JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH

How to cite this article:
Mansourian A R*, Ahmadi A R**, CORRELATION BETWEEN INVERSE AGE AND SERUM THYROXIN LEVELS AMONG CHILDREN AND ADOLESCENTS. Journal of Clinical and Diagnostic Research [serial online] 2010 October [cited: 2010 October x]; 4:3196-3200.

Available from
http://www.jcdr.in/article_fulltext.asp?issn=0973-709x&year=2010&volume=&issue=&page=&issn=0973-709x&id=934

ORIGINAL ARTICLE

Correlation Between Inverse Age And Serum Thyroxin Levels Among Children And Adolescents

Mansourian A R*, Ahmadi A R**

ABSTRACT

The aim of this research was to investigate whether serum thyroxin concentration, within the normal reference intervals were age-related among children and adolescents. This investigation was carried out on 243 subjects who were chosen randomly from all those patients who were referred during the one-year period from to the Danesh Medical Diagnostic Laboratory in Gorgan, northern Iran.
The thyroxin concentrations of the subjects were obtained from the outpatient records of the patients who were referred to the Laboratory during 2007-08. The thyroxin concentrations were determined by the Radio Immunoassay method by using standard laboratory kits. The sample population were divided into 4 age groups of 1-5 years, 6-10 years, 11-15 years and 16-21years. The results of this study showed that there is an inverse age correlation between thyroxin concentrations among children and adolescents in this region.

Key words: Children, Thyroid Hormone, Thyroxin, Iran

*Department of Biochemistry, Biochemistry and Metabolic disorder Research Center; **Department of laboratory Science. Biochemistry and Metabolic disorder Research Center; Golestan University of Medical Sciences. Gorgan- IRAN
Corresponding Author:
Dr Azad R Mansourian, Associate Professor, Gorgan Medical School, Biochemistry and Metabolic Disorder Research Center, Gorgan-IRAN Tel: +98 (171)4422652 FAX: +98(171)4440225
E-mail: azad_r_ mansourian@yahoo.com

Introduction

The thyroid gland plays a crucial role in the children's endocrinology and thyroid hormone deficiency can lead to mental and physical impairment among children. The assessment of serum thyroxin levels is a key factor for the evaluation of the thyroid function test. Many factors including the state of feeding, body mass index and serum iodine concentration may interfere with the levels of thyroid hormones [1],[2].Thyroid hormones are decreased as result of aging, but there are also conflicting reports as to whether the serum thyroxin concentration is altered during the normal life span [3],[4],[5],[6],[7],[8]. There are also some studies indicating that the mean serum thyroxin level is high in early infancy and that it is gradually decreased. Study on the status of the thyroxin levels of the subjects from 10 days to 2 years of age indicated a significant decrease during the first month of life. In another study which was carried out on all age groups including children, it was shown that from 1 year of age onwards, the concentration of all thyroid hormones tended to decrease until adulthood, but other investigations in this area of research were controversial and they were not universally acceptable. [9],[10],[11] Age and gender dependent variation among children and adolescents have been studied by many workers, with contradictory findings [7],[12],[13]. On the basis of all these universally unsatisfying and inhomogeneous observations, the following investigation was designed. The aim of the present study was to determine the significance of Serum thyroxin levels among children and adolescents of Gorgan in northern Iran and to establish whether thyroxin concentration is age related.

Material and Methods

Thyroxin (T4) concentrations of 243 subjects (72 males and 171 females) of about 1 year to 21 years of age were obtained retrospectively from the out patients records of the Danesh Medical Diagnostic Laboratory in Gorgan which is located in northern Iran.

The data belonged to the subjects who were chosen randomly from all the patients who were referred to the above laboratory during 2008-09 and the data were processed at the Danesh Medical Diagnostic Laboratory Research Center.

The names of the subjects were driven out of the center's laboratory records by a test code and their anonymity was maintained. The hypothyroid and hyperthyroid subjects based on standard kit reference intervals were excluded from this investigation. The ANOVA- Fisher Test was used to evaluate the correlation of the data for thyroxin concentration among the different age groups. Linear equation was applied to obtain the thyroxin mean value. The total sample population were divided into 4 groups as follows: A(1-5 years), B(6-10 years), C(11-15 years) and D(16-21 years).

