

# **FREQUENCY OF DYSLIPIDEMIAS IN 6-12 YEARS OLD PAKISTANI CHILDREN: A CROSS-SECTIONAL STUDY**

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## **Body**

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### **ABSTRACT**

**OBJECTIVES:** To estimate the frequency of dyslipidemias in 6-12 years old Pakistani children attending pediatric clinic.

**METHODS:** This cross-sectional study was conducted at private clinic Peshawar, Pakistan after parental consent, on 85 (42 male, 43 female) children, with age ranging 6-12 years. Measurement of height, weight, waist circumference, body mass index (BMI), blood pressure, fasting lipid profile and fasting blood glucose (FBG) were recorded. Children with diabetes, renal or lipid disorders and their sibs, and those using metabolic profile altering medications were excluded from study.

**RESULTS:** About 18% of the participants were either obese (n=8, 9.5%) or overweight (n=7, 8.3%). In male children, mean BMI was  $15.0 \pm 2.6$  and  $18.1 \pm 4.9$  for 6-8 years and 9-12 years age respectively. In female children, mean BMI was  $14.9 \pm 1.1$  and  $17.8 \pm 3.5$  for 6-8 years and 9-12 years age respectively. Mean FBG was  $4.5 \pm 0.5$  mmol/L. Total cholesterol (mmol/L) was  $3.98 \pm .79$  and  $4.20 \pm .46$  for males and females of 6-8 years age and  $4.27 \pm .48$  and  $4.22 \pm .54$  for males and females of 9-12 years age respectively. Similarly, low density lipoprotein cholesterol (mmol/L) was  $2.27 \pm .51$  and  $2.53 \pm .46$  for males and females of 6-8 years age and  $2.53 \pm .50$  and  $2.45 \pm .49$  for males and females of 9-12 years age respectively. Eighty-nine percent of children had at least one lipid abnormality. The most prevalent lipid abnormality was low levels of high density lipoprotein cholesterol (HDL-c), borderline low or low in 75% (95% CI: 64-84).

**CONCLUSION:** Low level of HDL-c is the most prevalent lipid abnormality in 6-12 years old Pakistani children.

**KEY WORDS:** Cardiovascular disease (MeSH), dyslipidemia (MeSH), cholesterol (MeSH), Cholesterol, HDL (MeSH), Cholesterol, LDL (MeSH), triglycerides (MeSH), cardiometabolic risk, lifestyle (MeSH).

### **INTRODUCTION**

Cardiovascular diseases are the leading causes of morbidity and mortality all over the world.<sup>1</sup> Previously prevalent among relatively affluent societies, these disorders are now observed to be declining in most high income countries, while rapidly increasing in many middle and low income societies.<sup>2</sup>

In 1990, 35% of the 14 million deaths from cardiovascular diseases in the world were reported to be from high-income countries while by 2020, only 24% of the projected 25 million of such deaths are expected to be from the rich countries, the remaining 76% being from middle and low-income ones.<sup>2</sup>

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These shifting proportions of the burden of cardiovascular disease are observed along with a general epidemiological transition of burden of disease from predominantly communicable to non-communicable diseases (NCDs), which has been observed globally, in parallel with social change and economic development.<sup>3</sup> In the Eastern Mediterranean region, the burden of disease from NCDs is projected to rise from 46% in 2004 to 60% by the year 2020, with the prevalence of Dyslipidemia reported as high as 50% in parts of the region.<sup>4</sup>

According to 2004 estimates, 50% of Disability Adjusted Life Years in Pakistan were from NCDs, a quarter of which were due to Cardiovascular Disease, of which, Ischemic Heart Disease constituted more than 50%.<sup>5</sup> With the projected increase of the burden of NCDs, these figures are expected to rise.

