e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2022; 14(4); 316-326

Original Research Article

Establishment of Biological Reference Interval for Liver Function Test in Tertiary Care Hospital in the Rural Area of Anand District

Patel Dharmik S[1], Chhatriwala Mitul N[2], Sodavadiya Kirankumar B[2], Patel Jainita[4]

[1,2,3]Associate Professor, Department of Biochemistry, Pramukhswami Medical College, Bhaikaka University, Karamsad, Gujarat.

[4]M.Sc. MLT Student, Bhaikaka University, Karamsad, Gujarat

Received: 09-01-2022 / Revised: 20-02-2022 / Accepted: 11-03-2022
Corresponding author: Dr. Chhatriwala Mitul N
Conflict of interest: Nil

Abstract

Background: The concept of reference intervals was introduced by the international federation of clinical chemistry IFCC to avoid the problems with normal values and values obtained from an individual under clinical investigation. In India, the reference value of LFT used in laboratories has been adopted from those reported for the western population. The reference range varies considerably from one laboratory to another and is dependent on the population diet, methodology, and selection of reference group needs of the clinicians.

Aims and Objectives: To establish reference intervals of LFT which include alkaline phosphatase, bilirubin (total, direct, indirect), total protein, albumin, globulin, A/G ratio, SGPT, SGOT in healthy individuals attending routine health checkups at rural tertiary care hospital of Gujarat.

Materials and Method: The posterior sampling was done over the period September 2018 to July 2019. The study was done at the clinical biochemistry department of tertiary care hospital in a rural area. In our study, we took 901 individuals who came to the hospital for their routine health check-ups after applying Inclusion & Exclusion criteria. The partitioning was done according to age (18-30, 31-40, 41-50, 51-60, 61-70, 70 and above years) and sex. Analysis was performed using the commercially available statistical software
Stata for each analyte.

Results: We compared the reference range derived with the biological reference interval being used currently in the laboratory. Values compared for ALP (u/l), Bilirubin Total (mg/dl), Bilirubin Direct (mg/dl), Bilirubin Indirect (mg/dl), Total protein (g/dl), Albumin (g/dl), A/G Ratio (g/dl), SGPT (u/l), SGOT (u/l). Values derived in our study for Males: - 54.07-87.70, 0.34-0.88, 0.08-0.22, 0.22-0.70, 6.91-7.81, 3.54-4.12, 0.91-1.27, 23.90-45.32, 17.41-30.39 and for Females: - 54.64-93.45, 0.28-0.70, 0.05-0.21, 0.17-0.53, 6.97-7.85, 3.45-4.01, 0.87-1.17, 20.44- 40.94, 16.15- 30.25 respectively.

Conclusion: It was seen that the reference range of most liver function test parameters varies when compared with other reference ranges and reference ranges being used in the laboratory. The reason for the same was that the liver function test may vary according to age groups, epidemiological areas, and ethnicity.

Keywords: Reference interval, LFT, Liver function tests, ethnic variations.

Introduction

The liver has to perform different kinds of biochemical synthetic and excretory functions. So, no single biochemical test can detect the global function of the liver. Liver function tests also referred to as hepatic panels, are a group of blood tests that provide information about the state of a patient's liver. These tests include prothrombin time, APTT, albumin, bilirubin (direct and indirect), and others. The ALT and AST tests measure enzymes that your liver releases in response to damage or disease. The albumin test measures how well the liver creates albumin, while the bilirubin test measures how well it disposes of bilirubin. ALP can be used to evaluate the bile duct system of the liver. Liver function tests are generally used to assess hepatocellular injury, cholestasis, infiltrative disease, biliary obstruction, or synthetic function of the liver. Liver function tests are also used to screen asymptomatic patients/ individuals, mostly during regular health check-ups, blood donation, and hospitalization for no liver-related diseases[1].

