Establishment of reference intervals of thyroid function test in healthy individuals

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Abstract

Aim: The central role of the laboratory is to aid the clinician, in interpreting observed values, by providing relevant reference values. To prevent ambiguities inherent in the term normal values, a laboratory should establish its own reference limits. Therefore, the current study was aimed at establishing the reference range of Thyroid function test in healthy population.

Study design: This was a retrospective cross sectional study on 1000 healthy individuals above 18 years of age, attending the routine health check-up.

Materials and Methods: Partitioning was done according to age and sex, inclusion and exclusion criteria were applied and T3, T4 and TSH levels were estimated on the study group.

Results: The values of T3 and T4 obtained were (mean and reference interval in nmol/L) 1.85 (1.15-2.55) and 100.58(57.35-143.81)respectively for males and 1.87(1.07-2.55) and 110.49(62.46-158.52) respectively for females. Similarly, TSH values were 1.23 (0.37-5.19) mIU/L and 1.37(0.27-5.63) mIU/L in males and females respectively.

Conclusion: We found that the value of serum Total T3 & serum Total T4 was higher as compared to the international values while that serum TSH was similar.

Keywords: Reference range, T3, T4, TSH.

Introduction

Interpretation of medical laboratory data is an example of decision making by comparision. Hence, reference values are required for tests performed in the clinical laboratory. A patient's laboratory result is not medically useful unless appropriate data for comparison is available. The central role of the laboratory is to aid the clinician, in interpreting observed values, by providing relevant reference values in a convenient and practical format. The concept of reference intervals was introduced by the International Federation of Clinical Chemistry (IFCC) to avoid problems with normal values and values obtained from individuals under clinical investigation. According to IFCC, it is necessary for every laboratory to have its own set of reference limits. However, in India most of the laboratories follow the reference intervals established in the western population; which usually do not match with the Indian population.[1] To prevent ambiguities inherent in the term normal values, the concept of reference values was introduced and implemented in the 1980s.[2,3] IFCC recommends the term reference values and related terms, such as reference individual, reference limit, reference interval, and observed values.[4-8] For most analytes, a laboratory should establish (or verify) its own reference limits. In the 2010 clinical and laboratory standards institute(CLSI) guidelines, this point has been emphasised.[5] Currently very few studies have been done for establishing reference range for TFT (thyroid function test) namely thyroid stimulating hormone(TSH), total thyroxine(T4), total triiodothyronine(T3); for healthy adult population in India. In our country, the reference values of TFT used in clinical laboratories have been adopted from those reported for the western population. But these reference intervals in most of the cases cannot be taken into acount in our set up because serum TFT levels even in healthy normal population are affected by a number of factor such as age, sex, racial differences, dietary factors, socio-economic status and geographic conditions. Moreover it is also important to take into account the method by which TFT was estimated. Thyroid diseases are, arguably, among the commonest endocrine disorders worldwide. India too, is no exception. According to a projection from various studies on thyroid disease, it has been estimated that about 42 million people in India suffer from thyroid diseases. Thyroid diseases are different from other diseases in terms of their ease of diagnosis, accessibility of medical treatment , and the relative visibility that even a small swelling of the thyroid offers to the treating physician. Early diagnosis and treatment remain the cornerstone of management.[6] Thyroid hormones have ubiquitous effects on growth and development in the fetus child ,and adolescent, and they regulate calorigenesis and metabolic rate throughout life. Thyroid hormones maintain the basal metabolic rate and thus regulates the metabolism of endogenous and exogenous substances.[7,8] Therefore, the current study was aimed at establishing the reference range of TFT in adult healthy population in Anand district, Gujarat, India.

Materials and Methods

This retrospective cross sectional study was done at a tertiary care center in the Anand district of Gujarat and samples were collected between April 2016 to February 2017. Before starting the study, a protocol was prepared and presented to Institutional Human Research Ethics Committee who subsequently approved the proposal. In the study 1000 individuals who attended the routine Health Check up were selected after applying the Inclusion & Exclusion criteria. Based on their T3,T4,TSH values we established thyroid hormone reference range. All the healthy individuals above 18 years of age, attending the routine health checkup were included in the study. Individuals below the age of the 18 years, with past history of hypertension, diabetes, renal failure, any thyroid disorder, on any thyroid medication and pregnant women were excluded from the study. During the course of 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 of the analytes. Tests were performed by electrochemiluminenscence principle.