The modifiable risk factors for cardiovascular risk i.e. atherogenic dyslipidemia,<sup>6</sup> dysglycemia, and high resting systolic blood pressure,<sup>7</sup> have been reported to originate in childhood<sup>8-15</sup> and early adulthood.<sup>16</sup> Addressing the pandemic of cardiometabolic risk<sup>17</sup> in adult populations will require preventive efforts aimed at upstream risks in pediatric age groups. In order to develop any effective preventive strategies in this respect, recent information about the prevalence of these risk factors in the relevant populations is necessary. The only two studies aimed at estimating the prevalence of dyslipidemias among children in Pakistan, both done at Karachi, are two decades old.<sup>18,19</sup>

Routine screening for Dyslipidemia in children has been controversial,<sup>20-23</sup> and although the 2011 guidelines from the Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents<sup>24</sup> do recommend universal screening for dyslipidemia in children with a non-fasting, non-HDL-C at 10 years of age, such screening may not be feasible for Pakistan, still placed in the lower half of the world ranking of projected gross domestic product.<sup>25</sup>

Insights into the magnitude and socio-demographic correlates of dyslipidemia can be very helpful in identifying clients with higher vulnerabilities to cardiometabolic risk in our community, where the prevalence of the metabolic syndrome has been reported as high as 16%.<sup>26</sup>

The objective of this study was estimating the prevalence of Dyslipidemias among school-age Pakistani children aimed at detecting the most prevalent form of lipid abnormalities in this population.

### METHODS

#### Sample:

The sample was taken from among the healthy school-age children of parents visiting the primary author's clinic. Based on the assumption of randomness regarding clinic visits,<sup>27</sup> all attending parents were requested to allow their healthy school age children to participate in the study. Not only the enrolled children were offered free examination but three free consultations at any time after enrolment were also offered to the family as an incentive. Children with known diabetes, renal and lipid disorders or those with such disorders among their sibs, as well as those using any metabolic profile altering medications were excluded. Data were collected over a period of 10 months in 2011-12 for 85 children ranging in age from 6 to 12 years.

#### Data Collection and Measurement Process:

Parents who agreed to participate used to bring their school age children to the clinic, any day they chose. The children, after a general physical examination, underwent standardized height, weight, waist circumference, and blood pressure measurements; and Information about their food habits and lifestyle was collected by interviewing the children along with their parents. Waist circumference of the children was measured in standing position, at a point midway between the lowest ribs laterally and the iliac crest. The information was reviewed and ambiguities clarified and corrections were made before the participants would leave the clinic.

Investigation requests were given to the parents without recommending any single laboratory, based on the assumption that lipid testing procedures are fairly uniform across the all major laboratories in the area.

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Early morning fasting blood glucose (FBG), and fasting lipid profile i.e. total cholesterol, low density lipoprotein cholesterol (LDL-c), high density lipoprotein cholesterol (HDL-c) and triglycerides, were recommended, as the child was almost fasting overnight.

### Sample Size:

With the prevalence of dyslipidemia in Pakistani children estimated to be 25%,<sup>18,19</sup> in order to estimate the population proportion within 10 percentage points of the true population proportion, a sample size of 73 would be required for a confidence level of 95%.<sup>28</sup>

### Data Entry

Data were entered in the computer using Epidata software.<sup>29</sup> For statistical analysis, R version 2.1.330, and Stata version 8.231 software programs have been used.

### Statistical Analysis:

Means $\pm$ standard deviations are reported as summary measures. Proportions are reported as percentages.

Confidence intervals for proportions are based on normal approximation of binomial distribution. All tests of significance are two-tailed and a significance level of 0.05 has been used.

### Definitions of Cutoff Points:

The cutoff points used for various categories of lipids are from the National Cholesterol Education Program (NCEP) Expert Panel on Cholesterol Levels in Children.<sup>24</sup>

## RESULTS

Out of 85 children, 42 (49%) were male while 43 (51%) were female, with age ranging 6 to 12 years. None of the morphometric measures differed significantly between the two genders (Table I).

