International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2013): 6.14 | Impact Factor (2013): 4.438

Lipid Profile and Liver Function Test Estimates in Saudi Females

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Abstract: ***Objective: To investigate the normal values of serum lipids and liver enzymes for adult Saudi females living within the restricted environment of western region of Saudi Arabia (Makkah). Materials and Methods: In this prospective cross-sectional, blood samples were collected from 169 female donors, their age ranged from 18-25 years. All study population were fasting for 10-12 hours before sample collection. Liver function tests and lipid profiles were tested. Results: The result obtained for cholesterol, triglyceride, HDL, total protein, albumin, ATL, AST and ALP showed a range that lies approximately within the global values, however, upper limits for cholesterol, triglyceride, HDL and ATL showed significantly low levels. LDL and bilirubin showed significantly lower range than the global values and the reference range values reported by the ministry of health Saudi Arabia. Conclusion: The variations produced in some parameters, as compared to the similar values mentioned in literature and the reference values reported by ministry of health, Saudi Aeabia, indicate that the social, environmental, nutritional and dietary factors as well as awareness of health and body mass index may have an effect on the normal liver function test in Saudi females.***

Keywords: Liver function test, lipid profile, Reference range, Saudi Arabia

1. Introduction

The liver is the site at which many drugs are removed from the circulation and subsequently metabolized and excreted. Through its portal circulation liver is exposed to greater concentrations of orally administered drugs than any other organ apart from the intestine itself. It is not surprising therefore that many drugs can produce hepatic injury including hepatocellular damage, cholestasis and even tumor production [1]. Consequently a major safety concern in any clinical study of a new chemical entity (NCE) will be the effect of the drug upon the liver. Such effects are monitored by changes in the so-called liver function tests. Liver function tests (LFTs) are useful tools in clinical practice to assess potential liver diseases, to monitor treatment responses, and to predict prognosis of the patients with liver diseases. As a battery, LFTs consists most commonly of serum total cholesterol (TC), total protein, albumin, alkaline phosphatase (ALP), total bilirubin (TB), aspartate amino transferase (AST), alanine aminotransferase (ALT), and γ-glutamyl transferase (GGT). However, the interpretation of LFTs should be comprehensive and careful because LFTs can be influenced by many personal and environmental factors, including age, gender [2], body mass index (BMI) [3], alcohol drinking [4], cigarette smoking, malnutrition, presence of extra hepatic diseases such as cardiac, musculoskeletal, or endocrine, and status of liver health in itself [5]. In addition, gamma glutamyl transferase (γGT), is a commonly measured sensitive marker of cholestasis.

Liver enzymes are useful for the assessment of patients suffering from ischemic heart disease or edema [6]**.** The values of normal liver function tests are expected to vary from one society to another. On the other hand serum lipids are becoming of great interest to physicians. These include cholesterol, triglyceride, low and high density lipoproteins. High level of these lipids may increase the risk of ischemic heart disease. Albumin, the major plasma protein, is synthesized almost exclusively by the liver. Also, the liver synthesizes many of the clotting factors necessary for blood coagulation.

The triglycerides, content of the liver vary widely depending on the state of nutrition. After feeding a high-fat diet, however, the triacylglycerol content of the liver rises to a very high value, between 25% and 50% of the total weight, the fat content also increases to 5-10% of the liver weight during fasting. On the other hand low cholesterol levels may be caused by many factors such as hyperthyroidism, liver disease, malabsorption (inadequate absorption of nutrients Cholesterol is carried in the blood by lipoproteins.

The normal range of high density lipoprotein (HDL) cholesterol levels has been described between 40 and 50 mg/dl in males, while the females have a range between 50 and 60 mg/dl with slight variations among different laboratories.

Low-density lipoprotein test measures how much low-density lipoprotein (LDL) is found in the blood where as very low density lipoprotein (VLDL) is composed mostly of cholesterol, with not much protein. The Normal Values of VLDL cholesterol level is between 5 and 40 mg/dl. Increased levels of VLDL are associated with atherosclerosis and coronary heart disease [7].