Reference value: a value obtained by observation or measurement of a particular type of quantity on a reference individual. The IFCC also defines other terms related to the concept of reference values reference population, reference sample group, reference distribution, reference limits, and reference interval[1]. The concept of reference intervals was introduced by the international federation of clinical chemistry IFCC to avoid the problems with normal values and values obtained from an individual under clinical investigation. In India, the reference value of LFT used in laboratories has been adopted from those reported for the western population.

Data collected during the medical interview, clinical examination, and supplementary investigation must be interpreted by comparison with reference data. The reference range varies considerably from one laboratory to another and is dependent on the population diet, methodology, and selection of reference group needs of the clinicians[0]. For the determination of reference ranges, the most important stage is the selection of the reference group and the standardization of preanalytical factors[4,5].

The latest edition of the clinical and laboratory standards institute-approved guideline, "Defining, establishing and verifying reference intervals in the clinical laboratory." Recognizes the reality that, in practice, very few laboratories perform their reference intervals studies, instead of performing a new reference interval study, laboratories and manufacturers refer to studies done many decades ago when both the methods and the population were very different[6].

At present, there are very few studies done for the reference range for LFT (liver function test) of an adult healthy population in India. Most of the worldwide studies for LFT reference range are done for European countries thus it's very much important to have a reference range of LFT for the healthy adult population in countries like India.

Materials and Method

The posterior sampling was done from September 2018 to July 2019. The study was done at the clinical biochemistry department, tertiary care rural center in Anand District. Before starting the study, the protocol was prepared and presented to

the institutional Human Research Ethics Committee which subsequently approved the proposal.

In our study, we took 901 individuals who attended tertiary care rural center in Anand District for their routine health check-ups after applying Inclusion & Exclusion criteria. Based on their alkaline phosphatase, bilirubin (total, direct, indirect), total protein, albumin, globulin, A/G ratio, SGPT, and SGOT values we established d normal reference range for Liver function tests a for a healthy population of the Anand district.

Inclusion Criteria

- All healthy individuals above 18 years of age attending the routine health checkup at the Hospital, Karamsad will be included in this study.

Exclusion Criteria

- Below the age of the 18 years,
- History of hypertension, diabetes, Renal failure, Alcoholic individuals, Liver failure, any other liver disorder on any liver medication, Pregnancy & cancer, Requirement of any investigations or interventions to be concluded on participants
- If exclusion details/ history will not be available for a specific individual, data for that individual will be excluded.

Detail history was taken from LIS – Laboratory Information System of the hospital with the consent of COD, the health check scheme in charge, & head of the central diagnosis laboratory-CDL.

During the study, there was no change in the equipment, reagent, calibration standards, and controls. Before starting the analysis, the instrument was calibrated using calibrators and the controls were checked at different concentrations (BioRad levels 1 and 2) of the analytes. As a part of external quality assurance, our laboratory is enrolled BioRad-USA external quality control program.

The healthy subjects obtained after applying the inclusion & exclusion criteria were used for establishing the reference intervals. The partitioning was done according to age (18-30, 31-40, 41-50, 51-60, 61-70, 70 and above years) and sex. Analysis was performed using the commercially available statistical software Stata 14. for each analyte (serum total ALP, Bilirubin (total, direct, indirect), Albumin, Globulin, A/G ratio, total protein, SGPT, SGOT) Mean ± SD values were presented. A P-value of less than 0.5 was considered statistically significant. Descriptive statistics were applied for frequency Mean ± SD. We will compare our derived reference range with the reference range being used as standard and we will look for a statistically significant difference.

Observation and results

In this study, a total number of 901 healthy individuals ‘’who attended the ‘whole body check-up scheme’ at tertiary care rural center in Anand District’’ were included after applying the inclusion and exclusion criteria and were selected for establishing the reference intervals.

Age and gender-wise partitioning of the subjects was done (Table 1). In this study, there were 443 males and 458 females. The maximum number of individuals was between the age group of 51-and 60 (see figure no-1). In each group female participants were more in number.

