

GENDER DIFFERENCES IN LIVER FUNCTION TESTS: A RETROSPECTIVE STUDY

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Abstract

Background: There are studies which have indicated the role of gonadal hormones in regulating structure and function of nearly every tissue and organ in the mammalian body, causing gender differences in a variety of characteristics. The objective of our study was to compare the gender differences in liver function tests in healthy individuals and to find the correlation between bilirubin and other liver markers.

Methodology: The retrospective study was conducted by collecting the data from the Clinical Biochemistry Laboratory of Adarsha Superspeciality Hospital, Udupi. Liver function tests were compared among 35 women and 35 men, who got their liver function tests done as a part of routine investigation panel. Comparison of liver parameters was done using the Mann Whitney U test. A correlation study was done by calculating Spearman's correlation coefficient.

Results: Total and direct bilirubin were very significantly high in males as compared to females ($P=0.001$ and $p < 0.0001$). A significantly high total protein ($p=0.039$), globulins ($p=0.0092$), AST ($p=0.0168$), ALT ($p=0.0010$) were observed in males. ALT was positively very highly significantly correlated with total and direct bilirubin ($p=0.0038$ and $p=0.0049$ respectively ($r=0.26$ and $r=0.256$ respectively).

Conclusion: A significantly high total and direct bilirubin, AST, ALT, total protein and globulin levels were observed in men compared to women. The causative factor is inconclusive and association of liver profile and female gonadal hormones needs further research.

Keywords: Bilirubin, AST, And ALT, plasma proteins, gender difference **Running title:** Liver profile and gender difference

Introduction

Gonadal hormones have a role in the development of gender-specific traits and affect primarily structure and function of

gender-specific organs. Studies have indicated their role in regulating the structure and function of nearly every tissue and organ in the mammalian body, causing

gender differences in a variety of characteristics. Sex hormones are associated with various aspects of reproduction, differentiation, development, growth, and homeostasis, influence the development of female and male-specific traits. Organs including brain, bones, liver, kidneys show differences in males and females (1). Protective role of estrogen has been well established in health and disease and it is responsible for the gender differences in various biochemical markers. There are a few studies available comparing liver parameters in both the genders (2,3). There is a limited availability of literature that provides information on this area to the best of our knowledge.

The objective of our study was to compare the gender differences in liver function tests in healthy individuals. We also aimed to find the correlation between bilirubin metabolism and other liver functions.

Methodology

Study design: The retrospective study was conducted by collecting the data from the Clinical Biochemistry Laboratory attached to Adarsha Superspeciality Hospital, Udupi. Ethics committee approval was sought before starting the study.

Liver function tests were compared among 35 women and 35 men. Their mean age was 52.71±2.05 years and 48.74±1.48 years respectively.

Inclusion criteria: healthy individuals who got their investigations done as a part of a routine check-up. Exclusion criteria: Liver disorders, diabetes mellitus, alcoholics, those with any known systemic illnesses.

Total bilirubin, direct bilirubin, aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), total protein (TP), albumin and globulin were estimated in liver function panel using commercially available kits with Transasia EM-200, automated chemistry analyzer. Comparison of the liver profile was done between females and males.

Statistical analysis was done by using GraphPad Instat version 3 software. Mann Whitney U test was used to compare the means. A correlation study was done by calculating Spearman's correlation coefficient, r (between -1 and +1). Level of significance was fixed at P<0.05.

Results

Total and direct bilirubin were very significantly high in males as compared to females (P=0.001 and p<0.0001). A significantly high total protein (p=0.039), globulins (p=0.0092), AST (p=0.0168), ALT (p=0.0010) were observed in males. ALT was positively very highly significantly correlated with total and direct bilirubin (p=0.0038 and p=0.0049 respectively) (Spearman's correlation, r=0.26 and r=0.256 respectively).

Table 1: Gender differences in liver function tests in normal individuals

Biochemical Parameters	Women (n=35)	Men (n=35)	P value
Total bilirubin	0.57±0.03	0.865±0.05	0.001**
Direct bilirubin	0.25±0.01	0.45±0.08	<0.0001***
Total protein	6.46±0.12	6.75±0.06	0.0390*
Albumin	3.69±0.05	3.74±0.03	0.46
Globulin	2.72±0.1	3.02±0.07	0.0092**
AST	27.92±2.38	36.13±3.24	0.0168*
ALT	34.47±5.65	48.63±6.059	0.0010**
ALP	71.07±4.06	71.12±2.69	0.9
FBS	97.89±2.06	96.83±1.18	0.85

PPBS	136.57±7.6	137.7±7.27	0.94
HbA1c	5.77±0.19	5.68±0.13	0.18

*significant

**highly significant

***very highly significant

Discussion

A significant gender difference in bilirubin (total and direct), AST, ALT, TP, and globulin were observed. There was no significant gender difference in other liver parameters. Our study is supported by Rosenthal and colleagues, who reported a declined bilirubin levels in females (2). This could be attributed to an increased rate of conjugation and excretion of bilirubin in females due to the influence of gonadal hormones. However, the above study contradicts our correlation between bilirubin and ALT. It states that bilirubin metabolism is independent of other functions of the liver, which are not concerned with bile pigment processing. However, we cannot justify this fact as our sample size is small. Our study is in accordance with that by Mera et al which also suggests a low AST level in women (3). But contrary to our study, they also found decreased ALT and high AST/ALT ratio in women. Discrepancies were noted in ALT in different genders with same living conditions (4-7). Comparatively, high ALT was reported in females (8-10). This variation in liver enzymes is attributed to the hormonal status and difference in the muscle mass (9). A similar study reported a higher liver enzymes and bilirubin in men (11). However, the role of female gonadal hormone in altering the biochemistry of liver could be inconclusive. Moore et al and Darj et al studied the effect of estradiol supplementation on liver markers (12, 13). They found no elevations in liver enzymes and bilirubin levels after hormone replacement therapy. Crippin and colleagues compared liver profile in postmenopausal

women with and without estrogen-containing hormone replacement therapy (14). They reported that there was no elevation in bilirubin levels in women on hormone replacement therapy. Contradictory reports were given by Guattery and colleagues who stated heightened bilirubin levels in biliary cirrhotic women treated with hormones, necessitating cessation of therapy (15). Our findings on plasma proteins are supported by the report by Devi and colleagues (16). Low albumin levels in women could be due to increased degradation. This study states that the rate of protein synthesis is lower in females compared to males (16). Limitation of the study: Small sample size is the limitation of our study.

Conclusion

A significantly high total and direct bilirubin, AST, ALT, total protein and globulin levels were observed in men compared to women. The causative factor for gender difference is inconclusive and the association of liver profile and female gonadal hormones needs further research.

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