In various liver diseases, serum levels of a number of cytolic, mitochondrial, and membrane-associated enzymes are increased, the degree of elevation varies with the type of liver disease. These enzymes include aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), γ-glutamyl transferase (GGT). Two key factors affect the degree of elevation and the pattern of changes includes the specific activity of the enzyme in the liver, and the relative rates of catabolic clearance of the enzyme from the blood stream. Clearance of liver enzyme from the plasma occurs at varied rates

Changes in LFTs of obscure origin have been noted during prolonged periods of residence. Such findings have been attributed to several factors including excess calorie intake due to lack of exercise [8], a high obesity index and/or a high γGT activity [9]. Alternatively [10] tentatively attributed trans aminase changes in healthy volunteers taking placebo to 'dietary factors and rest', and a more detailed paper from the same group, once again studying healthy volunteers taking placebo, came to a similar conclusion [11]. Indeed, there is evidence in the literature that diet can have an effect upon hepatic enzymes both in animals [12,13,14] and in healthy humans [15,16]. However, in patients receiving enteral nutrition, the observed changes in LFTs were considered more likely to be associated with clinical complications rather than with the enteral nutritional support itself [17].

The normal reference values for the liver function tests and lipid profile vary. They may also be different form normal ranges seen in other parts of the world. Hence it becomes of great interest to study the normal values of LFTs and lipid profile values in different parts of the world. Current study is therefore carried out to find the normal values of serum lipids and liver enzymes for adult Saudi females in the Western region of Saudi Arabia (Makkah) to correlate them with the possible social, environmental, nutritional or dietary factors.

2. Materials and Methods

This prospective cross-sectional study was done after getting approval by the ethics committee of the Faculty of the Medicine, Umm Al Qura University, Makkah, Saudi Arabia. All reference individuals enrolled in this study written informed consent prior to the study. Each candidate was required to complete a physical examination by a certified physician to check their health conditions. The exclusion criteria were as followings: presence of acute and chronic infections, digestive diseases, kidney disease, metabolic and nutritional diseases, rheumatic diseases, endocrine disease, circulation system diseases, burns and muscle trauma, hypertension (systolic pressure ≥140 mmHg and/or diastolic pressure ≥90 mmHg), excessive smoking (smoking>20 cigarettes/day), massive blood loss, malnutrition (lose weight, poverty, or special dietary habits) and symptoms (low BMI or significant weight loss), surgery undergone within six months, medication taken within two weeks, blood donation or blood transfusion within four months, strenuous exercise or heavy manual labor. Individuals were further excluded in accordance with one of the following criteria: Positive results for Hepatitis B surface antigen, Hepatitis C antibodies, or HIV antibodies. In addition menstruating, pregnant, and lactating females were also excluded from sampling.

About three to five milliliters of blood was drawn from 169 healthy female donors aged between 18-25 year, fasting for 10-12 hours before sample collection from the antecubital vein by means of vacutainers in the plain tube (no anticoagulant).

Samples were allowed to clot for half an hour at room temperature, then centrifuged using ALC centrifuge PK130 made in the U.S.A adjusted at 3400 r.p.m. for five minutes. Serum was transferred into sterile serum container for testing.

Some of the samples tested were excluded from analysis as they showed abnormal look such as visible hemolysis. Therefore in each parameter's result the number of the tested samples are indicated. The exact number of the samples tested for each parameter is indicated on each histogram.

Collected data was analyzed using SPSS program 17.0 (SPSS Institute, Inc.; Chicago, IL, USA) software for statistical analysis. Results were presented as mean ± standard deviation. A *P*-value of <0.05 was considered statistically significant on all analysis.

3. Results

Normal distribution curve for serum cholesterol level obtained by 157 samples in this study as shown in figure (1) indicated a value of 156.9 ± 29.9 mg/dl with a range of (127.0 - 186.8 mg/dl). Triglyceride in the tested samples was found to be 65.5 ± 23.7 mg/dl with a range of 41.8 - 89.2 mg/dl. The histogram with the normal distribution curve for serum high density lipoprotein (HDL) level from 119 samples in this study is shown in figure (1). HDL in the tested samples was found to be 49.8 ± 7.2 mg/dl with a range of 42.6 – 57.0 mg/dl. Normal distribution curve for serum low density lipoprotein (LDL) level obtained by 155 samples in this study as shown in figure (1) indicated a value of 90.3 ± 22.0 mg/dl with a range of 68.3 – 112.3 mg/dl.

