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Variation of Alkalinephosphatase and Transaminases Levels in Different Trimesters of Pregnancy Iraqi Women

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Abstract

The level of enzymes Alkaline phosphatase (ALP) and transaminase (AST &ALT) were measured in 99 Iraqi pregnant women from different areas in Baghdad city and compared with a control group comprising non-pregnant women (29women). Those pregnant women were classified into three groups according to the semester of pregnancy. (Group I to III). New inclusion and exclusion criteria were applied in this study to increase the specificity. The result revealed a significant increase in the corresponding enzymes ($p<0.001$) for each simester of pregnancy when compared with the control group(non pregnant women). There were no significant changes in enzymes activity between group1 (first trimester) and group II(second trimester) . The significant changes in ALP were observed between group1(first trimester) and group III (third trimester) $p<0.001$.The same trend was observed between group II (second trimester) and group III (third trimester). The result also revealed insignificant changes in AST/ALT ratio among all the groups including control group ($p>0.05$).

Conclusion: This study indicate the importance of the establishment of new reference values for the above mentioned enzyme during pregnancy and unsuitability of ALP in liver function test during pregnancy.

Key words: *Alkalinephosphatase, transaminases levels, different trimesters , pregnancy Iraqi women.*

Introduction

Pregnancy defined as a physiological state which occur physical change in the reproductive age of a woman. From the time of the reproductive system of a woman changes through the three trimesters of pregnancy. the reproductive system other systems of the body represent by the renal, endocrine, nervous, cardiovascular, respiratory, gastrointestinal system and hepatobiliary system are also affected. The levels of estrogens (estradiol) and progesterone increase cumulative during pregnancy[1]. These sex hormones have effects on hepatic metabolic, synthesis, and excretory functions[2]. The biliary excretion of bromo sulfo phthalein decreases during late pregnancy and the clearance of some compounds that are secreted into bile may therefore be impaired6. The liver has a central and critical biochemical role in the metabolism, digestion, detoxification and elimination of substances from the body[3].

Liver functions are determine by measuring the concentration of substances produced by hepatocytes or by estimating the serum content of substances released from these cells as a result of damage and determine the capability of liver to perform metabolic functions like detoxification, conjugation[4]. Serum aminotransferases assays are the most common laboratory tests for detection of liver diseases and these include aspartate aminotransferase (AST, E.C.2.6.1.1), and alanine aminotransferase (ALT, E.C.2.6.1.2). They are excellent markers of hepatocellular injury[5]. AST is found primarily in the heart, liver, skeletal muscles, kidney, brain, pancreas, lungs, leucocytes and red blood cell while ALT is found primarily in the liver, kidney, with lesser amount in the heart and skeletal muscles. ALT is thought to be more specific for hepatic injury because it is present mainly in the cytosol of the liver cells and in low concentration else where15 while AST is both cytosolic (20% of total activity) and mitochondria (80% of total activity), it is less sensitive and specific for the liver reference[6]. The pregnant woman physiological changes to support fetal growth and development. During pregnancy, the serum estrogen and progesterone levels increase progressively and reach a maximum

during the third trimester. These sex steroids have effects on metabolic, synthetic, and excretory hepatic functions[7]. The increase in plasma volume that occurs during pregnancy leads to haemodilution and decreases the serum protein concentrations. Serum alkaline phosphatase levels increase in late pregnancy because of both a production of the placental isoenzyme and an increase in the bone isoenzymes.It is therefore not surprising that changes in liver function tests (LFTs) occur during pregnancy[8].

Alkaline phosphatase ALP (E.C.3.1.3.1) is present in practically all tissues of the body, especially at or in cell membranes and it occurs in particularly high levels in intestinal epithelium, kidney tubules, bones (osteoblasts), liver and placenta[9]. It catalyzes the hydrolysis of phosphate esters in alkaline environment generating an organic radical and inorganic phosphate[10]. Hepatobiliary disease and bone disease associated with increased osteoblastic activity are linked to increased serum alkaline phosphatase.