Statistical analysis

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 T3,T4,TSH) Mean ± SD values were presented. p value of less than 0.05 was considered statistically significant. One way anova , 2 unpaired sample 't' test was applied for gender – specific and age – specific group comparisons for all markers. Descriptive statistics was applied for frequency Mean ± SD. Correlation analysis was performed using the pearson method. P values <0.05 were considered to be significant.

Results and Discussion

A total of 1000 healthy individuals who attended routine health check up were included in the study after applying inclusion and exclusion criteria. There were 485 males and 515 females. Age and gender wise partitioning of subjects was done and it was observed that there were more individuals between the age group of 51-60 and in each group female participants were more in number. (Table 1) (Fig. 1) (Fig. 2).

Table 1: Age and gender distribution

Age(years)	Total	Percent	Male	Female
18-30	94	9.4%	41(8.4%)	53(10.2%)
31-40	197	19.7%	100(20.6)	97(18.8%)
41-50	246	24.6%	115(23.7%)	131(25.4%)
51-60	265	26.5%	125(25.7%)	140(27.1%)
61-70	134	13.4%	63(12.9%)	71(13.7%)
>70	64	6.4%	41(8.4%)	23(4.4%)
Total	1000	100%	485	515

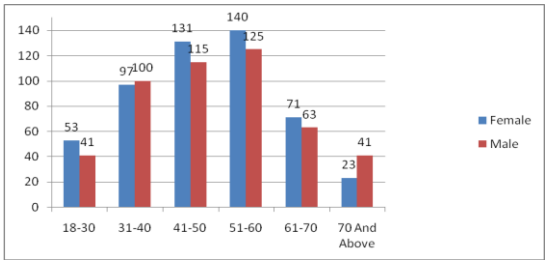

Fig. 1: Age Distribution

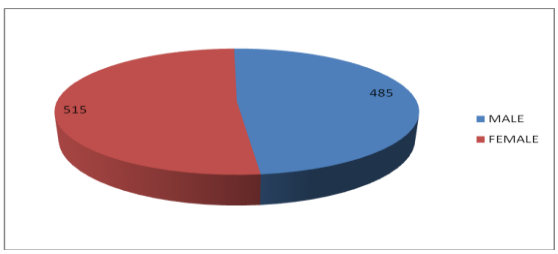

Fig. 2: Gender Distribution

Mean BMI values of male and female were calculated and the 'p' value was 0.2297 which indicated that there was no significant difference in the BMI values between females and males.(Table 2) (Fig. 2)

Table 2: Reference Interval of total value of BMI

Gender	Total no	Mean	Sd	Reference Interval	P value
Female	515	26.70	4.89	17.11-36.28	0.2297
Male	485	26.36	4.09	18.34-34.37	

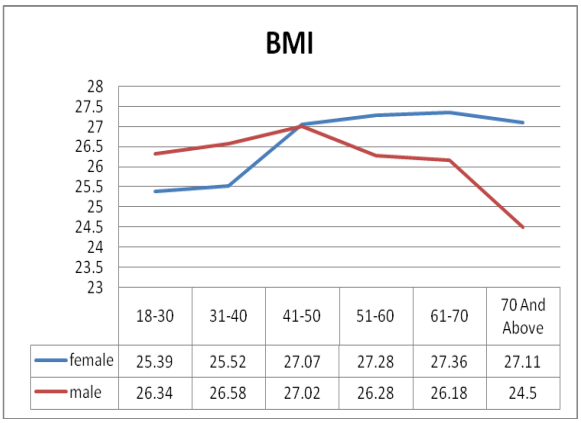

Fig. 3: Mean Value Of BMI in different age groups

Mean value of serum total T3 was calculated and it was observed that the value was higher in female age group of 18-30. (Fig. 4) (Table 3)

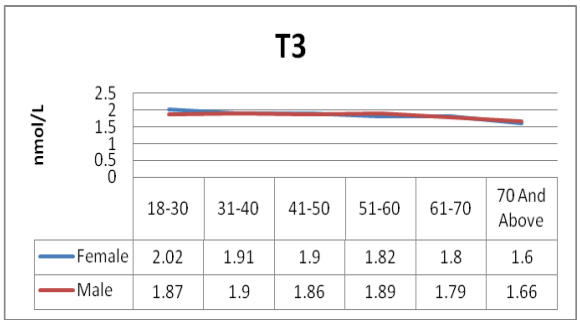

Fig. 4: Mean Value of Serum Total T3

Mean value of serum total T4 was calculated and it was seen that the value were comparable to each other in all age groups but the value was slightly higher in females as compared to males. (Fig. 5) (Table 3)