A total of 46 (54.1%) children had either systolic or diastolic blood pressure above 90th percentile for age and gender (95% CI: 43.0-65.0), considered a cardiometabolic risk by most definitions of Metabolic Syndrome in Children.<sup>32-37</sup>

Mean FBG for the participants was  $4.5\pm 0.5$  mmol/L. Three children (3.5%; 95% CI: 0.7 - 10%) had FBG  $\geq 5.6$  mmol/L or more, considered a cardiometabolic risk factor by International Diabetes Federation definition of Metabolic Syndrome (Table II).

In male children, mean BMI was  $15.0\pm 2.6$  and  $18.1\pm 4.9$  for 6-8 years and 9-12 years age respectively. In female children, mean BMI was  $14.9\pm 1.1$  and  $17.8\pm 3.5$  for 6-8 years and 9-12 years age respectively (Table 1). About 18% of the participants were either obese (8, 9.5%) or overweight (7, 8.3%) according to the latest definition of cutoff points, Overweight: Body Mass Index (BMI) for age between the 85th and 95th percentile and obesity for BMI-for-age at or above the 95th percentile.<sup>38</sup>

Twenty six (31%) of these children had their waist circumference above 75th percentile for age and gender (95% CI: 21.0 - 41.5%).

TABLE I: ANTHROPOMETRIC CHARACTERISTICS OF THE PARTICIPANTS BY AGE AND GENDER (MEAN  $\pm$ SD, RANGE)

Parameters		Male			
Female					
Age		6-8 years n = 19		9-12 years n = 23	
20	9-12 years n = 23				6-8 years n =
Height (cm)		124.2 $\pm$ 7.1	107-132	138.7 $\pm$ 8.5	129-159
135	140.0 $\pm$ 9.2	124-156			123.4 $\pm$ 4.8
					118-

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Weight (kg)	23.2±5.0 16-38	35.3±12.0 22-62	22.6±2.1 19-26
35.4±9.7 22-60			
Body Mass Index	15.0±2.6 9.8-22.5	18.1±4.9 13.2-29.9	14.9±1.1 13.2-
17.1 17.8±3.5 12.8-28.5			
Waist Circumference (cm)	56.2±6.9 47-77	64.9±12.5 48-95	59.6±3.7 53-68
66.7±9.1 50-89			
Hip Circumference (cm)	63.6±6.3 54-82	74.9±11.4 62-105	67.2±4.3 59-79
77.6±8.1 64-99			
Waist-Hip Ratio	.88±.06 .79-1.0	.86±.01 .76-.98	.89±.04 .80-.97
.86±.06 .75-.96			
Waist-Height Ratio	.45±.05 .39-.59	.47±.08 .37-.66	.48±.03 .44-.53
.48±.05 .36-.61			

TABLE II: SUMMARY OF BIOCHEMICAL PROFILE FOR THE PARTICIPANTS BY AGE AND GENDER (MEAN±SD, RANGE)

Parameters		6-8 years			
9-12 years					
		Male n = 19	Female n = 23	Male n =	
20	Female n = 23				
Total Cholesterol	Mean±SD	3.98±.79	4.20±.46	4.27±.48	
4.22±.54					
(mmol/L)	Range	1.28-4.96	3.45-4.94	3.10-5.19	
3.39-5.33					
LDL-c (mmol/L)	Mean±SD	2.27±.51	2.53±.46	2.53±.50	
2.45±.49					
	Range	.79-3.14	1.85-3.37	1.44-3.50	
1.68-3.41					
HDL-c (mmol/L)	Mean±SD	1.42±.38	1.40±.22	1.38±.35	
1.38±.26					
	Range	.41-2.12	1.08-1.85	.85-2.11	
.99-1.89					
Triglycerides	Mean±SD	.55±.21	.65±.19	.73±.38	
.75±.21					
(mmol/L)	Range	.21-.95	.34-1.04	.33-1.79	
.32-1.19					
Fasting Blood Glucose (mmol/L)	Mean±SD	4.46±.74	4.22±.28	4.71±.39	
4.57±.45					
	Range	2.5-5.9	3.7-4.7	3.9-6.0	
4.0-6.1					

