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Prevalence of Elevated Serum Aminotransferases among Asymptomatic Population of Tamil Nadu, India

CHEZHIAN ANNASAMY[1], KRISHNASAMY NARAYANASAMY[1]* and RAJENDRAN KARTHICK[2]

[1]Department of Hepatology, Madras Medical College, Chennai – 600003, Tamil Nadu, India.
[2]Research Scientist, Multidisciplinary Research Unit (MRU),
Madras Medical College, Chennai - 600003, Tamil Nadu, India.

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ABSTRACT

Studies carried out across several countries have shown that serum aminotransferases levels vary with various clinical and demographic factors such as age, sex, race, body mass index (BMI) etc. Our objectives were to estimate the prevalence of elevated serum aminotransferases among asymptomatic individuals in the population in Tamil Nadu, the southern region of India and also to identify the associated risk factors for the same. A total of 10765 individuals were included in this population-based study. Subjects were requested to report on an empty stomach in the morning and blood samples were collected. Those subjects who did not report were visited in their homes and blood collected. Subject's demographic, clinical and laboratory data such as serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), cholesterol, triglycerides, glucose, HDL cholesterol were analyzed. Univariate and multivariate logistic regression was done to calculate odds ratio with 95% confidence intervals. Among the 10765 participants, 18.0% (1938) had elevated aminotransferase. High proportion of elevated aminotransferase was seen in males (20.2%) compared to females (15.7%) ($p < 0.0001$). Univariate analysis showed a significant association of hypertriglyceridemia, hyperglycemia, diabetes mellitus, age and BMI with elevated aminotransferase in both genders. Multivariate analysis revealed that age, hypertriglyceridemia, hyperglycemia and BMI may be independently associated with elevated aminotransferase in both genders. This study revealed that 18% of the asymptomatic individuals in Tamil Nadu, South India had laboratory findings suggestive of possible liver damage. Middle aged and obese individuals having hypertriglyceridemia and hyperglycemia should be screened for elevated aminotransferase and clinically evaluated further for potential liver damage.

Keywords: Asymptomatic; Alanine aminotransferase (ALT); Aspartate aminotransferase (AST); Hypertriglyceridemia; Hyperglycemia.

INTRODUCTION

Liver diseases are a significant health burden due to their increasing morbidity and mortality rates worldwide. In the majority of the cases, a long and asymptomatic pathogenic duration of chronic liver diseases (CLD) leads to the end stage liver diseases such as cirrhosis, hepatocellular carcinoma (HCC), etc.,[1, 2]. The major risk factors for CLD and end stage liver diseases include excess alcohol consumption[3], hepatitis B or hepatitis C virus infection (4), Non-alcoholic fatty liver disease (NAFLD)[5]. However, several studies have shown that causes of cirrhosis remains cryptogenic in many individuals. Indeed, prevalence of liver diseases and diverse etiologies are closely related to different

geographical regions and populations hygienic, sanitary conditions, sedentary lifestyles and other indicators of the level of socioeconomic status[6]. In particular, NAFLD is emerging as one of the most important causes of CLD in various countries[7-9]. Understanding the causes of liver disease and its future projections is critically important for the planning of care pathways and the provision of healthcare.

Chronic liver disease is often diagnosed by asymptomatic elevations in serum aminotransferases, which include alanine aminotransferase (ALT) and aspartate aminotransferase (AST), as these are usually sensitive indicators of liver-cell injury and are helpful in recognizing CLD (10). Most of the published epidemiological studies on the prevalence and etiology of elevated aminotransferase levels have only been documented in restricted groups such as blood donors[11], health screening[12], primary care center[13] and in overweight and obese adolescents[14]. Moreover, changing lifestyle habits, food habits and urbanization in the recent times have increased the incidence of obesity in India. Several studies from different countries had shown variation in serum aminotransferases levels to be associated with various clinical and demographic factors such as age, sex, race, body mass index (BMI) etc. [15,16].

A population based screening of liver function test could provide a reliable tool to estimate the potential chronic liver diseases. However, to our knowledge, such a study has not been conducted on liver function test in Tamil Nadu, South India. This is the first population-based study and aims to determine the prevalence of elevated serum aminotransferases in asymptomatic individuals in a large population in urban, sub-urban and rural areas of southern region of India and identify associated risk factors.