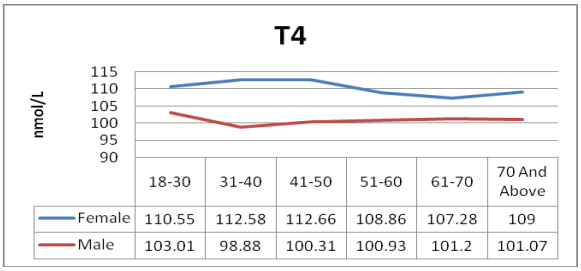

Fig. 5: Mean value of serum Total T4

Mean TSH values of male and female were calculated and it was seen that there was no significant difference in the TSH values among different age groups. (Fig. 6) (Table 3)

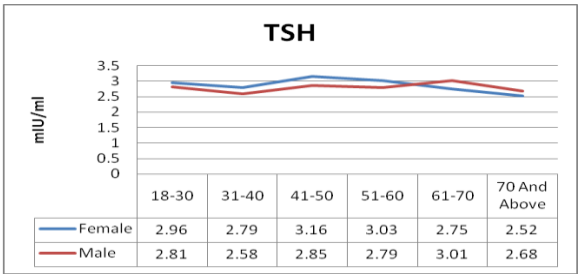

Fig. 6: Mean value of serum Total TSH

There was no significant difference in value of T3 and TSH between females and males while there was significant difference between in the total T4 values between males and females. (Table 3)

Table 3: Reference Interval of TFT

Analyte	Gender	Total	Mean	SD	Reference interval	P value
Serum Total T3	Male	485	1.85	0.36	1.15-2.55	0.4982
	Female	515	1.87	0.35	1.07-2.55	
Serum Total T4	Male	485	100.58	22.06	57.35-143.81	0.0420
	Female	515	110.49	24.51	62.46-158.52	
Serum TSH	Male	485	2.78	1.23	0.37-5.19	0.0282
	Female	515	2.95	1.37	0.27-5.63	

There was no significant difference in the total T3 values in all age groups between males and females but there was significant difference in the total T4 values between males and females in the age group of 31-60 years, while in the other age groups there was no significant difference in the values of total T4 in between males and females. There was no significant difference in the TSH values in all age groups between males and females. (Table 4)

Table 4: Reference Interval of TFT age-wise

Age	Sex	No	Total T3			Total T4			TSH		
			Mean	RI	p value	Mean	RI	p value	Mean	RI	p value
18-30	M	41	1.87 (0.32)	1.25-2.49	0.0597	103.01 (22.18)	59.54-146.48	0.1108	2.81 (0.91)	1.01-4.59	0.5217
	F	53	2.03 (0.44)	1.17-2.89		110.55 (22.79)	65.89-155.21		2.96 (1.29)	0.44-5.48	
31-40	M	100	1.90 (0.33)	1.26-2.54	0.9287	98.88 (23.23)	53.34-144.41	<0.0001	2.58 (1.16)	0.31-4.85	0.2367
	F	97	1.91 (0.29)	1.35-2.47		112.58 (20.81)	71.8-153.36		2.79 (1.27)	0.31-5.27	
41-50	M	115	1.86 (0.36)	1.16-2.56	0.3630	100.31 (23.60)	54.05-146.56	0.0002	2.85 (1.30)	0.31-5.39	0.0818
	F	131	1.90 (0.36)	1.2-2.6		112.66 (27.39)	58.98-166.34		3.16 (1.46)	0.3-6.02	
51-60	M	125	1.89 (0.40)	1.11-2.67	0.1756	100.93 (22.51)	56.82-145.04	0.0093	2.79 (1.25)	0.34-5.24	0.1446
	F	140	1.83 (0.34)	1.17-2.49		108.86 (26.28)	57.36-160.36		3.03 (1.39)	0.31-5.75	
61-70	M	63	1.79 (0.31)	1.19-2.39	0.9021	101.20 (18.17)	65.59-136.81	0.0778	3.01 (1.33)	0.41-5.61	0.2608
	F	71	1.80 (0.32)	1.18-2.42		107.28 (21.03)	66.06-148.49		2.75 (1.28)	0.25-5.25	
>70	M	41	1.66 (0.34)	1 - 2.32	0.5951	101.07 (19.40)	63.05-139.09	0.1611	2.68 (1.23)	0.27-5.09	0.6360
	F	23	1.62 (0.26)	1.12-2.12		109.00 (24.80)	60.4-157.6		2.52 (1.45)	0.3-5.36	