TABLE III: SUMMARY OF LIPIDS STATUS FOR THE PARTICIPANTS BY AGE AND GENDER; PROPORTIONS (%) AND 95% CONFIDENCE INTERVALS\*

Parameters		6-8 years			
9-12 years					
		Male n = 19	Female n = 23	Male n =	
20	Female n = 23				
Total Cholesterol	Acceptable	68.4 (43.4-87.4)	70.0 (45.7-88.1)	60.9	
(38.5-80.3)	63.6 (40.6-82.8)				
(mmol/L)	Borderline High	31.6 (12.6-56.6)	30.0 (11.9-54.3)	34.8	
(16.4-57.3)	31.8 (13.9-54.9)				
	High	--	--	4.3 (0.1-	
21.9)	4.6 (0.1-22.8)				
LDL-c (mmol/L)	Acceptable	89.5 (66.8-98.7)	75.0 (50.9-91.3)	73.9	
(51.6-89.8)	81.8 (59.7-94.8)				
	Borderline High	10.5 (1.3-13.1)	20.0 (5.7-43.7)	17.4 (4.9-	
38.8)	13.6 (2.9-34.9)				
	High	--	5.0 (0.1-24.8)	8.7 (1.1-	
28.0)	4.6 (0.1-22.8)				
HDL-c (mmol/L)	Acceptable	31.6 (12.6-56.6)	25.0 (8.6-49.1)	26.1	
(10.2-48.4)	18.2 (5.2-40.3)				
	Borderline Low	47.4 (24.4-71.1)	60.0 (36.0-80.9)	43.5	
(23.2-65.5)	54.6 (32.2-75.6)				

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	Low	21.0 (6.0-45.6)	15.0 (3.2-37.9)	30.4
(13.2-52.2)	27.2 (10.7-50.2)			
Triglycerides	Acceptable	89.5 (66.9-98.7)	80.0 (56.3-94.3)	73.9
(51.6-89.8)	81.8 (59.7-94.8)			
(mmol/L)	Borderline High	10.5 (1.3-33.1)	20.0 (5.7-43.7)	21.7 (7.4-
43.7)	18.2 (5.1-40.3)			
	High	--	--	4.4 (0.1-
21.9)	--			

TABLE IV: OVERALL SUMMARY OF ABNORMAL LIPIDS STATUS FOR THE PARTICIPANTS\*

Lipid Category	Adverse Category (Borderline/ High or Low) n (%)	95% Confidence Intervals
HDL-c (mmol/L)	63 (75.0)	64.4 - 83.8
Total Cholesterol (mmol/L)	29 (34.5)	24.5 - 45.7
LDL-c (mmol/L)	17 (20.2)	12.2 - 30.4
Triglycerides (mmol/L)	16 (19.0)	11.3 - 29.1

Cutoff values for the various categories of Lipids were based on the United States National Cholesterol Education Program (NCEP) Expert Panel on Cholesterol Levels in Children.<sup>24</sup> Total cholesterol (mmol/L) was  $3.98 \pm .79$  and  $4.20 \pm .46$  for males and females of 6-8 years age and  $4.27 \pm .48$  and  $4.22 \pm .54$  for males and females of 9-12 years age respectively (Table II). Similarly, low density lipoprotein cholesterol (mmol/L) was  $2.27 \pm .51$  and  $2.53 \pm .46$  for males and females of 6-8 years age and  $2.53 \pm .50$  and  $2.45 \pm .49$  for males and females of 9-12 years age respectively.

More than 89% of these children had at least one lipid abnormality, the most common being abnormal HDL-c, found in 63 (75%, 95% CI: 64.4-83.8). Among these, the Borderline Low category was the one more prevalent, comprising 65 (77%, 95% CI: 67-86) of the children from this sample (Table III).