MATERIALS AND METHODS

Study Design and Target Population

A large population survey was carried out for screening of liver disease among the South Indian population in the period of 2013 to 2016 by the Department of Hepatology, Madras Medical College, Chennai. The study protocol has been approved by the Institutional ethics committees. Randomly selected areas of urban, rural and suburban regions of Tamil Nadu South India were included (Pannaipuram in Theni district, Royapuram, Madhavaram, Porur, Poonamalle areas of Chennai District, Tambaram area of Kanchipuram District, Uthukottai, Velliyur, Manavur, Periyapalayam, Palavedu areas of Tiruvallur District, Sholurmattam of Nilgris District and Vellore District). The local population was informed a day before of conducting the study via press, loud speaker and local newspapers.

Screening

A written informed consent was obtained from each participant. During the screening, participants were asked to complete a comprehensive questionnaire regarding their basic demographic information, medical history, medication use and social information which includes age, sex, alcohol intake, history of diabetes, history of hypertension and history of previous liver disease. Heights and weights were measured and body mass index was calculated. Subjects were excluded during the analysis if they had a known history of viral hepatitis, any other liver disease, alcoholic (consumed >20 g/day) or an identified cause of LFT elevation (ie, drug toxicity).

Biochemistry

Five millilitres of fasting venous blood sample was collected in the morning from all individuals who participated in sterile dry syringes. All blood tests were undertaken within a few hours of sampling. Blood samples were tested for serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), cholesterol, triglycerides, serology for viral hepatitis. In our analyses, ALT levels were considered to be abnormal if they exceeded 31 IU/L (men), 24 IU/L (women); AST levels were considered to be abnormal if they exceeded 37 IU/L (men), 31 IU/L (women); these values are consistent with the upper limits of normal established by our lab.

Statistical Analysis

Data for continuous variables were expressed as mean ± SD and categorical variables were expressed as frequencies. The continuous variables were evaluated by Student's t-tests and

categorical variables were evaluated by Pearson's chi-square test. P value of less than 0.05 was considered to be significant as the distributions were normal. To identify variables associated with elevated aminotransferases crude and adjusted odds ratios (ORs) were calculated using univariate and multivariate logistic regression analyses. Only those variables that were statistically significant effect at the 0.05 level in the univariate analyses remained in the multivariate model. Ninety-five percent confidence intervals (CIs) were also determined. All statistical calculations were conducted using SPSS version 20.0.

RESULTS

Demographic details of participants

The laboratory and demographic features of the study participants are presented in Table 1. A total of 10765 subjects were included. The mean age was 39.8 years. There were more males 5477 (50.9%) than females 5288 (49.1%). Among the subjects, 11.7% (1257) were below 20, 31% (3339) were between 21 and 30, 21.6% (2322) were between 31 and 40, 24.8% (2667) were between 41 and 50, 11% (1180) were over 51. Two third of

Table 1: Data distribution of age, body mass index, laboratory values among the study subjects

Characteristic	Total (N = 10,765)	Males (N=5477)	Females (N=5288)	P Value
Age (yr)	39.80±13.813	40.8±13.78	38.76±13.76	< 0.002*
< 20	1257 (11.7)	930 (17)	327 (6.2)	< 0.0001*
21-30	3339 (31)	1267 (23.1)	2072 (39.2)	
31-40	2322 (21.6)	1225 (22.4)	1097 (20.7)	
41-50	2667 (24.8)	1354 (24.7)	1313 (24.8)	
>51	1180 (11)	701 (12.8)	479 (9.1)	
BMI	26.68±4.41	26.77±4.44	26.59±4.39	< 0.039*
<18.50	477 (4.4)	247 (4.5)	230 (4.3)	< 0.001*
18.50 - 24.99	3790 (35.2)	2007 (36.6)	1783 (33.7)	
25.00 - 29.99	3781 (35.1)	1830 (33.4)	1951 (36.9)	
≤30.00	2717 (25.2)	1393 (25.4)	1324 (25)	
Area				< 0.0001*
Urban	3807 (35.4)	2491 (45.5)	1316 (24.9)	
Suburban	3640 (33.8)	1662 (30.3)	1978 (37.4)	
Rural	2717 (25.2)	1052 (19.2)	1665 (31.5)	
Tribal	601 (5.6)	272 (5)	329 (6.2)	
ALT (IU/L)	28.96±15.67	29.78±16.33	28.11±14.92	< 0.0001*
AST (IU/L)	31.65±13.01	33.04±14.36	30.22±11.26	< 0.0001*
Total cholesterol	209.44±66.68	204.84±66.31	214.19±66.74	< 0.0001*
Total cholesterol ≤200 mg/dL	1869 (17.4)	1266 (23.1)	603 (11.4)	< 0.0001*
Triglyceride	155.39±54.48	145.65±49.01	165.48±57.92	< 0.0001*
Triglyceride ≤150 mg/dL	4310 (40)	1923 (35.1)	2387 (45.1)	< 0.0001*
HDL cholesterol	35.78±9.67	35.13±9.71	36.46±9.58	< 0.0001*
HDL cholesterol ≥40mg/dL	2130 (19.8)	1073 (19.6)	1057 (20.0)	0.605
Glucose	98.15±32.66	88.91±19.9	107.72±39.77	< 0.0001*
Glucose ≤100 mg/dL	2176 (20.2)	1241 (22.7)	935 (17.7)	< 0.0001*
Diabetes Mellitus	2238 (20.8)	1152 (21.0)	1086 (20.5)	0.526
Hypertension	2059 (19.1)	1207 (22)	852 (16.1)	< 0.0001*