Results

The thyroxin mean concentration for each group is presented in [Table/Fig 1]. The ANOVA-Fisher test revealed the inverse correlation of thyroxin with chronological age (p<o.o5).

[Table/Fig 1]: Thyroxine Concentration of different age groups (A-D).

Group	Age (year)	numbers	thyroxin mean:nmol/L
A	1-5	41	113.5
B	6-10	38	107.38
C	11-15	39	102.92
D	16-21	123	99.21

The mean value of thyroxin was higher in males than females in the same age group, but this correlation was not found in group(C). In this study, we found that the thyroxin concentration inversely correlated with the ages in group A-D.(P<.005). Within the group (A), thyroxin levels were found to have a significant reverse correlation (P<0.05) In group (B), there was no significant correlation, but there was an inverse correlation between the ages and thyroxin levels. The mean of the thyroxin levels was higher in females among all the age groups, except for the age group of 5-10 years. The mean thyroxin value for females and males in the groups A-D were as follows: 106.60, 122.54-105.95, 113.37-107.75, 96.00 and 98.37, 94.40 nmol/l respectively.

The findings of this investigation showed the there were no significant differences between thyroxin concentration and gender. (P>0.05), but within each age group, the following findings was obtained: In groups A andC, the thyroxin levels did not indicate any significant

alteration with gender, but in this present study, as a whole, it was demonstrated that there was an inverse correlation between thyroxin concentration and age in all age groups [Table/Fig 1]. Also, in this study, we found that in general, the T4 levels in males were slightly higher than that in the female subjects [Table/Fig 2], which may be related to the male sex hormone levels at the time of puberty.

Limitation of the present study

The sample population in this study was not large enough to demonstrate a comprehensive conclusion and consequently, the power of the current study cannot be correlated in a wide spectrum in the society, because our population was a sample of convenience, which can be considered to be another limitation of the present study.

[Table/Fig 2]: The mean thyroxin concentration value for males and females as a whole.

Thyroxin mean nmol/L	gender	numbers
101.53	Female	170
103.23	Male	72

Discussion

Thyroxin (T4) is a key factor among the thyroid function tests, which can provide information about thyroid disorders. Age and gender specific normal ranges are important for the interpretation of thyroid hormone assessment among children. There are many reports about the normal ranges in children for the thyroid hormone as a whole. In one study, the thyroid stimulating hormone (TSH) was considered as the best single test which could explain the status of the thyroid gland [14]. Although this latter study is correct, if the thyroid gland was to be assessed on the basis of one single test, then TSH measurement alone cannot provide enough information as to whether the thyroid gland is working properly. There are many cases with abnormal levels of TSH, but the serum T4 levels still is at its normal value and if the patient is to be treated, for either high or low TSH for the sake of hypothyroidism and hyperthyroidism, then it is clearly a misdiagnosis, and the patient is gone under drug therapy for subclinical thyroid dysfunction, which may not be necessary.

T4 seems to be the best single test for the thyroid function test, although the picture is clear when all the thyroid function tests including TSH, T4, T3, T3 uptake, AntiTpo, AntiTg and other anatomical tests are done, but when the health cost-effectiveness is also the main concern along with medical treatment, then, T4 can be considered as a single test which can provide satisfactory information on the thyroid function. T4 is one of the most important hormones which are required for the mental and physical growth of children, and T4 deficiency among children at an early age leads to mental retardation [15]. There are many studies on the status of thyroid hormones among children and adolescents. [11],[16]

The normal range of the thyroid hormone in adults, also, has been under heavy investigation in various parts of the world, with some variation in the findings. [17],[18],[19],[20],[21] The normal ranges from a small sample population of subjects cannot satisfactorily report the proper functioning of the thyroid gland hormone, which is mostly age and gender dependent. Also, a small size population has been recommended for the study of thyroid hormones [22].