The histogram with the normal distribution curve for serum total bilirubin level from 169 samples in this study is shown in figure (2). Total bilirubin in the tested samples was found to be 0.3 ± 0.15 mg/dl with a range of 0.15 - 0. mg/dl. Total protein in the tested samples was found to be 7.7 ± 0.7 mg/dl with a range of 7.0 – 8.4 . mg/dl. Serum Albumin tested in 168 samples showed a value of 4.4 ± 0.7 g/dl with a range of 3.7 – 5.1 g/dl (Figure 2).

Alanine Aminotransferase (ALT) analysis in 168 samples showed a value of 8.14 ± 3.31 with a range of 4.8 – 11.4 u/l (Figure 2). Asparate aminotransferase (AST) analysis in 168 samples as shown in Figure 9, found to be 16.40 ± 4.0 u/l with a range of 12.4 -20.4 u/l. Serum Alkaline Phosphate (ALP) analysis in 167 samples showed a value of 68.5 ± 17.82 u/l with a range of 50.7 -86.3 u/l (Figure 2).

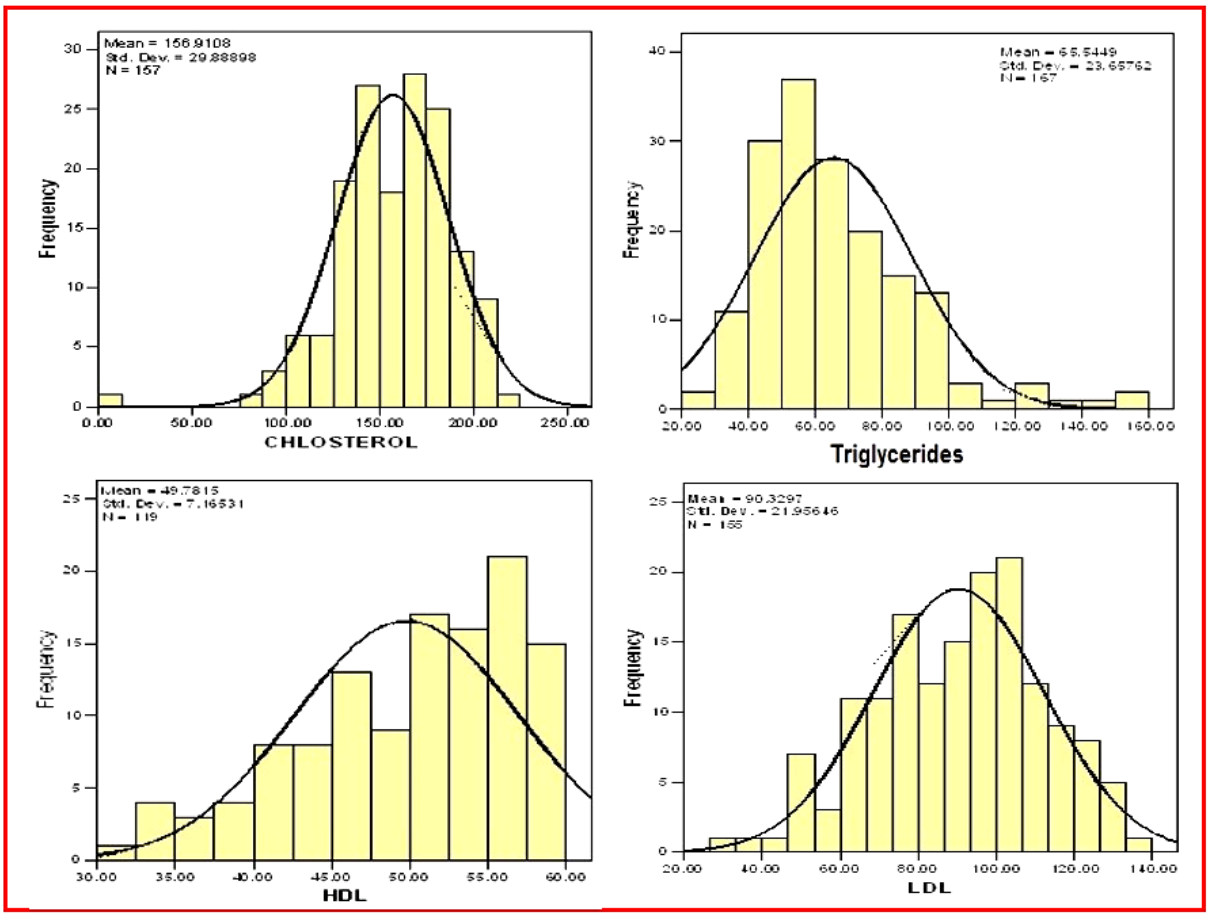

Figure 1: Results of lipid profile (Cholesterol, Triglyceride, HDL and LDL) in adults Saudi females