The other lipid abnormalities in descending order of prevalence were those of total cholesterol HDL-c, and triglycerides (Table IV).

No statistically significant difference was found between genders regarding any of the lipid categories.

## DISCUSSION

Our main finding is that 89% of these children carried at least one lipid abnormality i.e. borderline or high / low levels. The most prevalent (75%) of these disorders was low HDL-c, reported to be similar in physicochemical characteristics to that related to adult coronary heart disease albeit more susceptible to intervention.<sup>39</sup> The fact that lifestyle interventions are effective in this situation is quite encouraging as most of these children with low HDL-c are in the borderline high category.

Badrudin et al<sup>18,19</sup> reported higher mean levels of TC, LDL-c, and HDL-c among girls; we have found the gender differences regarding lipid abnormalities to be non-significant. They reported 33% of girls and 22% of boys to be in the borderline high or high categories regarding total cholesterol, our figures are 33% and 36% respectively, statistically non-significant albeit higher among boys. Both these studies included children 5-19 years of age, so we cannot make direct comparisons but lipid abnormalities may differ in various cultural subgroups based on the differences in lifestyles as well as socio-economic factors.

While 20% of the U.S. children have been reported to be in the adverse category of total cholesterol, LDL-c or HDL-c,<sup>40</sup> we had almost 30% of children in our sample (29.8%, 95%CI: 20.1-40.7) belonging to this category.

The finding of low HDL-c being the most prevalent anomaly among these children may be an indicator of the lifestyle issues in this population. These children, being from relatively affluent families, may not be representative of the general population but still this finding requires clinicians' attention not only for further confirmatory studies but also for interventional initiatives.

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Emergence of low HDL-c as a prominent lipid abnormality has been an unexpected finding in this study. As this abnormality is known to be related to sedentary lifestyle,<sup>41,42</sup> the study has brought to the forefront the need for incorporating preventive initiatives in the clinical practice of pediatrics.

A broad, multifaceted and multipronged concerted effort is required to address this emerging threat. Health education for the society in general, social dialogue regarding lifestyles, relevant adjustments in the education system and policy decisions in many different areas of the existing socioeconomic structures is required through a collaborative effort of professionals in the relevant fields.

It is important to note that 48 (77%; 65-87%) of the children with low HDL-c were not obese or even overweight and without any apparent indications of a metabolic problem of potentially serious long term health consequences. Almost 35% of these dyslipidemic children had waist circumference above 75th percentile. The fact highlights the importance of assessing measures of cardiometabolic risk other than weight, height or BMI. The non-obese child is the least likely to be screened for cardiometabolic risk or lipid disorders. Nothing in his physique or appearance will induce anyone, even his physician, to extend to him any help in this respect.

These silent victims of a demon running in their young blood, consuming them from within, need and deserve the attention of healthcare planners, clinicians and the decision makers.

### LIMITATIONS

The sample was chosen from among the families that visited the author's private clinic. Generally, these families are relatively affluent and the findings cannot be generalized to general population.

Higher values of blood pressure reported here may be the result of the measurement process / environment but children with abnormal metabolic profiles may be prone to exhibit abnormal adrenergic responses and further studies are needed to clarify this.

### CONCLUSION

This study has provided estimates of frequency of dyslipidemias in 6-12 years old Pakistani children attending a pediatric clinic. Dyslipidemia is very common in these children and 89% of children had at least one lipid abnormality. Low level of HDL-c is the most prevalent lipid abnormality in this population. About 18% of the participants were either obese or overweight. The fact that the dyslipidemic profile of our school age children is suggestive of lifestyle issues has highlighted the need for addressing this issue through multi-sector efforts. Pediatricians need to work with public health professionals, healthcare planners and decision makers to initiate public awareness and health education. Political involvement needs to be generated in order to make selective screening facilities available for an average Pakistani child. There is also a need for further, larger, population based studies to document the true prevalence and patterns of dyslipidemia in Pakistani children.

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