The ratio of AST to ALT is of use in Wilson disease, CLD and alcoholic liver disease and a ratio of more than 2 is usually observed. The lack of ALT rise is probably due to pyridoxine deficiency. In NASH the ratio is less than one in the absence of fibrosis on liver biopsy [11]. In viral hepatitis the ratio is usually less than one. The ratio invariably rises to more than one as cirrhosis develops possibly because of reduced plasma clearance of AST secondary to impaired function of sinusoidal cells[12]. ALT exceeds AST in toxic hepatitis, viral hepatitis, chronic active hepatitis and cholestatic hepatitis.

Many previous studies dealing with liver function test in different trimesters of pregnancy were carried out . most of these studies lack specificity because there were no clear exclusion and inclusion criteria involvement . Also the relation ship between alkaline phosphatase and transaminase enzymes were elucidated in order to draw some conclusions for the lab. Investigation of those parameters in different trimesters of pregnancy In this study new introduced **inclusion criteria** :

1- 1-All antenatal cases between 18 to 40 years of age.

2- spontaneous conception.

3- 3-singleton pregnancy.

4- No history of hypertension , diabetes or liver diease.

Also all pregnant women with the following criteria were excluded from our study:

1- Known liver disease .

2- Hypertensive patients.

3- Assisted conception.

4- Multiple pregnancy.

Method

Study Design and Subjects

This study was a hospital based cross sectional in vitro study collected specimens at private Hospital, Al-kadra'a hospital over a period of seven months (between November 2017 to June 2018). A cross sectional study consists of 102 pregnant women and 31 matched control (age matched non pregnant women).

Among the 102 pregnant women, 32 were in first trimester (within 1-3 month), 34 were in second trimester (within 4-6 month) and 36 were in third trimester (within 7-9 month). Subjects were recruited according to simple random sampling method meeting the selection criteria.

A written consent were taken from the pregnant women and control group before recuiting them in this study.

Blood Sample Collection

A volume of 3 ml of venous blood was drawn from each volunteer using a disposable vacutainer system in Plain and separator serum (SST) tubes vacutainer. Serum or plasma separated within half an hour and stored at -20 C temperature till analysis was carried out.

Analysis of Specimens

Serum alanine transaminase (ALT) activity was measured by modified IFCC UV enzymatic kinetic method. Serum aspartate transaminase (AST) activity was measured by modified IFCC UV enzymatic kinetic method. Serum alkaline phosphatase (ALP) activity was measured by DGKC colorimetric Kinetic method. AST/ ALT ratio was also calculated. All biochemical analysis was carried out on spectrophotometer UV/VIS clinical chemistry analyser using kits (LINEAR CHEMICALS) .

Results and Discussion

Table (1) : Serum AST,ALT,ALP enzymes in nonpregnant and pregnant women (first, second and third trimester)

All data are expressed as mean ± SD. p value < 0.001 considered as statistically significant .

varaibles	**Controls(non pregnant women) N=29 (mean+ SD)**	**Cases pregnant women**		
		1st trimester N=31 (mean+ SD)	**2nd trimester N=33 (mean+ SD)**	**3rd trimester N=35 (mean+ SD)**
AST(U/L) Limited range	15.1 + 5.6 (13.02+17.2)	22.1+ 6.7 (19.6-24.6)	21.3 + 6.8 (18.9-23.8)	20.4 + 5.7 (18.5-22.4)
ALT(U/L)	13.8 + 3.9 (12.3-15.4)	19.7+ 6.2 (17.5-22.05)	20.4 + 7.8 (17.6-23.1)	20.8 + 7.3 (18.3-23.4)
ALP(U/L)	76.01 + 14.9 (70.3-81.7)	100.8+ 47.6 (83.3-118.2)	108.9+32.0 (97.6-120.3)	152.5 + 45.1 (137-168)
AST/ALT	1.3 ± 0.5	1.2 ± 0.7	1.3 ± 0.6	1.2 ± 0.5

Table(2) The probability according to Kruskal-Wallis test for AST, ALT , APL AST/ALT among the studied groups

Probability				
Groups	AST	ALT	ALP	AST/ALT
Total patients group vs. controls	P < 0.001	P < 0.001	P < 0.001	P > 0.05
Group1 vs. group2	NS	NS	NS	P > 0.05
Group1 vs. group3	NS	NS	P < 0.001	P > 0.05
Group1 vs. controls	P < 0.001	P < 0.001	P < 0.001	P > 0.05
Group2 vs. group3	NS	NS	P < 0.001	P > 0.05
Group2 vs. controls	P < 0.001	P < 0.001	P < 0.001	P > 0.05
Group3 vs. controls	P < 0.001	P < 0.001	P < 0.001	P > 0.05