The continuous variables are mean±sd and categorical variables are frequency. t test for continuous variables or chi-squared test for categorical variables (*P<0.05)

Table 2: Proportion of elevated aminotransferase levels in the Tamil Nadu population by various demographic, body mass index and laboratory characteristics

Characteristic	Population Distribution (%)	Proportion of elevated aminotransferase (N=1937)	P Value
Gender			< 0.0001*
Male	50.9	1108 (20.2)	
Female	49.1	829 (15.7)	
Area			< 0.0001*
Urban	35.4	822 (21.6)	
Suburban	33.8	712 (19.6)	
Rural	25.2	362 (13.3)	
Tribal	5.6	41 (6.8)	
Age			< 0.0001*
< 20	11.7	119 (9.5)	
21-30	31	355 (10.6)	
31-40	21.6	384 (16.5)	
41-50	24.8	904 (33.9)	
>51	11	175 (14.8)	
Body mass index			< 0.0001*
<18.50	4.4	18 (3.8)	
18.50 - 24.99	35.2	316 (8.3)	
25.00 - 29.99	35.1	634 (16.8)	
≤30.00	25.2	969 (35.7)	
Total cholesterol			< 0.018*
<200 mg/dL	82.6	1569 (17.6)	
≤200 mg/dL	17.4	372 (19.9)	
Triglyceride			< 0.0001*
<150 mg/dL	60	518 (8)	
≤150 mg/dL	40	1419 (32.9)	
HDL cholesterol			0.863
>40mg/dL	80.2	1551 (18.0)	
≥40mg/dL	19.8	386 (18.1)	
Glucose			< 0.0001*
<100 mg/dL	79.8	1243 (14.5)	
≤100 mg/dL	20.2	694 (31.9)	
Diabetes Mellitus			< 0.0001*
No	79.2	1430 (16.8)	
Yes	20.8	507 (22.7)	
Hypertension			0.924
No	80.9	1568 (18)	
Yes	19.1	369 (17.9)	

The continuous variables are mean±sd and categorical variables are frequency. t test for continuous variables or chi-squared test for categorical variables (*P<0.05)

the subjects (62%) were either overweight (35.1%) (BMI between 25 and 29.9) or obese (26.9%) (BMI ≤ 30). Of subjects screened, 3807 (35.4%) came from urban, 3640 (33.8%) came from sub urban areas, 2717 (25.2%) came from rural areas and 601 (5.6%) came from tribal areas. In the study subjects, 20.8% and 19.1% had a diagnosis of diabetes mellitus and hypertension, respectively. The mean serum alanine aminotransferase level was 28.96±15.67 IU/L and the mean serum aspartate aminotransferase level was 31.65±13.01 IU/L for the total group.

Abnormal liver function tests

The distribution of the different possible causes of elevated aminotransferase by demographic characteristics and other factors were shown in Table 2. Overall, 18.0% had elevated aminotransferase (1938 out of 10765 subjects). The abnormal aminotransferase was very high in male gender (20.2%) when compared to female gender (15.7%) ($p < 0.0001$). The aminotransferase elevation was very high between the age group of 41 - 50 years (33.9%). This was followed by the age group of 31 - 40 years (16.5%) and minimal level were observed among the individuals falling below the age group of 20 years (9.7%) ($p < 0.0001$). However, elevated aminotransferase increased gradually with increasing BMI ($p < 0.0001$). The elevated aminotransferase was higher in urban populations (21.6%) than suburban (19.6%), rural (13.3%), tribal (6.8%) ($p< 0.0001$).

