|| Print ISSN: 2589-7837 || Online ISSN: 2581-3935 ||
International Journal of Medical Science and Diagnosis Research (IJMSDR)
Available Online at www.ijmsdr.com
NLM (National Library of Medicine ID: 101738825)
Original Research Article
Volume 4, Issue 5; May: 2020; Page No. 01-04

ROLE OF TRANSTHYRETIN LEVELS IN INDIAN CHILDREN AND ADOLESCENTS.

Srinivasa Nageswara Rao.G[1], E. Sruti[2]
[1]Associate Professor, Dept. of Biochemistry, Tomo Riba Institute of Health & Medical Sciences, Naharlagun.
[2]Tutor, Department of Biochemistry, Tomo Riba Institute of Health & Medical Sciences, Naharlagun
Conflicts of Interest: Nil
Corresponding author: Dr. Srinivasa Nageswara Rao. G

Abstract:
Reports from different parts from India suggested a rising trend prevalence in overweight and obesity among children and adolescents. The serum transthyretin and its correlation with biochemical parameters were analysed in 296 children and adolescents (103 control 96 obese, 97 overweight) of age group 10-17 years. Clinical and anthropometric parameters were also evaluated in all the children. The levels of serum transthyretin were measured by immuno turbidimetric assay. One of the major observations of this study was no significant differences of serum transthyretin between the groups and there was no association between serum transthyretin and Apo AI, Apo B and Lp(a) levels among the study groups. Therefore, the available information suggests that transthyretin levels were not affected by overweight and obesity related inflammation.
Keywords: Transthyretin, Overweight, Obesity.

INTRODUCTION

There was a rising trend in the prevalence of overweight and obesity among children and adolescents in both developed and developing countries. Many studies have reported that, it is most serious health problem of 21st century (1). A statistical survey on obesity reveals that this is more prevalent in urban population, when compared to the rural population (2). Furthermore, it is well established that, overweight children and adolescents have an increased risk of adult obesity (3). A handful of recent reviews and epidemiological studies have implicated that, obesity is a risk factor for insulin resistance, metabolic syndrome and atherosclerotic coronary heart diseases in children (4,5). To prevent the future development of type 2 diabetes or CHD it is better to identify children who are at high risk for these disorders. These is compelling evidence that obesity during childhood and adolescence is a determinant of a number of cardiovascular risk factors including atherogenic dyslipidemia, hypertension, left ventricular hypertrophy atherosclerosis. An average increase of 0.5 kg/m2 of BMI in children increase the risk for hypertension, dyslipidemia and type 2 diabetes mellitus a decade later(4,6,7). It is important to note that in most previous clinical studies have indicated that, transthyretin was found to be associated with lipoproteins in particular both HDL and LDL fractions were reported to contain transthyretin. Transthyretin cleave blood compound called apolipoprotein AI(Apo AI) which can produce structures called fibrils that are shaped like strands and accumulate in blood vessels that may accelerate the development of atherosclerosis(8,9,10). Transthyretin(TTR) is a 55-KDa homotetramer with a dimer of dimmers configuration that is synthesized in the liver, choroid plexus and retinal pigment epithelium. Each monomer is a 127-residue polypeptide rich in beta sheet structure. It is a serum and cerebrospinal fluid carrier of the thyroid hormone, it transports thyroxine and retinol. Majority of transthyretin circulates as a part of 1:1 molar complex with retinol binding protein 4(RBP4) (11,12,13). Previous studies have produced mixed results concerning transthyretin levels in obesity. Some studies reported higher levels of serum transthyretin in obese subjects, while others have not detected any correlation (14,15). Unfortunately, the role of serum transthyretin levels especially in children and adolescents with overweight and obesity is not clear.

The aim of this study was to investigate the relationship between serum transthyretin and biochemical, anthropometric parameters in overweight and obese children of Indian population. To date, no published data are available on the serum transthyretin levels in Indian children and adolescents.