Table 1: Age and gender distribution

N0	AGE(YEARS)	Gender	PERCENT	Total
1	18-30	M	29 (3.2%)	57 (6.3%)
		F	28 (3.1%)	
2	31-40	M	46 (5.1%)	106 (11.8%)
		F	60 (6.7%)	
3	41-50	M	85 (9.4%)	174 (19.3%)
		F	89 (9.9%)	
4	51-60	M	111 (12.3%)	254 (28.2%)
		F	143 (15.9%)	
5	61-70	M	121 (13.4%)	225 (25.0%)
		F	104 (11.5%)	
6	70-80	M	37 (4.1%)	62 (6.9%)
		F	25 (2.8%)	
7	80 and Above	M	14 (1.6%)	23 (2.6%)
		F	9 (1.0%)	
8	Total	M	443 (49.2%)	901 (100.0%)
		F	458 (50.8%)	

Age and gender-wise partitioning of the subject was done. We observed that there were more individuals between the age group of 51-and 60.

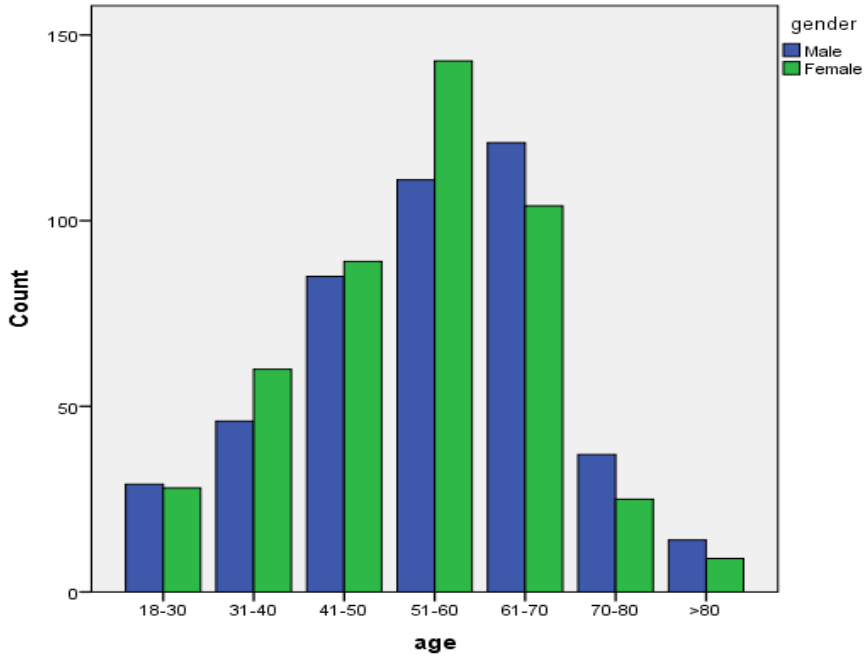

Figure 1: Gender Distribution

In this study, there were 443 males and 458 females. A maximum number of individuals were between the age group of 51-and 60 (see figure no-1). In each group female participants were more in number.

Table 2: Reference Interval for Alkaline phosphatase (ALP)

NO	AGE	GENDER	MEAN	SD	REFERENCE INTERVAL
1	18-30	M	73.00	18.52	54.47-91.53
		F	63.82	15.49	48.32-79.32
2	31-40	M	69.52	20.03	49.48-89.56
		F	63.75	18.37	45.38-82.12
3	41-50	M	73.11	15.24	57.87-88.35
		F	72.47	20.81	51.65-93.29
4	51-60	M	71.33	16.25	55.07-87.59
		F	79.69	17.75	61.94-97.45
5	61-70	M	69.47	16.92	52.55-86.08
		F	76.23	19.22	57.00-95.46
6	71 -80	M	69.16	17.13	52.02-86.30
		F	72.12	17.64	54.48-89.76
7	81 and Above	M	71.00	14.63	56.37-85.63
		F	80.44	16.74	63.70-97.18
8	TOTAL	M	70.89	16.81	54.07-87.70
		F	74.05	19.40	54.64-93.45