As a small population cannot be trusted, therefore, many studies have concentrated on large sample populations which have been derived from the database of medical and laboratory centers, to obtain proper numbers of the subjects for comprehensive research projects**.** [23]**,[**24],[25]

In this present study, we also used the database from a clinical diagnosis laboratory to have enough sample size. Our method of sampling is in agreement with the latter study also, as the age and gender of the children and the adolescents were the two main keys in the interpretation of the clinical diagnosis and the requirements of any medical treatment. We carried out this investigation to elaborate on the status of age and gender related parameters on children and adolescents in this region which is located in northern Iran. Although the study was based on laboratory databases, the population was large enough for the T4 measurement test to be applied to the inhabitants of this region. Such studies based on the database of clinical centers, have also been carried out by other investigators

[23],[24]. Laboratory - based data obtained for this and other similar studies can be considered as a limitation, but due to the problems faced with community based studies, the databases from clinical centers have been used in many reports [26],[27].We assume that this method of sampling can satisfy the aim of such study, but with the limitation which has already been mentioned**.**

In this study, our main concern was to find out whether serum thyroxin levels were age-related. Studies have been done on age related alterations in serum thyroxin levels by various researchers, but with contradictory results. [3], [8]. In our study, we found that serum thyroxin levels were inversely associated with age, which was in agreement with the results of other investigations. [28],[11] The mean of serum thyroxin levels among females and males was almost similar, ie 101.53 nmol/l vs 10.3.23 nmol/l for females and males respectively. Our results showed a progressive reduction of serum thyroxin levels from 113.5 ;107.38, 102.92 and 99.21 nmol/l for the age groups of 1-5 , 6-10 , 11-15 and 16-21 of years respectively. Our results are in agreement with some studies [11],[8], but on the other hand, a study on Chinese neonates and infants indicated that the mean serum thyroxin concentration was high in newborns of up to seven days and it reduced in their pre-school ages within a few months [29],[30], which did not match with our findings. We found that within our group which consisted of infants of < 1 year upto 5 years of age, there was a significant reverse correlation with age, ($P<0.05$) which contradicted the latter study in China, which indicated that the pre-school thyroxin levels were reached at 6-9 months of age [29].The other finding in this present investigation was the higher mean value for male thyroxin levels in the age group of 5-10 years, which may be related to the extra demand of thyroxin for male subjects during this period of life, [31] but another study indicated that the thyroxin concentration showed no difference between the different sexes. [15],[30] Although the differences in the mean T4 values among our female and male subjects were slight, males were found to have higher mean levels of T4, which was not in agreement with a latter study, although they had done a study on different age groups.

Another study in France indicated that there was no alteration in mean T4 levels between the ages of one month and 2 years, which is different from the results of the Chinese study [9],[10],[20].

Studies in China and France have mostly been carried on in subjects up to 2 years of age but contradicting each other ,but they relay on a key point that serum T4 level gradually decrease as the children getting older. The common key point in the above studies can be found in our investigation, as our sample population too consisted of children of about less than one year of age up to 21 years, but the message that comes through, is that thyroxin levels are inversely related to age among children and that the exact T4 concentration should be assessed in various parts of the world, due to the slightly variation which might be present in different regions...

Conclusion

From this present study, we found that in our region, serum thyroxin levels were inversely associated with age in children. Abnormality in the thyroid function disrupts normal physiological development, particularly among children. Many studies in various parts of the world have been carried out without a comprehensive match in the results on the status of serum thyroxin levels. Whether the serum thyroxin levels are steadily age related from infancy through adolescence is still unclear, even though all the studies are in agreement that serum thyroxin levels are age-related. The comprehensive literature review in this study and the findings from this present investigation emphasized once again that the status of serum thyroxin alteration and its age-related dependence in each country and even in each state of the country should be assessed carefully in order to prevent any misdiagnosis with respect to a vital hormone such as thyroxin in growing children. .

Acknowledgment:

The authors sincerely thank The Danesh Medical Diagnostic Laboratory in Gorgan for providing the database for this study.