Materials and Methods:

The entire work was conducted in 296 school going children with in the age groups of 10-17 years from different schools in Chennai and Jabalpur were enrolled as study participants. Informed written consent from the parents and children were obtained before the start of the study. A detailed questionnaire regarding medical history of the parents and children were recorded. This study was approved by institutional ethics committee. Overweight and obese children were included. Children with secondary causes of obesity, insulin dependent diabetes mellitus and insulin independent diabetes mellitus and children with relevant drug treatment were excluded. Anthropometric measurements such as height, weight, body mass index (BMI) and waist to hip ratio (WHR) were recorded. Weight was measured using a beam balance to the nearest centimeter using a tape stuck to the wall. Abdominal girth

was measured at the level of umbilicus with the subject relaxed and in a standing posture. Hip girth was measured at the widest point of the hips at the level of the greater tronchanter with the patient standing with the both feet together. Waist to hip ratio was calculated from these measurements. Children with >85th percentile for age and gender were considered as overweight and children with >95th percentile for age and gender were considered as obese by using centers for disease control and prevention growth charts. Blood pressure levels were also recorded for all children using mercury sphygmomanometer.

12 hours fasting venous blood samples were collected from all the children, serum separated and the samples were stored at -20^{0}c until analysis. Serum transthyretin , Lp(a), Apo AI and Apo B levels were measured by immuno turbidimetric method (Spin React, Spain). 12 hours fasting venous blood samples were collected from all the children, serum separated and the samples were stored at -20^{0}c until analysis.

Statistical analysis:

Statistical analysis of the data was carried out using SPSS package 9.0. Results are expressed as Mean ± SD and p value of < 0.05 was considered to be statistically significant. Data of significance among the groups were analysed by one way ANOVA and Bonferroni comparison. Correlation analysis was done by Pearson's correlation at 5% level of significance. Since some of the parameters are slightly skewed, we have applied logarithmic transformations for all statistical analysis.

Results:

The present study examined 296 subjects (103 control, 96 obese and 97 overweight children and adolescents. The biochemical and anthropometric characteristics of study subjects are shown in table 1.

Table 1: Comparison between controls and overweight, obese children.

Parameter	Group I	Group II	Group III
Age	14.45±1.36	13.93±1.47	14.07±1.56
BMI(Kg/m^2)	18.04±2.14	24.09±1.42**	28.35±2.56**
WHR	0.85±0.09	0.99±0.13**	1.02±0.13**
SystolicB.P(mmHg)	117.57±5.51	120.52±7.13†	124.48±8.81**
DiastolicB.P(mmHg)	75.44±6.68	77.94±9.01 NS	76.56±9.04 NS
TC(mg/dl)	140.93±18.22	151.93±21.76**	164.19±22.05**
TG(mg/dl)	75.72±26.85	90±32.31†	103.26±36.18**
LDL-C(mg/dl)	87.93±12.27	90.70±12.28 NS	92.57±12.34 NS
HDL-C(mg/dl)	39.46±4.83	38.99±4.03 NS	38.36±3.46 NS
Fasting glucose(mg/dl)	87.83±6.55	81.98±6.16**	80.97±6.5**
Transthyretin(mg/dl)	25.4 ± 3.2	25.0 ± 3.7 NS	24.7± 3.1 NS
Apo AI	153.1±17.9	130.9±9.2**	132.3±10.8**
Apo B	73.5±12.0	88.5±11.4**	82.6±12.6**
Lp(a)	16.1 ± 5.7	23.5 ± 4.8*	20.0 ± 5.1**

**P<0.001; †P<0.05; NS-non - significant. < 0.05 (Control Vs Other Groups)
Group I – Healthy Children and Adolescents
Group II – Overweight Children and Adolescents
Group III – Obese Children and Adolescents

On further comparison between boys and girls, no marginal differences of serum transthyretin levels were observed between boys and girls. The mean levels of serum transthyretin in boys and girls of different groups are summarized in table 2.

Table 2: Mean levels of Transthyretin in boys and girls of different groups

	Group I N = 103		Group II N= 96		Group III N = 97	
	Boys (55)	Girls (48)	Boys (54)	Girls (42)	Boys (47)	Girls (50)
Transthyretin (mg/dl)	25.5±3.2	25.3±3.3	25.4±4.2 NS	24.5±3.0 NS	25.1±3.3 NS	24.3±2.8 NS

**P<0.001; †P<0.05; NS-non - significant. < 0.05 (Control Vs Other Groups)
Group I – Healthy Children and Adolescents
Group II – Overweight Children and Adolescents
Group III – Obese Children and Adolescents

Among the overweight and obese children and adolescents the parental history of obesity, hypertension, diabetes and heart diseases was 56%, 35%,33% and 8.5% respectively.