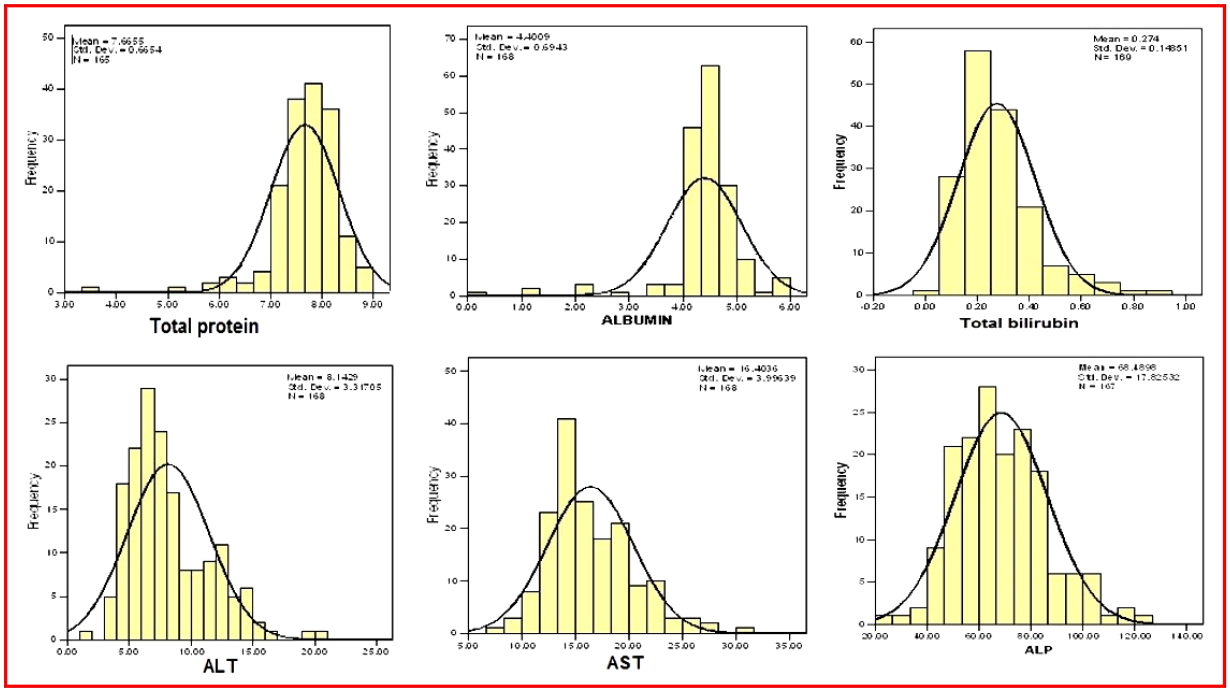

Figure 2: Results of liver function test (Total, protein, Albumin, bilirubin ALT, AST and ALP) in adults Saudi females.

4. Discussion

Liver function tests, including assays for alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), γ-glutamyltansferase (GGT), total protein, albumin, and total bilirubin, are generally used to assess hepatocellular injury, cholestasis, infiltrative disease, biliary obstruction, or synthetic function of the liver. Normally, liver function tests are also used to screen asymptomatic patients/individuals, mostly during regular health check-ups, blood donation, and hospitalization for non-liver related diseases [18]**.** Appropriate reference intervals of those tests are the most important elements for health evaluation, disease diagnosis, therapy monitoring, and prognosis assessment.

According to Cobas Integra 400 instruction sheet (Basel, Switzerland, F.Hoffmann-La Roche) for the conversion of units of cholesterol (mmol/l = mg /dl ÷33.66), cholesterol value in our results is equivalent to 4.0 ± 0.8 mmol/l with a range of (3.2 - 4.8 mmol/l) with a lower limit of 3.2 mmol/l is in conformity with the previous findings [19], who gave a value of 4.8 ± 1.1 mmol/l. However, the upper limit in this study is significantly low ($p>0.0001$) than the upper limit described by [19] and the ministry of health, kingdom of Saudi Arabia (unpublished data).