Table 3: Reference Interval for Bilirubin total

NO	AGE	GENDER	MEAN	SD	REFERENCE INTERVAL
1	18-30	M	0.60	0.30	0.3-0.9
		F	0.49	0.26	0.23-0.75
2	31-40	M	0.56	0.33	0.23-0.89
		F	0.44	0.19	0.25-0.63
3	41-50	M	0.63	0.31	0.32-0.94
		F	0.48	0.21	0.27-0.69
4	51-60	M	0.60	0.23	0.37-0.83
		F	0.49	0.18	0.31-0.67
5	61-70	M	0.62	0.27	0.35-0.89
		F	0.50	0.24	0.26-0.74
6	70-80	M	0.68	0.20	0.48-0.88
		F	0.56	0.24	0.32-0.80
7	80 and Above	M	0.65	0.18	0.47-0.83
		F	0.50	0.07	0.43-0.57
8	TOTAL	M	0.61	0.27	0.34-0.88
		F	0.49	0.21	0.28-0.70

Table 4: Reference Interval for Bilirubin Direct

NO	AGE	GENDER	MEAN	SD	REFERENCE INTERVAL
1	18-30	M	0.14	0.06	0.08-0.20
		F	0.13	0.05	0.08-0.18
2	31-40	M	0.14	0.08	0.06-0.22
		F	0.11	0.05	0.06-0.16
3	41-50	M	0.15	0.06	0.09-0.21

		F	0.13	0.08	0.05-0.21
4	51-60	M	0.15	0.06	0.09-0.21
		F	0.13	0.06	0.07-0.19
5	61-70	M	0.15	0.07	0.08-0.22
		F	0.14	0.11	0.03-0.25
6	71 -80	M	0.16	0.05	0.11-0.21
		F	0.14	0.06	0.08-0.20
7	81 and Above	M	0.17	0.06	0.11-0.23
		F	0.15	0.05	0.10-0.21
8	TOTAL	M	0.15	0.07	0.08-0.22
		F	0.13	0.08	0.05-0.21

Table 6: Reference Interval for Bilirubin Indirect

NO	AGE	GENDER	MEAN	SD	REFERENCE INTERVAL
1	18-30	M	0.47	0.28	0.19-0.75
		F	0.36	0.22	0.14-0.58
2	31-40	M	0.42	0.28	0.14-0.70
		F	0.32	0.17	0.15-0.49
3	41-50	M	0.47	0.27	0.20-0.74
		F	0.35	0.18	0.17-0.53
4	51-60	M	0.45	0.21	0.24-0.66
		F	0.36	0.16	0.20-0.52
5	61-70	M	0.46	0.23	0.23-0.69
		F	0.36	0.18	0.18-0.54
6	71-80	M	0.52	0.18	0.34-0.70
		F	0.42	0.20	0.22-0.62
7	81 and Above	M	0.48	0.15	0.33-0.63
		F	0.35	0.05	0.30-0.40
8	TOTAL	M	0.46	0.24	0.22-0.70
		F	0.35	0.18	0.17-0.53

Table 7: Reference Interval for Albumin

NO	AGE	GENDER	MEAN	SD	REFERENCE INTERVAL
1	18-30	M	4.05	0.23	3.82-4.28
		F	3.80	0.22	3.58-4.02
2	31-40	M	3.96	0.27	3.69-4.23
		F	3.80	0.36	3.44-4.16
3	41-50	M	3.88	0.33	3.55-4.21
		F	3.73	0.27	3.46-4.00
4	51-60	M	3.78	0.25	3.53-4.03
		F	3.71	0.27	3.44-3.98
5	61-70	M	3.79	0.26	3.53-4.05
		F	3.70	0.25	3.45-3.95
6	71-80	M	3.71	0.27	3.44-3.98
		F	3.76	0.33	3.43-4.09