The relationship between serum transthyretin and Apo AI , Apo B and Lp(a) for all the subjects are shown in table 3.

Table 3: Pearson's correlation analysis between Serum serum transthyretin and Apo AI , Apo B and Lp(a) of the study subjects.

	Overall (296) rho	pvalue	Boys (156) rho	pvalue	Girls (140) rho	pvalue
Apo AI	0.1068	0.049	0.10	0.19	0.14	0.07
Apo B	0.0517	0.343	0.04	0.56	0.44	0.58
Lp(a)	0.0715	0.189	0.11	0.13	0.02	0.74

Discussion:

Obesity is a chronic and non communicable disease affects both young and old equally. There is now evidence from many studies that, the overall prevalence of overweight among the urban adolescents was 10 times higher than that of rural counter parts. Socioeconomic background is increasing rapidly in India leads to changes in diet pattern, decreased physical activity due to improved transportation leads to more prevalence of overweight and obesity especially in high socioeconomic background population (16). Infact data from animal experiments suggest, elevated transthyretin concentrations may play a role in maintaining the very high RBP4 concentrations observed in ob/ob mice (17). The focus of the paper is to dissect the relationship between serum transthyretin and other

biochemical, anthropometric parameters in obese and overweight children.

Data reported in the present study shows no marginal differences of transthyretin levels between the groups. Similar to our findings, earlier studies also stated that transthyretin levels are not affected by obesity and may play a permissive role in the regulation of RBP4 (15). However, some studies have not supported these findings (9,18).

On further comparison between boys and girls, no marginal differences of transthyretin were observed between boys and girls. The results of our study strongly suggest that transthyretin levels are not altered by hormonal changes.

In the present study we observed significantly elevated BMI,WHR in both obese and overweight children and adolescents than controls, this is natural as per the diagnostic criteria.

Our previous studies shows significantly elevated Apo B and Lp(a) levels in both obese and overweight children adolescents on comparison with the controls. We also observed decreased Apo AI levels in both obese and overweight children and adolescents on comparison with the controls. Our observations strongly suggest that atherosclerotic process begins very early in life and although clinical manifestations of cardiovascular diseases do not usually emerge until middle age and our data agree with those reported by others (19,20,21). Here we also observed elevated serum TC, TG, LDL-c and systolic blood pressure in obese and overweight children and adolescent. On the other hand, serum glucose, HDL-c and diastolic blood pressure levels are decreased. It is generally believed that childhood obesity is associated with dyslipidemia, hypertension in obese children may occur due to increased intravascular volume, sodium retention and hyperinsulinemia(22,23). Additionally in this study we also observed no significant correlation between serum transthyretin levels and Apo B, Apo AI and Lp(a) levels. Current data suggest that transthyretin levels were not affected by overweight and obesity related inflammation.

Conclusion:

The present data confirms no marginal differences of serum transthyretin levels between the groups and also no significant association between serum transthyretin and Apo B, Apo AI and Lp(a) levels. Our findings reinforce the notion that, transthyretin levels are not affected by obesity related inflammation and may play a permissive role in the regulation of RBP4. Furthermore, future research should endeavour to build upon the findings of this study.

References:

1. Barness LA, Opitz J, Gilbert-Barness E.Obesity: Genetic, Molecular, and Environmental Aspects. American Journal of Medical Genetics. 2007; 143A (24):3016-34.
2. Supreet Kaur, Umesh Kapil and Preeti Singh. Pattern of chronic diseases amongst adolescent obese children in developing countries. Current Science.2005; 88(7):1052-56.
3. Krassas GE, Tzotzas T. Do obese children become obese adults: childhood predictors of adult disease. Pediatr Endocrinol Rev. 2004;3:455-9.
4. David S. Freedman, William H. Dietz, Sathanur R. Srinivasan, and Gerald S. Berenson. The Relation of Overweight to Cardiovascular Risk Factors Among Children and Adolescents: The Bogalusa Heart Study. Pediatrics. 1999;103(6):1175-82.
5. Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. N Engl J Med. 2005; 352(16):1685-95.
6. Daniel J Hoffman, Zimian Wang, Dympna Gallagher, Steven B Heymsfield. Comparison of Visceral Adipose Tissue Mass in Adult African Americans and Whites. Obesity research. 2005;13(1):66-74.
7. Yoshihide Asato, Keisuke Katsuren, Tadashi Ohshiro, Kazuhide Kikawa. Relationship Between Lipid Abnormalities and Insulin Resistance in Japanese School Children. Arteriosclerosis Thrombosis and Vascular Biology.2006;26(12):2781-6.
8. William C.Nichols, Richard E.Gregg H, Bryan Brewer Jr, Merrill D.Benson. A mutation in apolipoprotein A-I in the Iowa type of familial amyloidotic polyneuropathy. Genomics. 1990;8(2): 318-23.
9. Liz MA, Faro CJ, Saraiva MJ, Sousa MM. Transthyretin, a new cryptic protease. J Biol Chem. 2004;279(20):21431-8.
10. Tanaka Y, Ando Y, Kumamoto T, Miyazaki A, Nakamura M, Nakayama M, Araki S, Ando M. Changed affinity of apolipoprotein AII to high density lipoprotein (HDL) in patients with familial amyloidotic polyneuropathy (FAP) type I. Biochim Biophys Acta. 1994;1225(3):311-6.
11. Goodman DS.Plasma retinol-binding protein. In: Sporn MB, Roberts AB, Goodman DS (eds) The retinoids. 1984;2:41–88.
12. Monaco, H., Menico, R., and Alessandro, C.. Structure of a Complex of Two Plasma Proteins. Science.1995; 268: 1039-41.
13. Soprano DR, Blaner WS: Plasma retinol-binding protein. The Retinoids: Biology, Chemistry and Medicine. 2nd edit. Raven Press Ltd., New York, 1994, pp 257-281.
14. Kloting N, Graham TE, Berndt J, Kralisch S, Kovacs P, Wason CJ, Fasshauer M, Schon MR, Stumvoll M, Blüher M, Kahn BB. Serum retinol-binding protein is more highly expressed in visceral than in subcutaneous adipose tissue and is a marker of intra-abdominal fat mass. Cell Metab. 2007;6(1):79-87.
15. Astride Altomare, Timothy E Graham, Barbara B Kahn, Donald George, Vicky Funanage and Prabhakaran Balagopal. Serum Transthyretin (TTR) In Obese Children And Relationship To Serum Retinol Binding Protein (RBP4) And Inflammation After Lifestyle Changes That Improve Insulin Sensitivity - A Randomized Controlledintervention. Circulation. 2007;116:16-18.
16. Ramachandran A. Diabetes & Obesity- The Indian Angle. Indian J Med Res 2004;120(5):437-9.
17. Van Bennekum AM, Wei S, Gamble MV, Vogel S, Piantedosi R, Gottesman M, Episkopou V, Blaner WS. Biochemical basis for depressed serum retinol levels in transthyretin-deficient mice. J Biol Chem. 2001;276(2):1107-13.
18. Kunitake ST, Chen GC, Kung SF, Schilling JW, Hardman DA, Kane JP. Pre-beta high density lipoprotein. Unique disposition of apolipoprotein A-I increases susceptibility to proteolysis. Arteriosclerosis. 1990;10(1):25-30.
19. Srinivasa Nageswara Rao G.,Prema Gurumurthy,Priya Gururajan,Saibabu R.,Kirthivasan V.,K. M. Cherian. Clinical and Biochemical Parameters in Relation to Serum Lp(a) Levels in Indian Children and Adolescent. Int J Pharm Bio Sci. 2010;1(2) 1-11.

20. Srinivasa Nageswara Rao.G, Prema Gurumurthy And Sruti.E. Role Of Serum Apolipoprotein Levels In Indian Children And Adolescents. Int J Pharm Bio Sci .2013;4(1):387-94.

21. Barbara Glowinska, Miroslawa Urban,Alicja Koput,Marzena Galar. New atherosclerosis risk factors in obese, hypertensive and diabetic children and adolescents. Atherosclerosis.2003;167(2):275–86.

22. Laroia D, Sharma M, Diwedi V, Belapurkar KM, Mathur PS. Profile of blood pressure in normal school children. Indian Pediatr. 1989;26(6):531-6.

23. Chu NF, Makowski L, Chang JB, Wang DJ, Liou SH, Shieh SM. Lipoprotein profiles, not anthropometric measures, correlate with serum lipoprotein(a) values in children: the Taipei children heart study. Eur J Epidemiol. 2000;16(1):5-12