AST/ALT ratio greater than 1.5 is diagnostic for alcohol-induced liver injury (Correia *et al*., 1981; Salaspuro, 1987). In normal individuals, ALT levels are higher than those of AST (Sheth *et al*., 1998; Imperiale *et al*., 2000; Park *et al*., 2000; Siddiqi *et al*., 2007) though not higher than 1.5 times the upper reference limit (Torezan-Filho *et al*, 2004). We found AST level correlating positively with ALT level for both males and females. The calculated mean AST/ALT ratio of 1.38 and 1.36 for males and females respectively fell short of the 1.5 value for alcohol-induced hepatic injury. This suggests that in general, alcohol-related hepatic injury was not present in the participants. A careful look at the individual AST/ALT ratio values revealed that about 37% and 32% of the male and female participants respectively had AST/ALT ratio values above 1.5, which may appear to suggest alcohol-induced liver cirrhosis. Although majority of our respondents (data not shown) indicated that they drink locally brewed alcohol (akpeteshie) and self-medicate with paracetamol sometimes, none admitted the habit to be regular for fear of being branded alcoholic which the communities frown upon.

Studies elsewhere (Correia *et al*., 1981; Salaspuro, 1987; Torezan-Filho *et al*., 2004) that found AST/ALT ratio greater than 1.5 to be strongly associated with alcohol-induced hepatic injury also observed clinically significant higher levels of AST and/ or ALT in their respondents. In the current study, those exhibiting AST/ALT ratio values of more than 1.5 did not give clinically significant higher levels of AST and/or ALT. Thus, altogether, our respondents did not experience any clinically significant hepatic injury as a result of their lifestyle.

The serum urea levels of 9.04mmol/L and 8.72 mmol/L obtained for males and females respectively, were higher than the reference upper limit with the males recording a slightly higher but statistically insignificant level than the females. These figures appear to suggest renal-related pathological process in participants since they were chosen based solely on physical appearance and information provided by respondents on their health status. As a result, further investigations are required to confirm the renal status of the study group.

CONCLUSION

The levels of ALT, AST and urea of a sample of apparently healthy-looking Ghanaian rural dwellers have been determined. The results suggest normal liver function but the status of their kidney is ill-defined.

REFERENCES

Akkaya, O., Kiyici, M., Yilmaz, Y., Ulukaya, E. and Yerci, O. (2007). Clinical significance of activity of ALT enzyme in pa-

tients with hepatitis C virus. *World J. Gastroenterol* 13(41): 5481-5485.

Al-Quaiz, M. N., Madani, T.A., Karawi, M.A. (2003). The natural history of hepatitis C virus infection. *Saudi Med J.* 24 (2): S67-S70.

Anand, B. S. and Velez, M. (2004). Assessment of correlation between serum titers of hepatitis c virus and severity of liver disease. *World J Gastroenterol* 10 (16): 2409-2411.

Beld, M., Penning, M., McMorrow, M., Gorgels, J., van den Hoek, A. and Goudsmit, J. (1998). Different hepatitis C virus (HCV) RNA load profiles following seroconversion among injecting drug users without correlation with HCV genotype and serum alanine aminotransferase levels. *J. Clin. Microbiol* 36: 872-877.

Correia, J. P., Alves, P. S. and Camilo, E. A. (1981). SGOT-SGPT ratios. *Digestive Diseases and Sciences* 26: 284.

Fuad, A. M. H. and Salim, O. (2003). Interpretation of liver chemistry tests *Bull Kuwait Inst Med Spec* 2: 27-31.

Goldie, D.J. and McConnell, A.A. (1990). Serum alanine aminotransferase reference range estimated for blood donors. *J. Clin. Path. 43 (11):929-31*.

Green, R. M. and Flamm, S. (2002). AGA technical review on the evaluation of liver chemistry tests. *Gastroenterology* 123: 1367-84.

Imperiale, T. F., Said, A.T., Cummings, O. W. and Born, L. J. (2000). Need for validation of clinical decision aids: use of the AST/ ALT ratio in predicting cirrhosis in chronic hepatitis C. *Am J Gastroenterol* 95(9): 2328-2332.

Ito, H., Yoshioka, K., Ukai, K., Watanabe, K., Yano, M., Ishigami, M., Mizutani, T., Sasaki, Y., Katano, Y. and Goto, H. (2004). The fluctuations of viral load and serum alanine aminotransferase levels in chronic hepatitis C. *Hepatol Res* 30: 11-17.

Kamath, P. S. (1996). Clinical approach to the patient with abnormal liver test results. *Mayo Clin Proc* 71: 1089-95.

Kanai, P. (2005). Renal function. *Am J Clin. Path.* 13: 156-169.