We conducted further analyses to determine specific characteristics associated with asymptomatic aminotransferase elevations in male gender and female genders (Table 3-6). Male with elevated aminotransferase were slightly younger ($p < 0.004$) and were having higher BMI when compared to that of males with normal aminotransferases ($p < 0.001$).

Table 3: Demographic and Laboratory Characteristics of Male by Elevation of Aminotransferase

Characteristic	Normal (N=4369)	Male Aminotransferase Elevation (N=1108)	P value
Age	41.48±13.61	38.13±14.12	< 0.004*
< 20 (930)	840 (90.3)	90 (9.7)	< 0.00001*
21-30 (1267)	1034 (81.6)	233 (18.4)	
31-40 (1225)	1036 (84.6)	189 (15.4)	
41-50 (1354)	849 (62.7)	505 (37.3)	
>51 (701)	610 (87)	91 (13)	
Body mass index	26.1±4.24	29.43±4.19	< 0.001*
<18.50	236 (95.5)	11 (4.5)	< 0.0001*
18.50 - 24.99	1816 (90.5)	191 (9.5)	
25.00 - 29.99	1477 (80.7)	353 (19.3)	
≤30.00	840 (60.3)	553 (39.7)	
ALT (IU/L)	24.67±12.9	49.95±12.32	< 0.0001*
AST (IU/L)	29.29±11.98	47.81±13.43	< 0.0001*
Total cholesterol ≤200 mg/dL	846 (20.1)	262 (20.7)	0.639
Triglyceride ≤150 mg/dL	287 (8.1)	821 (42.7)	< 0.0001*
HDL cholesterol ≥40mg/dL	884 (20.1)	224 (20.9)	0.557
Glucose ≤100 mg/dL	605 (14.3)	503 (40.5)	< 0.0001*
Diabetes Mellitus	797 (18.4)	311 (27)	< 0.0001*
Hypertension	856 (20)	252 (20.9)	0.526

The continuous variables are mean±sd and categorical variables are frequency. t test for continuous variables or chi-squared test for categorical variables (*P<0.05)

Male with elevated aminotransferase had higher mean levels of AST and ALT than male with normal aminotransferases ($p < 0.0001$). An important finding is that elevated levels were almost twice as high as those in normal individuals. Comparison of other profile in males having normal aminotransferases level with elevated aminotransferase level had shown notifiable results, higher number of males with elevated aminotransferase were having high fasting triglyceride ($p < 0.0001$), glucose levels ($p < 0.0001$) and a greater number of diabetes ($p < 0.0001$) than normal level of aminotransferase.

On the other hand, compare to males, females with asymptomatic aminotransferase elevations were in the slightly higher age ($p < 0.006$). Similar to male, female with asymptomatic aminotransferase elevations had higher BMI ($p < 0.001$), higher number of increased fasting triglyceride levels ($p < 0.001$), number of diabetics ($p < 0.001$) and glucose levels ($p < 0.001$).

Neither history of hypertension nor total and HDL cholesterol levels were shown to have significant association in both the genders.

Univariate analysis had shown that there was a significant association in age, hypertriglyceridemia, hyperglycemia, diabetes mellitus and BMI with elevated aminotransferase in both genders, however, multivariate analysis had revealed that age, hypertriglyceridemia, hyperglycemia and BMI may be the common independent predictors of elevated aminotransferase. Diabetes mellitus was again significant risk factors for males but not females.

DISCUSSION

Majority of the epidemiological studies on liver diseases were conducted in a highly selected hospital based populations and this leads to referral

Table 4: Demographic and Laboratory Characteristics of Female by Elevation of Aminotransferase