NS: Non-significant at the level ≥ 0.05

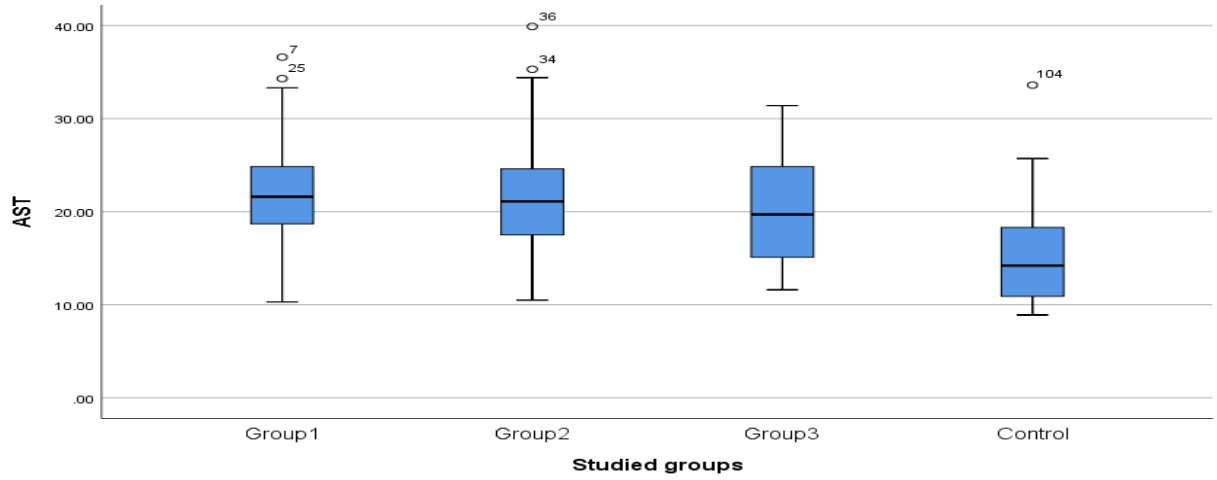

Figure (1): AST level in patients subgroups compared to controls

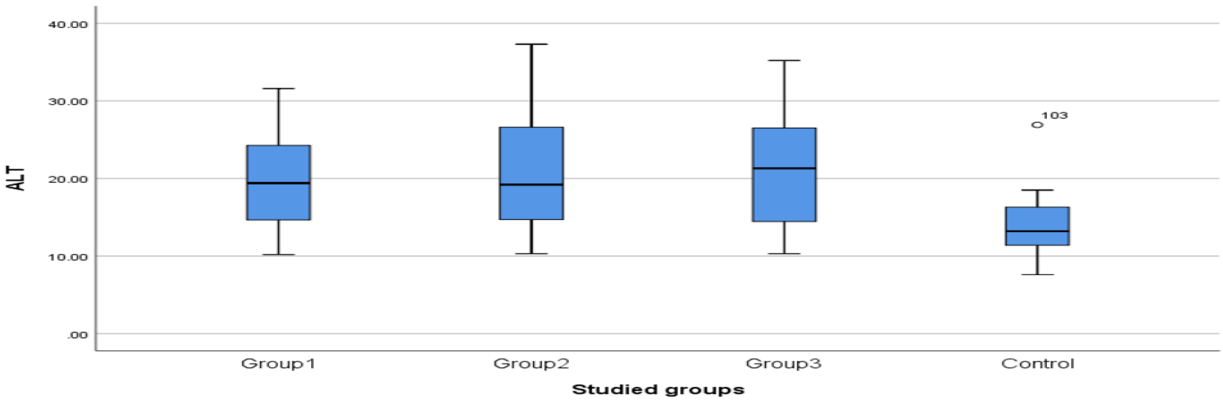

Figure (2): ALT level in patients subgroups compared to controls

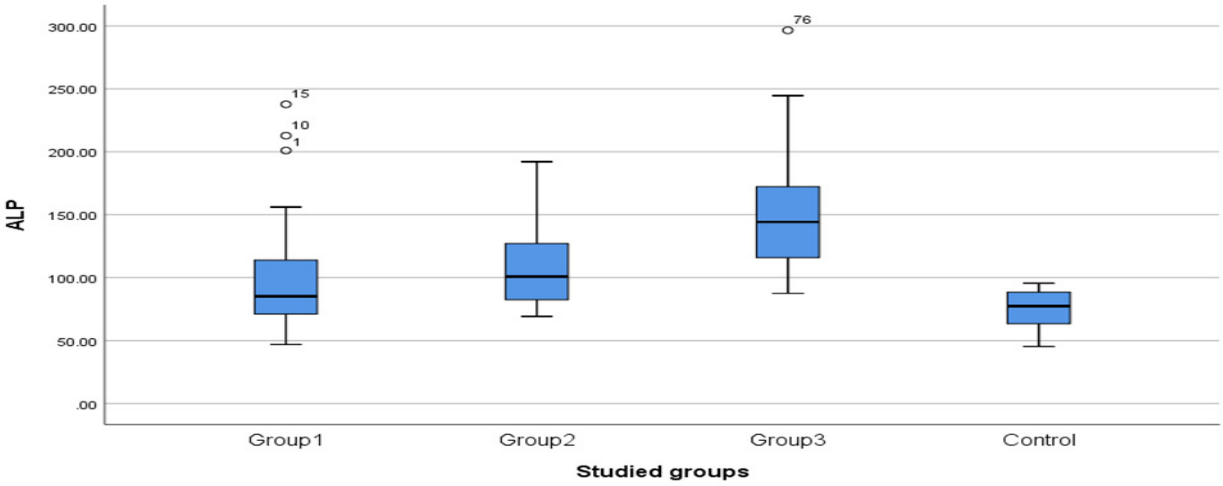

Figure (3): ALP level in patients subgroups compared to controls

The result shown in table(1)(2) revealed a significant increase in the serum levels of AST, ALT and in the successive these trimesters of pregnancy in comparison to the control group. This result agree with Mdhurima Bora,etal in case of ALT, there is gradual increase in 1st , 2nd and 3rd trimester when compared with control non pregnant group. P<0.001.This supports few studies, a slight increase in ALT and or AST has been found in third trimester [13,14,15]. This may be attributed to hormonal factors that may lead to changes in such enzyme. It is well known that sex steroids have diverse effects on metabolic synthetic and excretory hepatic function.

Some previous studies didn't indicated the differences in the level of those enzymes during pregnancy. such changes in our result to can be attributed to the inclusion and exclusion criteria outlined in our study.

The results also showed a significant increase in ALP level with the progress of pregnancy. This change in the level of the corresponding enzyme can be attributed to the increase rather than elevation of hepatic isoenzyme. In addition to that, there is an increased production of bone isoenzyme with gestational age as a result of fetal bone development .such diversity of the source of serum ALP shows that it is not a reliable or