7	81 and Above	M	3.80	0.42	3.38-4.22
		F	3.69	0.39	3.30-4.08
8	TOTAL	M	3.83	0.29	3.54-4.12
		F	3.73	0.28	3.45-4.01

Table 8: Reference Interval for Globulin

NO	AGE	GENDER	MEAN	SD	REFERENCE INTERVAL
1	18-30	M	3.61	0.45	3.16-4.06
		F	3.62	0.31	3.31-3.93
2	31-40	M	3.49	0.30	3.19-3.79
		F	3.61	0.42	3.19-4.03
3	41-50	M	3.51	0.38	3.13-3.89
		F	3.70	0.36	3.34-4.06
4	51-60	M	3.58	0.36	3.22-3.94
		F	3.70	0.38	3.32-4.08
5	61-70	M	3.51	0.36	3.15-3.87
		F	3.70	0.41	3.29-4.11
6	71-80	M	3.44	0.32	3.12-3.76
		F	3.74	0.48	3.26-4.22
7	81 and Above	M	3.61	0.58	3.03-4.19
		F	3.63	0.20	3.43-3.83
8	TOTAL	M	3.53	0.37	3.16-3.90
		F	3.69	0.39	3.30-4.08

Table 9: Reference Interval for Total Protein

NO	AGE	GENDER	MEAN	SD	REFERENCE INTERVAL
1	18-30	M	7.67	0.44	7.23-8.11
		F	7.42	0.35	7.07-7.77
2	31-40	M	7.45	0.36	7.09-7.81
		F	7.41	0.50	6.91-7.91
3	41-50	M	7.35	0.48	6.87-7.83
		F	7.44	0.40	7.04-7.84
4	51-60	M	7.38	0.40	6.98-7.78
		F	7.41	0.41	7.00-7.82
5	61-70	M	7.31	0.42	6.89-7.73
		F	7.40	0.45	6.95-7.85
6	71-80	M	7.15	0.43	6.72-7.58
		F	7.42	0.49	6.93-7.91
7	81 and Above	M	7.42	0.69	6.73-8.11
		F	7.36	0.43	6.93-7.79
8	TOTAL	M	7.36	0.45	6.91-7.81
		F	7.41	0.44	6.97-7.85

Table 10: Reference Interval for A/G RATIO

NO	AGE	GENDER	MEAN	SD	REFERENCE INTERVAL
1	18-30	M	1.14	0.16	0.98-1.30
		F	1.06	0.11	0.95-1.17
2	31-40	M	1.14	0.13	1.01-1.27
		F	1.05	0.15	0.90-1.20
3	41-50	M	1.08	0.25	0.83-1.33
		F	1.02	0.13	0.89-1.15
4	51-60	M	1.06	0.17	0.89-1.23
		F	1.01	0.16	0.85-1.17
5	61-70	M	1.09	0.14	0.95-1.23
		F	1.01	0.14	0.87-1.15
6	71-80	M	1.06	0.21	0.85-1.27
		F	1.03	0.16	0.87-1.19
7	81 AND Above	M	1.09	0.21	0.88-1.30
		F	0.99	0.16	0.83-1.15
8	TOTAL	M	1.09	0.18	0.91-1.27
		F	1.02	0.15	0.87-1.17

Table 11: Reference Interval for SGPT (ALT)

NO	AGE	GENDER	MEAN	SD	REFERENCE INTERVAL
1	18-30	M	37.14	12.26	24.88-49.40
		F	26.96	9.39	17.57-36.35
2	31-40	M	39.04	9.70	29.34-48.74
		F	29.13	11.13	18.00-40.26
3	41-50	M	38.73	11.07	27.66-49.80
		F	31.69	11.17	20.52-42.86
4	51-60	M	35.13	9.99	25.14-45.12
		F	32.82	10.14	22.68-42.96
5	61-70	M	31.12	10.02	21.10-41.14
		F	28.81	7.77	21.04-36.58
	71-80	M	31.00	8.75	22.25-39.75
		F	31.40	12.17	19.23-43.57
6	81 AND Above	M	25.43	5.83	19.60-31.26
		F	29.00	12.64	16.36-41.64
7	TOTAL	M	34.61	10.71	23.90-45.32
		F	30.69	10.25	20.44-40.94