Characteristic	Normal (N=4459)	Female Aminotransferase Elevation (N=829)	P value
Age	38.53±13.643	39.97±14.372	< 0.006*
< 20	298 (91.1)	29 (8.9)	< 0.0001*
21-30	1950 (94.1)	122 (5.9)	
31-40	902 (82.2)	195 (17.8)	
41-50	914 (69.9)	399 (30.4)	
>51	395 (82.5)	84 (17.5)	
Body mass index	26.06±4.21	29.45±4.24	< 0.0001*
<18.50	223 (97)	7 (3)	< 0.0001*
18.50 - 24.99	1658 (93)	125 (7)	
25.00 - 29.99	1670 (85.6)	281 (14.4)	
≤30.00	908 (68.6)	416 (31.4)	
ALT (IU/L)	24.35±12.46	48.34±9.97	< 0.0001*
AST (IU/L)	27.27±7.58	46.08±14.18	< 0.0001*
Total cholesterol ≤200 mg/dL	719 (15.3)	110 (18.2)	0.066
Triglyceride ≤150 mg/dL	231 (8)	598 (25.1)	< 0.0001*
HDL cholesterol ≥40mg/dL	667 (15.8)	162 (15.3)	< 0.726
Glucose ≤100 mg/dL	638 (14.7)	191 (20.4)	< 0.0001*
Diabetes Mellitus	633 (15.1)	196 (18)	< 0.016*
Hypertension	712 (16.1)	117 (13.7)	0.088

The continuous variables are means±sd and categorical variables are frequency. t test for continuous variables or chi-squared test for categorical variables (*P<0.05)

bias. To avoid such bias in the studies related to the liver diseases, we have assessed the elevations in the levels of aminotransferases and its etiology among population of a South India, Tamil Nadu; such a population has dietary and cultural habits that are different from those of populations in northern India and other states of Indian country.

In the present study, we found a high proportion of elevated serum aminotransferase levels (18.0%) in the population of South India, Tamil Nadu including 20.2% of male gender, 15.7% of female gender.

To our knowledge, this is the first and largest cross-sectional population based study to analyze the level of aminotransferases among the population of south India. A study from Punjab showed that the elevation of serum aminotransferases was found in 46.15% of non insulin dependent diabetes mellitus

Table 5: Univariate logistic regression analysis to evaluate the association of risk factors predicting elevated aminotransferase

Characteristic	Male OR (95% CI)	P value	Female OR (95% CI)	P value
Age				
< 20		R		R
21-30	2.103 (1.622-2.727)	< 0.0001*	0.643 (0.421-0.981)	< 0.041*
31-40	1.703 (1.304-2.224)	< 0.0001*	2.222 (1.472-3.352)	< 0.0001*
41-50	5.552 (4.351-7.084)	< 0.0001*	4.486 (3.010-6.685)	< 0.0001*
>51	1.392 (1.022-1.897)	< 0.036*	2.185 (1.396-3.421)	< 0.001*
Body mass index				
<18.50		R		R
18.50 - 24.99	2.257 (1.211-4.206)	< 0.01*	2.402 (1.108-5.208)	< 0.026*
25.00 - 29.99	5.128 (2.77-9.49)	< 0.0001*	5.360 (2.5-11.595)	< 0.0001*
≤30.00	14.124 (7.644-26.099)	< 0.0001*	14.595 (6.817-31.247)	< 0.0001*
Total cholesterol ≤200 mg/dL	1.038 (0.889-1.213)	0.639	1.231 (0.986-1.536)	< 0.066*
Triglyceride ≤150 mg/dL	8.481 (7.294-9.86)	< 0.0001*	3.864 (3.282-4.549)	< 0.0001*
HDL cholesterol ≥60mg/dL	1.051 (0.891-1.239)	0.557	0.967 (0.802-1.166)	0.726
Glucose ≤100 mg/dL	4.091 (3.548-4.716)	< 0.0001*	1.495 (1.249-1.789)	< 0.0001*
Diabetes Mellitus	1.637 (1.407-1.904)	< 0.0001*	1.242 (1.041-1.481)	< 0.016*
Hypertension	1.052 (0.899-1.232)	0.526	0.833 (0.674-1.028)	0.089

*Significant by logistic regression analysis (*P<0.05).

Table 6: Multivariate logistic regression analysis to evaluate the association of risk factors predicting elevated aminotransferase

Characteristic	Male OR (95% CI)	P value	Female OR (95% CI)	P value
Body mass index	2.41 (2.184-2.659)	< 0.0001*	2.487 (2.236-2.756)	< 0.0001*
Triglyceride ≤150 mg/dL	8.481 (7.180-10.017)	< 0.0001*	4.093 (3.435-4.876)	< 0.0001*
Glucose ≤100 mg/dL	4.069 (3.428-4.829)	< 0.0001*	1.312 (1.073-1.605)	< 0.008*
Diabetes Mellitus	1.682 (1.396-2.026)	< 0.0001*	1.151 (0.945-1.402)	0.162
Age	1.273 (1.194-1.356)	< 0.0001*	1.716 (1.591-1.851)	< 0.0001*

*Significant by logistic regression analysis (*P<0.05).

patients[17]. In our study the observed high proportion 18.0% of elevated serum aminotransferase levels were relatively lower among the population without any symptom of the disease.