Kariv, R., Leshno, M., Beth-Or, A., Strul, H., Blendis, L., Kokia, E., Noff, D., Zelber-Sagie, S., Sheinberg, B. and Oren, R. (2006). Halpern, Z. Reevaluation of serum alanine aminotransferase upper normal limit and its modulating factors in a large-scale population study. *Liver Int* 26: 445-450.

Lozano, M., Cid, J., Bedini, J. L., Mazzara, R., Gimenez, N., Mas, E., Ballesta, A. and Ordinas, A. (1998). Study of serum alanine-aminotransferase levels in blood donors in Spain. *Haematologica* 83: 237-239

Mahl, T.C., (1998). Approach to the patient with abnormal liver test. *Prim. Care Pract.* 2(4): 379-89.

Marshall, E.K. Jr. (1998). Evaluation of serum transaminases. *J. Biol. Chem.* 15:487.

Mateescu, R.B., Rimbas, M., Staniceanu, F., Zurac, S., Dragomir, P., Voiosu, M.R., Tataru, M., Zota, M. and Bucurica, S. (2006). Histological and nonhistological criteria in the evaluation of liver involvement in chronic hepatitis C. *Rom J Intern Med* 44: 117-130

McCormick, S. E., Goodman, Z.D., Maydonovitch, C.L. and Sjogren, M. H. (1996). Evaluation of liver histology, ALT elevation, and HCV RNA titer in patients with chronic hepatitis C. *Am J Gastroenterol* 91: 1516-1522

Mohamadnejad, M., Pourshams, A., Malekzadeh, R., Mohamadkhani, A., Rajabiani, A., Asgari, A. A., Alimohamadi, S. M., Razjooyan, H. and Mamar-Abadi, M. (2003). Healthy ranges of serum alanine aminotransferase levels in Iranian blood donors. *World J. Gastroenterol* 9(10): 2322-2324.

Nyblom, H., Berggren, U., Balldin, J. and Olsson, R. (2004). High AST/ALT ratio may indicate advanced alcoholic liver disease rather than heavy drinking. *Alcohol & Alcoholism* . 39 (4): 336–339.

Park, G. J., Lin, B. P., Ngu, M. C., Jones, D. B. and Katelaris, P.H. (2000). Aspartate aminotransferase: alanine aminotransferase ratio in chronic hepatitis C infection: is it a useful predictor of cirrhosis? *J. Gastroenterol Hepatol* 15(4): 386-390.

Phillip, M.A. and Graham, R. P. (1995). Designing a coupled assay system for aspartate aminotransferase. *Biochem Edu*. 23:40 -41.

Pratt, D. S., and Kaplan, M .M. (2000). Evaluation of abnormal liver enzyme results in asymptomatic patients. *N. Engl J Med* 342 (17): 1266-1271.

Prati, D., Taioli, E., Zanella, A., Della, Torre, E., Butelli, S., Del Vecchio, E., Vianello, L., Zanuso, F., Mozzi, F., Milani, S., Conte, D., Colombo, M., and Sirchia, G. (2002).Updated definitions of healthy ranges for serum alanine aminotransferase levels. *Ann Intern Med* 137: 1-10.

Salaspuro, M. (1987). Use of enzymes for the diagnosis of alcohol-related organ damage. *Enzyme J*. 37: 87–107.

Sheth, S. G., Flamm, S. L., Gordon, F. D. and Chopra, S. (1998). AST/ALT ratio predicts cirrhosis in patients with chronic hepatitis C virus infection. *Am J Gastroenterol* 93 (1): 44-48.

Shiffman, M. L., Diago, M., Tran, A., Pockros, P., Reindollar, R., Prati, D., Rodriguez-Torres, M., Lardelli, P., Blotner, S. and Zeuzem, S. (2006). Chronic hepatitis C in patients with persistently normal alanine transaminase levels. *Clin Gastroenterol Hepatol* 4: 645-652

Siddiqi, A.I., Siddiqeh M., Mehmood, A. and Siddiqui, M.A. (2007). Alanine aminotransferase/aspartate aminotransferase ratio reversal and prolonged prothrombin time: a specific indicator of hepatic cirrhosis. *J. Ayub Med Coll Abbottabad* 19 (3): 22-24.

Tietz, N.W., Shuey, D.F. and Wekstein, D.R. (1992). Laboratory values in fit aging individuals- sexagenarians through Centenarian. *Clinical Chem* 38 (6): 1167-85.

Torezan-Filho, M.A., Alves, V. A.F. Almeida, N.C., Fernandes, H.S. and Strauss, E. (2004). Chemical significance of elevated alanine aminotransferase in blood donors: a follow-up study. *Liver Int* 24:575-581.

Valentine, B.A., Blue, J.T., Shelley S.M. and Cooper, B.J. (1990). Increased serum alanine aminotransferase activity associated with muscle necrosis in the dog. *J Vet Intern med* 4:140-143.