The value of triglyceride in our study showed a non significant difference when compared with the results by previous investigations [20]. However, the upper and lower limit in our study (0.4 - 1.0 mmol/L) is significantly lower ($p>0.005$) than that which was given by the above mentioned investigators (0.7 - 1.3 mmol/L) and the ministry of health, Saudi Arabia. This could be related to the fact that our samples were collected from healthy volunteers who performed fitness exercises, were slim, non smokers, taking care of their body weights and mostly avoiding fatty meals and were free from diseases such as the cardiovascular diseases, obesity, metabolic syndrome, or diabetes which may be associated with hypertriglyceridemia [21].

Accordingly it might be possible to suggest a new range value of 186.8 and 89.2 mg/dl respectively as a new reference value for serum cholesterol and serum triglyceride in Saudi females.

High density lipoprotein (HDL) values in our results was found to be approximately in similar limit of the range that was given by while the result of low density lipoprotein (LDL) was found to be lower ($p>0.005$) as described by [22].

Although these results lies in the range of high to moderate risk for ischemic heart disease according to the ranges stated in the sheets of Cobas Integra 400, we feel that these result are in the normal range as our volunteers are younger aged female, fit and free from diseased conditions suggesting that for HDL (42.6 – 57.0 mg/dl) and for LDL (68.3 – 112.3 mg/dl) may be considered as the new reference value for these Saudi females. Similar suggestions have been made previously for other global populations [23].

In our study total bilirubin level was found to be significantly lower ($p>0.005$) than the findings of previous investigators [24]. Our bilirubin result thus execlude the possibilities of coronary heart disease or renal disease in our volanteers. Similar suggestions have been made previously [25].

The result of total protein in our study lies within the ranges as coated by previous workers [26,27], thus suggesting that our volunteers were healthy, taking good diet rich in proteins and that they had healthy liver and kidney.

Alkaline aminotransferase (ALT) range in our study (4.8 – 11.4 u/l), though lies within the range value given as reference by ministry of health KSA (<31u/l), its upper limit was found to be significantly lower ($p>0.005$) is in conformity with the previous findings [28]. On the other hand, the result of Aspirate aminotransferase (AST) showed approximately similar values when compared with the previous investigators [29]. These findings are also within the range stated by ministry of health, Saudi Arabia (<31 u/l) thus indicating that the donors were healthy and not taking medications that increase liver enzymes nor they suffer from liver diseases.

Alkaline phosphatase (ALP) result in ours study were in conformity with the previous findings [30], also lies within the range that is stated by ministry of health, Saudi Arabia. However the highest range value in this study seems to be far below the upper values in both conditions. The variations produced in some parameters, as compared to the similar values mentioned in literature indicates that the diet, cultural factors for eating habits and awareness of health and body weight factors may have an effect on the normal liver function test in Saudi females [31].

With the increasing degree of standardization of laboratory, members of the scientific community are now proposing that it is now feasible to establish common reference intervals [32]. For example, the international community has established common reference intervals through several multi-center studies, based on the populations of five Nordic countries, seven Southeastern African countries and multiple ethnic groups from different countries respectively [33, 34] However, it is not appropriate to directly apply these reference intervals to the Saudi population, because some parameters may vary significantly among different races [35, 36, 37]. Moreover, currently there is no large sample multi-center based reference intervals developed for the Saudi population.

Nevertheless, taking into account the large diversity of the Saudi population in age structure, geographical, nutritional and occupational status, these local reference intervals cannot be applied to the whole Saudi population. Therefore, it is necessary to establish liver function tests reference intervals which are specific for the Saudi population and can be universally applied in most hospitals across Saudi Arabia.

In conclusion, it is suggested to establish a normal reference ranges for Saudi adult females in the laboratories

of ministry of health KSA taking in account the results concluded in this study in near future.