Reference:

[1]. Ahmadinejad Z. Ziaee V. Rezaee M. Yarmohamadi L. Shaikh H.Bozergi F .Yousefi R and Behjatiardekani J.
The effect of Ramadan Fasting on Thyroid hormone Profile:A cohort Study. Pakistan Journal of Biological Sciences 2006, 9(10):1999-2002
DOI:10.3923/pjbs.2007.905-909

[2]. Mansourian A R. Ghaemi E. Ahmadi A R. SaifiA. Moradi A Bakhshadeh-Nosrat S. A survey of Urinary Iodine concentration in South –east Caspian Sea in Northen Iran.Pakistan Journal of Biological Sciences 10(13):2166-2171
DOI: 10.3923/pibs.2007.2166.2171

[3]. Van den Beld ,AW. Visser TJ. feelders RA, Grobbee DE. Lamberts SW. Thyroid hormone concentrations. disease, physical function and mortality in elderly men. J Clin Endocrinol Metab. 2005, 90 (12):6735-37
PMID:16174720

[4]. Lipson A, Nickoloff LE, Tah HH et al,: A study of age dependent changes in thyroid function tests in adults. J Nuclear Medicine; 1979, 20: 1124-30
PMID:536771

[5]. Westgren . Burger A . lngemansson S .et al. Blood levels of 3,5,3-triiodothyronine and thyroxine: Difference between children , adults and elderly subjects, Acta Med Scand ,1976, 200:493-95
PMID:1015359

[6]. Fleury Y, Van G, Melle JA, Woringer V. et al. Sex dependent variations and timing of thyroid growth during puberty. J Clin Endocrinol Metab, 2001, 86:750-54
PMID:11158041

[7]. Michand P, Foradori A Rodriguez-Portales JA et al ,: A prepubertal surge of thyrotropin proceeds an increase in thyroxin and 3,5,3 -triiodothyronine in normal children . J Clin Endocrinol Metab,1991, 72:979-81
PMID:2022717

[8]. Nishikawa M , Inada M, Naito K et al ,. Age related changes of serum 3,3 –iiodothyronine, 3,5 –diiodothyronine and 3, 5 –diiodothyronine concentrations in man. J Clin Endocrinol Metab 1981, 52;517-22
PMID:7462399

[9]. Liappis, N , and A Starke . Reference Value for the Concentration of free thyroxine and free triiodothyronine in the serum of euthyroid children, Klin padiatr 1987 sep-oct;199(5):366-9.
PMID:3682710

[10]. Liappis N Schlebusch H Von peryes M Berg I . Reference Values for blood levels of free thyroxine , free triodothyronine and thyronine-binding globulins in euthyroid children method: Lumineseinee-enhanced enzyme Immunoassay. 1991, Mar - Apr : 203(2): 113-5 .
PMID:1903468

[11]. Nelson JC . Clark SJ . Borut DL . Tomei RT. Carlton EI. Age-related changes in Serum free thyroxine during childhood and adolescence , J Pediatr, 1993, 123(6): 899-905.
PMID:8229522

[12]. Parra A . Villalpando S. Junco E. Orquieta B. Alatorre S
Garcia-Bulnes G.
Thyroidgland functioning during childhood and adolescence. Chang in Serum TSH,T4,T3,Thyroxin-binding globulin, revers T3 ,free T4 and T3 concentration. Acta.Endocrinol(Copenh). 1980, 93:306-314
PMID:6769275

[13]. Chanione.JP,,. Toppet V,.Lagasse R,.Speh M,.Delange F
Determination of thyroid volume by ultrasound from the neonatal period to late adolescent. Euro Pediatr. 1991, 150:395-399
PMID:2040346

[14]. Surks. MI ,. Chopra IJ ,. Mariash CN,. Nicaff JT. American Thyroid Association guidelines for use of Laboratory tests in thyroid disorders. 1990, 263:1529-1532.
PMID:2308185

[15]. Elmlinger. MW Kuhnel, W. Lambrecht HG, Ranke MB, Reference intervals From birth to adulthood for serum thyronine (T4) , triiodothyronine (T3), free T3 , Free T4, thyroxine binding globulin (TBG) and thyrotropin (TSH). Clin Chem. Lab Med, Oct; 2001, 39 (10): 973-9 .
PMID: 1178614