suitable test for liver disease especially during the pregnancy. This results agree with Mdhurima Bora, Arpana Hazarika etal ALP values of the experimental group (all three trimesters). In case of 1st trimester it is significant ($P < 0.05$) and in case of 2nd and 3rd trimester the increase in ALP values become highly significant, $P < 0.001$. This increase during pregnancy is not due to an increase in the hepatic isoenzyme but rather largely due to the production of the placental isoenzyme[16,17]. During the third trimester there is also an increase in the production of the bone isoenzyme as documented by an increase in its serum level up to six weeks post-delivery.

The revealed that AST/ALT ratio is statistically insignificant. This can be attributed to the fact that there is a concomitant changes in the level of both these two enzymes and This will tend to keep the numerical value of the ratio AST/ALT nearly similar to its value in the control group.

Finally establishment of reference values for aminotransferases is quiet essential for the diagnosis of liver disease and other diseases associated with the changes in the level of these enzymes . in addition to that ,ALP is not suitable for diagnostic purposes in pregnancy and this may be substituted by other diagnostic tools.

Conflict of interest : Nil

Source of funding: Self –funded

Ethical Clearance: Ethical approval for this study was obtained from the scientific committee of university of Al-Farahidi /college of pharmacy before any measurements were carried out. Written informed consents were obtained from the pregnancy Iraqi women.

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