References

[1] Stricker B, Spoelstra P, "Drug-induced hepatic injury. In: Dukes MNG, editor. Drug-induced disorders," *Amsterdam: Elsevier*, vol. 1, pp.1-10, 1985.
[2] Rahmioglu N, Andrew T, Cherkas L, Surdulescu G, Swaminathan R, Spector T, Ahmadi K, "Epidemiology and genetic epidemiology of the liver function test proteins," *PLoS One*, vol.4, pp. 4435, 2009.
[3] Adams L, Knuiman M, Divitini M, Olynyk J, "Body mass index is a stronger predictor of alanine aminotransaminase levels than alcohol consumption," *J Gastroenterol Hepatol*, vol. 23, pp. 1089-1093, 2008.
[4] Sharpe P, "Biochemical detection and monitoring of alcohol abuse and abstinence," *Ann Clin Biochem*, vol. 38, pp. 652-664, 2001.
[5] Nathwani R, Pais S, Reynolds T, Kaplowitz N, "Serum alanine aminotransferase in skeletal muscle diseases," *Hepatology*, vol. 41, pp. 380-382, 2005.
[6] Michael M, "Association of Serum Bilirubin Concentration with Risk of Coronary Artery Disease," *Clinical Chemistry*, vol. 46, pp.1723-1727, 2000.
[7] Law M, Wald N, Rudnicka A, "Quantifying effect of statins on low density lipoprotein cholesterol, ischaemic heart disease, and stroke: systematic review and meta-analysis," *BMJ* , vol. 28, pp. 326(7404) 1423, 2003.
[8] Kanamaru M, Nagashima S, Uematsu T, Nakashima M, "Influence of 7-day hospitalization for Phase I study on the biochemical laboratory tests of healthy volunteers," *Jpn J Clin Pharmacol Ther*, vol. 20, pp.493–50, 1989.
[9] Kobayashi M, Yamada N, Shibata H, Nishikawa T, "Elevation of serum transaminase value after administration of non-toxic drugs in some volunteers for Phase I trials: a study on the selection of volunteers," *Jpn J Clin Pharmacol Ther*, vol. 22, pp.497–500, 1991.
[10] Rosenzweig P, Brohier S, Zipfel A, "Data on placebo in healthy volunteers: impact of experimental conditions on safety, and on laboratory and physiological variables during phase I trials," *Therapie*, vol. 51, pp. 356–7, 1996.
[11] Rosenzweig P, Miget N, Brohier S, "Transaminase elevation on placebo during Phase I trials: prevalence and significance," *Br J Clin Pharmacol*, vol.48, pp.19–23, 1999.
[12] Bidlack W, Brown R, Mohan C, "Nutritional parameters that alter hepatic drug metabolism, conjugation and toxicity," *Fed Proc*, vol. 45, pp.142–8, 1986.
[13] Dannenberg AJ, Yang EK, "Effect of dietary lipids on levels of UDP glucuronosyl transferase in liver," *Biochem Pharmacol*, vol. 44, pp.335–40, 1992.
[14] Yang E, Radominska A, Winder BS, "Dannenberg AJ. Dietary lipids coinduce xenobiotic metabolizing enzymes in rat liver," *Biochem Biophys Acta*, vol.1168, pp. 52–8, 1993.
[15] Irwin M, Staton A, "Dietary wheat starch and sucrose. Effect on levels of five enzymes in blood serum of young adults," *Am J Clin Nutr*, vol. 22, pp.701–9, 1969.
[16] Porikos KP, Van Itallie TB, "Diet-induced changes in serum transaminase and triglyceride levels in healthy adult men," *Am J Med*, vol.75, pp. 624–30, 1983.
[17] Richardson R, Garden O, Shenkin A, "Enteral nutrition and liver function test abnormalities," J Human Nutrition Dietetics, vol. 1, pp. 227–32, 1988.
[18] Green M, Flamm S, "Technical review on the evaluation of liver chemistry tests," *Gastroenterology*, vol. 123, pp. 1367–1384, 2002.
[19] Dubois C, Armand M, Mekki N, et al, "Effects of increasing amounts of dietary cholesterol on postprandial lipemia and lipoproteins in human subjects," *J Lipid Res*, vol. 35, pp. 1993–2007, 1994.
[20] Anja S, Lindman, M. Veierød B, Tverdal A, Pedersen I, Selmer R, "Nonfasting triglycerides and risk of cardiovascular death in men and women from the Norwegian Counties Study," *Eur J Epidemol*, vol. 25, no. 11, pp. 789-798, 2010.
[21] Lars B, John D, Brunzell A, Anne C, Goldberg I, Mohammad H, Anton F, "Evaluation and Treatment of Hypertriglyceridemia: An Endocrine Society Clinical Practice Guideline," *J Clin Endocrinol Metab*, vol. 97, no. 9, pp. 2969-2989, 2012.
[22] Elisabetta L, Annalisa G, Giuseppina T, Bela F, Katalin V, Angela A, "Markers of systemic inflammation and Apo-Al containing HDL subpopulations in women with and without diabetes," *Int J Endocrinol*, Sept 2: (in press), 2014.
[23] Danny J, Girish L, Christina A, Nadya M, Bobby V, "Raising HDL cholesterol in women," *Int J Womens Health*, vol.1, pp. 181–191, 2009.
[24] Berk, P, Howe, R, Bloomer, J, Berlin, N, "Studies of bilirubin kinetics in normal adults," *J Clin Invest*, vol. 48, pp. 2176, 1969.
[25] Braxton D, Keith T, Brain W, Patrick F, Afshin P, Alan R, "Association between bilirubin and cardiovascular disease risk factor: using mendelian randomization to assess casual inference," *BMC Cardiovasc Disord*, vol, 12, pp. 16, 2012.
[26] Audrey E, Micheal A, "Protein Synthesis in Liver, Muscle and Gill of Mullet (Mugil Cephalus L.) in Vivo," *Biol Bull*, vol.156, pp. 93-102, 1979.
[27] Kayla H, Melissa A, Somaieh A, Kristin M, Amy P, Stefan E, Timothy J, "A feasibility study to identify proteins in the residual pap test fluid of women with normal cytology by mass spectrometry based proteomics," *Clin Proteomics*, vol.11, no.1, pp. 30, 2014.
[28] Tao X, Linlin W, Shuping Q, Husijum N, Zhengtao L, "Complex association between alanine aminotransferase activity and mortality in general population: A systematic review and meta-analysis of prospective studies," *PLoS One*, vol. 9, no. 3, pp. e.9 1410, 2014.
[29] Goldie D, McConnell A, "Serum alanine transaminase (ALT) reference ranges estimated from blood donors," *J Clin Pathol*, vol.43, pp. 929-931.