M=male; F=female No. in brackets indicate SD

There has been a significant change in the lifestyle and work environment of present day with that of our forefathers. This has led to a tremendous change even in our biological workup. Endocrinological disorders have become rampant in today's scenario. In our study we tried to set up thyroid hormone reference intervals for healthy individuals of Anand district in Gujrat. We evaluated the data collected from 1000 healthy individuals after applying inclusion and exclusion criteria, who attended routine health check up scheme. The population was categorized into various age groups (18-30,31-40,41-50,51-60,61-70,≥70). Mean and SD values of T3,T4,TSH, of total data was 1.86±0.35, 105.69±23.86,2.87±1.31 respectively.

R.K Marwaha et al.[9] in 2013 studied and evaluated 4349 participants. The mean age of total population was 41.2±18.1. The reference population was categorized into various age groups 18-30, 31-40, 41-50, 51-60, 61-70, ≥70 and TSH values for females was 2.17±0.86, 2.10±0.93, 2.34±0.95, 2.33±0.94, 2.21±0.95, 2.21±0.95, and for males 2.25±0.86, 2.35±0.92, significant difference between any age categories in both men and women. In our study mean age of total population was 49.11± 13.64. Our reference population was categorized into various age groups and the TSH values for females was 2.96±1.29, 2.79±1.27, 3.16±1.46, 3.03±1.39, 2.75±1.28, 2.52±1.45 and that for males was 2.81±0.91, 2.58±1.16, 2.85±1.30, 2.79±1.25, 3.01±1.33, 2.68±1.23 respectively. As compared to their study there was no significant difference between age or gender wise results.

In 2014 P.wang et al.[10] studied 211 normal healthy zhengzhou population, the study subjects were partitioned into 4 age groups and the mean total T3 ,total T4 and TSH value for females was 1.57±0.20, 109.13±16.38, 3.63±2.69 and males was 1.67±0.29, 114.29±18.57, 3.04±1.95 respectively. We partitioned study subjects into 6 age groups and total T3, total T4, and TSH mean values for females was 1.87± 0.35, 110.49±24.51, 2.95±1.37 and males was 1.85±0.36, 100.58±22.06, 2.78±1.23 respectively .When we compared our results with their data we found that there was no significant difference gender wise and correlation analysis showed that not all markers correlated with age.

As per the standard guidelines for thyroid hormones normal reference range for T3, T4 & TSH is 0.77-2.33nmol/l, 58.05- 140.61nmol/l, 0.3-5.0mlu/l,respectively. As compared to this, in our study the reference ranges for T3, T4, TSH was 1.18-2.54, 58.93-152.45, 0.31-5.43 respectively. Hence, the value of T3 & T4 was higher, while that of TSH was found to be similar with that of the standard values.[11]

Pasupathi et al.[12] compared pregnant with non-pregnant women. The mean age of non pregnant women was 25±15 years and their body mass index was 26±3.4. Their T3, T4 & TSH values were 2.95±1.06, 89.75± 32.53, 2.54±1.32, while in the present study the mean BMI of females was 26.70±4.89 and mean values of T3, T4 & TSH of female was 1.87±0.35, 110.49±24.51 and 2.95±1.37. As compared to their data our TSH and total T4 values were higher.

In another study done on normal pregnant Indian women by Marwah et al.[13] FT3, FT4, & TSH values in pregnant women were evaluated trimester wise. The mean values of TSH for each trimester was 2.42±1.65,2.49±1.9,2.6±1.9 respectively.

In a subsequent study done in the Third Trimester in pregnant Flipino Women by Bautista A, et a, mean TSH value 1.44±0.70, while in the recent study the mean TSH value was 2.96±1.29 these results could not be compared since physiological changes such as hemodilution, increased serum thyroid-binding globulin alongwith its decreased clearance, increased human chorionic gonadotrophin and increased urinary iodide excretion, can affect the functioning of thyroid gland and interpretation of thyroid function tests.[14,15]

Conclusion

We found that the value of serum Total T3& serum Total T4 was higher as compared to the international values while that serum TSH was similar. The reason for same was that Thyroid Function Test may vary according to age groups, epidemiological areas, ethinicity. Decade wise group of individuals provided a clearer picture in setting reference range.

Limitations

Though we had taken a large sample size, it is still advisable to conduct similar studies with more participants, there by confirming the reference range for the Indian population and using our own data to establish reference range.

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