Table 12: Reference Interval for SGOT (AST)

NO	AGE	GENDER	MEAN	SD	REFERENCE INTERVAL
1	18-30	M	23.90	5.27	18.63 - 29.17
		F	21.11	5.72	15.39 - 26.83
2	31-40	M	23.89	5.27	18.17 - 29.61
		F	20.75	6.37	14.38 - 27.12
3	41-50	M	24.34	5.61	18.73 - 29.95

		F	21.93	7.90	14.03 - 29.83
4	51-60	M	24.31	7.38	16.93 - 31.69
		F	24.47	6.69	17.78 - 31.16
5	61-70	M	23.31	7.04	52.55 - 86.39
		F	23.29	6.09	17.20 - 29.38
6	71-80	M	23.38	5.74	17.64 – 29.12
		F	27.48	8.78	18.70 - 36.26
7	81 and Above	M	24.64	7.42	17.22 – 32.06
		F	25.56	8.17	17.39 - 33.73
8	TOTAL	M	23.90	6.49	17.41 - 30.39
		F	23.20	7.05	16.15 - 30.25

Discussion

In many cases, military recruits, medical students, or other more or less institutionalized, young and non-diseased people have constituted the reference population. In those cases, the reference population is a poor representative of individuals seeking health care and who might suffer from normal conditions[7].

The question of whether clinical laboratory standards, in particular, the reference intervals practiced in western, European, and other Asia-pacific countries are applied to the Indian population needs to be evaluated.

Alice juma et al. (2011) studied a total of 400 who consented to be part of the study were further evaluated. Reference ranges for Total protein (g/dl), Albumin (g/dl), ALP (u/l), SGPT (ALT) (u/l), SGOT (AST) (u/l), Bilirubin Total (mg/dl), Bilirubin Direct (mg/dl) were respectively Males values: - 6.7-9.2, 3.8-5.1, 45-147, 9-42, 16-47, 0.2-1.7, 0.0-0.2 and Female values: - 6.7-9.2, 3.8-4.8, 43-126, 6-27, 12-33, 0.1-1.5, 0.0-0.2. In our study, reference values of Total Protein (g/dl), Albumin (g/dl), ALP (u/l), SGPT (ALT) (u/l), SGOT (AST) (u/l), Bilirubin Total (mg/dl), Bilirubin Direct (mg/dl) were respectively in Males: - 6.91-7.81, 3.54-4.12, 54.07-87.70, 23.90-45.32, 17.41-30.39, 0.43-0.88, 0.08-0.22 and in females: - 6.97-7.85, 3.45-4.01, 54.64-93.45, 20.44-40.94, 16.15-30.25, 0.28-0.70, 0.05-0.21. We found that there was no significant difference between reference range of few parameters of our study while few reference ranges have significant differences[8].

Sultana furruqh et al. (2004) studied total 200 who consented to be part of the study. They partitioned the study subject mainly in 5 groups (21-30, 31-40, 41-50, 51-60, 61-70 years). The reference value of total Protein (g/dl), Albumin (g/dl), A/G Ratio, Bilirubin Total (mg/dl), Bilirubin Direct (mg/dl), AST (u/l), ALT(u/l), ALP (u/l) for Males were:- 6.6-8.6, 3.4-4.7, 0.7-1.7, 0.2-1.3, 0.1-0.4, 11-43, 25-86, 56-148 respectively and for Females were:- 6.6-8.8, 3.2-4.6, 0.7-1.6, 0.2-1.0, 0.1-0.4, 10-39, 22-75, 52-144 respectively[9].