The causes of elevated aminotransferases may vary across different geographic areas which has been supported by the data obtained in our studies. The level of aminotransferase varied significantly between the two genders in the present study. Our present study revealed that male subjects had high proportion of elevated aminotransferase. Hypertriglyceridemia, hyperglycemia, metabolic factor ie., body mass index were associated with elevated serum aminotransferase in both genders. However, gender differences have been reported in different studies worldwide including Japan[18, 19], USA in various ethnicity[20, 21].

Similar to our result, previous Asian studies also could not the find gender based differences in BMI for liver enzyme elevation[22]. However, we found that aminotransferase levels very high among middle aged 41-50 individuals in both genders and they are 4 to 5 fold more prone to develop liver disease. These important findings were not observed in other studies. This clearly explained that aminotransferase levels may vary by race and ethnicity. Hence, we conclude that this could be due to South Indian origin and might be different for other ethnicities. However, it should be stressed that in both men and women, asymptomatic aminotransferase elevation is strongly associated with excess BMI, one of the possible abnormalities related to the asymptomatic elevation of liver function test.

We suspect that most cases of aminotransferase elevations may be caused by nonalcoholic fatty liver disease (NAFLD). To support this, aminotransferase elevations was significantly associated with hypertriglyceridemia, hyperglycemia, diabetes and which is consistent with other studies on NAFLD[23 - 25]. However, we did not find an association between aminotransferase elevations hypercholesterolemia and HDL cholesterol, as seen in prior studies.

CONCLUSIONS

The results of this population-based survey indicate that a high proportion of the population in a Tamil Nadu, South India has laboratory findings suggestive of possible liver damage even though they are asymptomatic. Hypertriglyceridemia, hyperglycemia and excess BMI in the middle age is becoming an increasingly important etiological factor for individuals with elevated aminotransferase. It may be suggested based on these findings that obese individuals with diabetes and hypertriglyceridemia should be investigated for liver damage and managed accordingly.

REFERENCES

1. Simonetti RG, Camma C, Fiorello F, Politi F, D Amico G, Pagliaro L. Hepatocellular carcinoma. A worldwide problem and the major risk factors. *Dig Dis Sci;* **36**(7): 962-72 (1991).
2. Detlef Schuppan and Nezam H. Afdhal, Liver Cirrhosis. Lancet. 2008; 371(9615): 838–851. 3) Jose Altamirano and Javier Michelena. Alcohol Consumption as a Cofactor for Other Liver Diseases. *Clinical Liver Disease,* **2**(2): 72-75 (2013).
4. Joseph F. Perz, Gregory L. Armstrong, Leigh A. Farrington, Yvan J.F. Hutin, Beth P. Bell. The contributions of hepatitis B virus and hepatitis C virus infections to cirrhosis and primary liver cancer worldwide. *Journal of Hepatology;* **45**: 529–538 (2006).
5. Anstee QM , Targher G , Day CP. Progression of NAFLD to diabetes mellitus, cardiovascular disease or cirrhosis. *Nat Rev Gastroenterol Hepatol*; **10**: 330 – 44 (2013).
6. Geoffrey C. Nguyen and Paul J. Thuluvath. Racial Disparity in Liver Disease: Biological, Cultural, or Socioeconomic Factors. *Hepatology*; **47**(3): 1058-66 (2008).
7. Leon A. Adams, James F. Lymp, Jenny St. Sauver, Schuyler O. Sanderson, Keith D. Lindor, Ariel Feldstein, *et al*. The natural history of nonalcoholic fatty liver disease: a population-based cohort study. *Gastroenterology;* **129**: 113–121 (2005).