[16]. Soldin SJ. Brugnara C. Gunter KC. Hicks JM. Pediatric reference range , 1997, 2nd ed 139-146

[17]. Surks. MI ,. Goswami G ,. Daniels, GH. The thyrotropin reference range should remain unchanged. J chin Endocrinol Metab , 2005, 90: 5489-5496.
PMID: 16148346

[18]. Baskin HJ, Cobin RH , Duick DS , Gharib H, Cutter RB, Kaplan MM, Segal RL, . American Association of clinical Endocrinologists medical guide lines for clinical practice For the evaluation of treatment of hyperthyroidism and hypothyroidism, Endocr Prac , 2002, 8 : 457-467
PMID:12432434

[19]. Zophel K, Wundelich, G. Gruning T . Koch, R . Doge H. Kotzerke Y ,. {where does subclinical hypothyroidism start ? Implication for the definition of the Upper reference limit for thyroid stimulating hormone} , Nuklearmedizin, 2005 44: 56-61
PMID:15861273

[20]. Zophel K , Wunderlich G, Kotzerke Y ,. Should we really determine a reference population for the definition of thyroid-stimulating hormone reperence interval ? Clinl Chem. , 2006 52:329-330.
PMID:16449219

[21]. Kratzsch J . Fiedler CM. Leich A. Brugel M .Buchbinder S. Otto L . Sabri O. Matthes G. Thiery Y . : New referece Intervals For thyrotropin and thyroid hormones based on National Academy of clinical Biochemistry criteria and regular utrasonography of the thyroid . Clin Chem 2005, 51: 1480-1486
PMID:15961550

[22]. Virtanen A, kairisto V , Uusipaikka E, .Regression - based reference Limits : determination of sufficient sample size 1998, 44: 2353-2358.
PMID:9799764

[23]. Harwood. SJ ,.Cole GW, 1978, Reference Values based on hospital admission Laboratory data. JAMA 240: 270-274.
PMID: 351227

[24]. Kouri T . Kairisto V.virtanen A. Uusipaikka E. Rajamaki A .
Finneman H .etal. . Reference intervals developed from data for hospitalized patients: Computerized method based on combination of Laboratory and diagnostic data. Clin chem, 1994 40: 2209-2215
PMID:7988006

[25]. Lezzoni LI, Assessing quality using administrative data 1997:127:666-674
PMID: 9382378

[26]. Zurakowski , D , Di Canzio Y, Majzoub, JA .Pediatric reference intervals for serum thyroxine, triiodothyronine , thyrotropin and free thyronine , Clinical Chemistry, 1999, 45, 1087-1091. ,PMID:10388488, PMID:7628078

[27]. Cioffi MP. Gazzerro M.T. Vietri R. Magnetta. A. Durante A Auria D. Puca, GA. Molinari A.M. Serum

Concentration of Free T3 , free T4 and TSH in healthy children. Journal of pediatric Endocrinology and metabolism, 2001, 14, 1635-1639 PMID: 11795654

[28]. Gurmeet. K. kalsotra,L . Sadhoo AK. Age and Sex Related
Changes in thyroid Functions in normal healthy subjects of Jammu Region JK Science, 9(3); July-September: 2007, 132-136 .

[29]. Tsai WY . Lee, JS. Chou YH. Yau KI. Thyroid Function in normal neonates and in fants. Zhonghua Min Guo Xiao, Er ke, Yi Xue , Hui Za Zhi , Jal-Aug: 1994,35(4) : 261-5 .
PMID:8085445

[30]. Taulier-Raybaud. C,. Rabaud, Y. lucas C ,. Simonin G, Carayon P.,. Course of Serum Levels of free thyroid hormones in children from 10 days to 2 years of age , pediatric 1985, Jan-Feb; 40(1): 27-34.
PMID:4022714

[31]. Murthy. JN. Hicks JM. Soldin, SJ. Evaluation of the Techicon Immuno I Radom Access Immunoassay Analyzer and Calculation of Pediatric reference range for endocrine tests, T-Uptake, and ferritin , Clin Biochem 1995; 28: 181-5.