[30] Beckingham I and Ryder S, "Investigation of liver and biliary disease," *BMJ*, vol. 322, no. 7277, pp 33–36, 2001.
[31] Jing Y, Huan G, Li Z, Yunfeng H, Handong Y et al, "Genome-wide association study on serum alkaline phosphatase levels in a Chinese population," *BMC Genomics*, vol, 14, pp. 684, 2013.
[32] Ceriotti F, Hinzmann R, Panteghini M, "Reference intervals: the way forward," *Ann Clin Biochem*, vol. 46, pp. 8–17, 2009.
[33] Rustad P, Felding P, Franzson L, Kairisto V, Lahti A, et al, "The Nordic Reference Interval Project 2000: recommended reference intervals for 25 common biochemical properties," *Scand J Clin Lab Invest*, vol. 64, pp. 271–284, 2004.
[34] Karita E, Ketter N, Price A, Kayitenkore K, Kaleebu P, et al, "CLSI-derived hematology and biochemistry reference intervals for healthy adults in eastern and southern Africa," *PLoS One*, vol. 4, pp. e440, 2009.
[35] Schnabl K, Chan MK, Gong Y, Adeli K, "Closing the gaps in pediatric intervals: the CALIPER initiative," *Clin Biochem Rev*, vol. 29, pp. 89–96, 2008.
[36] Ceriotti F, Henny J, Queralto J, Ziyu S, Ozarda Y, et al, "Common reference intervals for aspartate aminotransferase (AST), alanine aminotransferase (ALT) and gamma-glutamyl transferase (GGT) in serum: results from an IFCC multicenter study," *Clin Chem Lab Med*, vol. 48, pp. 1593–1601, 2010.
[37] Colantonio DA, Kyriakopoulou L, Chan MK, Daly CH, Brinc D, et al, "Closing the gaps in pediatric laboratory reference intervals: a CALIPER database of 40 biochemical markers in a healthy and multiethnic population of children," *Clin Chem*, vol. 58, pp. 854–868, 2012