8. Bedogni G, Miglioli L, Masutti F, Tiribelli C, Marchesini G, Bellentani S. Prevalence of and risk factors for nonalcoholic fatty liver disease: the Dionysos nutrition and liver study. *Hepatology;* **42**: 44–52 (2005).
9. Giovanni Targher and Christopher D. Byrne. Nonalcoholic Fatty Liver Disease: A Novel Cardiometabolic Risk Factor for Type 2 Diabetes and Its Complications. *J Clin Endocrinol Metab;* **98**(2): 483– 495 (2013).
10. Dufour DR, Lott JA, Nolte FS, Gretch DR, Koff RS, Seeff LB. Diagnosis and monitoring of hepatic injury. Recommendations for use of laboratory tests in screening, diagnosis and monitoring. *Clin Chem*; **46**: 2050-68 (2000).
11. Satish Kumar, Anjali Amarapurkar, Deepak Amarapurkar. Serum aminotransferase levels in healthy population from western India. *Indian J Med Res*; **138**(6): 894-899 (2013).
12. Cary H. Patt, Hwan Y. Yoo, Kourosh Dibadj, Y John Flynn, and Paul J. Thuluvath. Prevalence of Transaminase Abnormalities in Asymptomatic, Healthy Subjects Participating in an Executive Health-Screening Program. *Digestive Diseases and Sciences.;* **48**(4): 797–801 (2003).
13. Jonathan Diez-Vallejo and Angel Comas-Fuentes. Asymptomatic hypertransaminasemia in patients in Primary Care. *Rev Esp Enferm Dig* (Madrid); **103**(10): 530-535 (2011).
14. Ajay Kumar Das, Prasanna Chandra, Akash Gupta, Naved Ahmad. Obesity and the levels of liver enzymes (ALT, AST & GGT) in East Medinipur, India. Asian *Journal of Medical Sciences,* **6**(1): 40-42 (2015).
15. Bellentani S, Tiribelli C, Saccoccio G, Sodde M, Frattin N, De Martin C, *et al*. Prevalence of chronic liver disease in the general population of Northern Italy: the Dionysos Study. *Hepatology;* **20**: 1442-1449 (1994).
16. Bellentani S, Tiribelli C. The spectrum of liver disease in the general population: lesson from the Dionysos Study. *J Hepatol;* **35**: 531-537 (2001).
17. Ekta Chitkara. Alarming high levels of transaminases in non insulin dependent diabetes mellitus. *Indian Journal of Basic and Applied Medical Research*; **3**(2): 544-548 (2014).
18. Hamaguchi M, Kojima T, Takeda N, Nakagawa T, Taniguchi H, *et al*. The metabolic syndrome as a predictor of nonalcoholic fatty liver disease. *Ann Intern Med*; **143**: 722–728 (2005).
19. Omagari K, Kadokawa Y, Masuda J, Egawa I, Sawa T, *et al*. Fatty liver in non-alcoholic non-overweight Japanese adults: incidence and clinical characteristics. *J Gastroenterol Hepatol;* **17**: 1098–1105 (2002).
20. Weston SR, Leyden W, Murphy R, Bass NM, Bell BP, *et al*. Racial and ethnic distribution of nonalcoholic fatty liver in persons with newly diagnosed chronic liver disease. *Hepatology;* **41**: 372–379 (2005).
21. Kallwitz ER, Kumar M, Aggarwal R, Berger R, Layden-Almer J, *et al*. Ethnicity and nonalcoholic fatty liver disease in an obesity clinic: the impact of triglycerides. *Dig Dis Sci;* **53** : 1358–1363 (2008).
22. Hye Soon Park, Jee Hye Han, Kyung Mook Choi, and Seon Mee Kim. Relation between elevated serum alanine aminotransferase and metabolic syndrome in Korean adolescents. *Am J Clin Nutr;* 82: 1046 –51 (2005).
23. Giulio Marchesini, Elisabetta Bugianesi, Gabriele Forlani, Fernanda Cerrelli, Marco Lenzi, Rita Manini, *et al*. Nonalcoholic fatty liver, steatohepatitis and the metabolic syndrome. *Hepatology;* **37**: 917–923 (2003).
24. Erifili Hatziagelaki, Drosos E. Karageorgopoulos, Athina Chounta, Anastasia Tsiavou, Matthew E. Falagas, and George Dimitriadis. Predictors of Impaired Glucose Regulation in Patients with Non-Alcoholic Fatty Liver Disease. *Experimental Diabetes Research*; 351974, 1-7 (2012).
25. Parijat Gupte, Peepak Amarapurkar, Subhash Agal, Rajiv Baijal, Pramod Kulshrestha, Snehansu Pramaniket, *et al*. Non-alcoholic steatohepatitis in type 2 diabetes mellitus. *J Gastroenterol Hepatol;* **19**: 854–858 (2004).