Liangyu Xia, et al (2016) studied a healthy normal population and evaluated the reference interval of liver function test parameters. Total Protein (g/dl), Albumin (g/dl) , ALP (u/l), AST (u/l), ALT (u/l) for males were:- 6.5-7.9, 2.1-5.2, 50-124, 16-39, 10-59, and for females were:- 6.5-7.9, 2.1-5.2, 39-96, 6-34, 14-34[10]. As we can see in the above studies the reference values derived in our study are significantly different from other studies for most of the parameters.

Conclusion

Our study was a hospital-based study in which we tried to establish the reference interval for a liver function test. We included different parameters of liver function tests such as ALP, Bilirubin (total, direct, indirect), Total Protein, Albumin, Globulin, A/G ratio, ALT, and AST.

It was seen that the reference range of most liver function test parameters varies when compared with other reference ranges and reference ranges being used in the laboratory. The reason for the same was that the liver function test may vary according to age groups, epidemiological areas, and ethnicity. Discrepancies in liver function tests play a pivotal role in the functioning of the human body. Keeping this in mind the present study was undertaken and a reference range based on its population was derived.

Limitations

Though we have taken a large sample size, it is advisable to conduct similar studies with more participants and in diverse geographical areas, thereby confirming the reference intervals for the entire Indian population based on our data.

Acknowledgment

We are thankful to the institute and management of Bhaikaka University for providing all required assistance for performing our study.

References

1. Green RM, Flamm S.AGA technical review on the evaluation of liver chemistry tests. Gastroenterology.2002; 123:1367-1384.
2. international federation of clinical chemistry, expert panel on theory of reference values. Approved recommendation on the theory of reference values. part 1. The concept of reference values. J Clin chem Clin biochem 1987;25:337-42; part 2 selection of individual for the production of reference values. J Clin Chem Biochem 1987;25:693-43: part 3.preparation of individuals and collection of specimens for the production of reference values. J Clin chem Clin biochem 1988: 26:593-8: part 4. Control of analysis variation in the production transfer and application of reference values. Eur J Clin chem Clin Biochem 1991:29: 531-5, part-5. Statistical treatment of collected reference values: determination of reference limits. J Clin Chem Biochem 1987; 25:645-56; part-6. Presentation of observed values related to reference values. J Clin Chem Biochem 1987; 25:657-62.
3. Burtis CA, aswood ER, Eds, Establishment, and use of reference values: Tietz textbook of clinical biochemistry, WB saunders company,1990.
4. Solberg HE. International federation of clinical chemistry, expert panel on the theory of reference values: approved recommendation on the theory of reference values. Part 1-The concept of reference values. Journal of clinical chemistry and clinical biochemistry. 1987; 25:337-42.
5. Jorgensen LGM, Stahl M, brandslund I, Petersen HP, Jensen BK, olivaceous N plasma glucose reference interval in a low–risk population. 2 Impact of the WHO ADA recommendations on the diagnosis of diabetes Mellitus. Scand J Clin chem lab invest 2001;61 181-90.
6. Clinical and laboratory standards institute, defining, establishing, and verifying reference intervals in the clinical laboratory; Approved guideline.3rd edition. CLSI document C 28-A3. Wayne, PA; clinical and laboratory standards institute 2008.

7. Burtis, C.A. and aswood, E.R. Establishment and use 0f Reference Values. In: Tietz Textbook of clinical chemistry. Chapter 14 3rd edition W.B. saunders company, Philadelphia U.S.A, 1999; 336-356.
8. Alice J, Eliud NM, Joseph JN. Estimation of reference values for liver function tests for the adult population in North-Rift Valley, Kenya. Asian J Med Sci 2011; 3:243–249.
9. Sultana Furruqh, D. Anitha, and T. Venkatesh, Estimation of Reference Values In Liver Function Test In Health Plan Individuals Of An Urban South Indian Population. Indian journal of clinical biochemistry,2004,19(2):72-79.
10. L. Xia, L. Qiu, X. Cheng, et al. Nationwide multicenter reference interval study for 28 common biochemical analytes in China. Medicine (Baltimore). 2016 Mar;95(9): e2915.