Sex, Ethnicity, and Socioeconomic Status Affect Israeli Pediatric Lipid Testing Despite Equality in National Healthcare Services

Hagar Interator MSc RD[1,2,3]*, Avivit Brener MD[1,2]*, Moshe Hoshen PhD[4], Inbar Safra MD[1], Ran Balicer MD PhD MPH[4], Moshe Leshno MD PhD[1], Raanan Shamir MD[1,5] and Yael Lebenthal MD[1,2]

[1]Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
[2]Pediatric Endocrine and Diabetes Unit, Dana–Dwek Children's Hospital, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel
[3]Nutrition and Dietetics Unit, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel
[4]Health Planning and Policy Wing, Clalit Health Services, Tel Aviv, Israel
[5]Institute of Gastroenterology, Nutrition, and Liver Diseases, Schneider Children's Medical Center of Israel, Petah Tikva, Israel

ABSTRACT: **Background:** In Israel, coronary heart disease mortality rates are significantly higher among the Arab population than the Jewish population. Dyslipidemia prevention should begin in childhood.
Objectives: To identify sociodemographic disparities in the preventive health measurement of lipid profile testing and lipoprotein levels among Israeli children and adolescents.
Methods: A cross-sectional analysis of 1.2 million children and adolescents insured by Clalit Health Services between 2007 and 2011 was conducted using sociodemographic data and serum lipid concentrations.
Results: Overall, 10.1% individuals had undergone lipid testing. Those with male sex (odds ratio [OR] = 0.813, 95% confidence interval [95%CI] 0.809–0.816), Arab ethnicity (OR = 0.952, 95%CI 0.941–0.963), and low socioeconomic status (SES) (OR = 0.740, 95%CI 0.728–0.752) were less likely to be tested. By 2010, differences among economic sectors narrowed and Arab children were more likely to be tested (OR = 1.039, 95%CI 1.035–1.044). Girls had higher total cholesterol, triglyceride, low-density lipoprotein-cholesterol, and non-high-density lipoprotein-cholesterol levels compared to boys ($P < 0.001$). Jewish children had higher cholesterol and low-density and high-density lipoprotein-cholesterol, as well as lower triglyceride levels than Arabs ($P < 0.001$). Children with low SES had lower cholesterol, low-density and high-density lipoprotein-cholesterol, and non-high-density lipoprotein-cholesterol levels ($P < 0.001$).
Conclusions: We found that boys, Arab children, and those with low SES were less likely to be tested. Over time there was a gradual reduction in these disparities. Publicly sponsored healthcare services can diminish disparities in the provision of preventive health among diverse socioeconomic groups that comprise the national population.

IMAJ 2019; 21: 369–375

KEY WORDS: healthcare disparities, lipid profile testing, lipoprotein levels, socioeconomic status, pediatric healthcare

*The first and second authors contributed equally to this study

Coronary heart disease (CHD) is a major worldwide health concern. It is a multifactorial disease with its foundations in childhood [1], suggesting that primary prevention should ideally be targeted to children and adolescents [2,3]. In Israel, CHD mortality rates are significantly higher among the Arab population compared to the Jewish population [4,5]. Sociodemographic factors affect health outcomes on multiple levels and can interfere with prevention.

There are several reports on child healthcare disparities by sex, ethnicity, and socioeconomic status (SES) [6,7]. This disparity may stem from discrimination related to these sociodemographic factors. The extension of such discrimination to affect lipid profile testing will invariably influence the efficacy of targeted screening in detecting hyperlipidemia and providing early treatment. The effects on pediatric lipid screening may also reflect the effect of sociodemographic factors on other preventive healthcare measurements.

In Israel, healthcare service is mandated for all residents by the 1994 National Health Insurance Law [8]. However, a publicly funded healthcare system and free screening do not rule out potential disparities based on ethnic origin, sex, or socioeconomic factors [9]. In the present study, we examined whether there are sociodemographic disparities in lipid profile testing in the Israeli pediatric population.

PATIENTS AND METHODS

COMPUTERIZED DATABASE AT CLALIT HEALTH SERVICES

This cross-sectional study was based on the computerized database of the Clalit Health Services for 2007–2011. Clalit Health Services is the largest health maintenance organization (HMO) in Israel and the second largest worldwide. It serves 54% of the entire population of Israel, which is composed of two main ethnic groups (Jews and Arabs). The HMO supplied healthcare to approximately 1.2 million children and adolescents each study year. Its database is a comprehensive state-of-the-art computerized data warehouse

that aggregates most of the data on medical services used by members of Clalit Health Services. It can be queried and linked down to the level of an individual member. Data are aggregated by continuous real-time input from physicians and health service providers. In addition to diagnoses, the data include anthropometric measurements (weight and height measured during clinic visits), laboratory records, and pharmaceutical information. The diagnoses of chronic diseases in the HMO's database are validated by systematic methodology based on the diagnosis by the primary care physician, chronic medication use, laboratory results, hospitalization diagnosis, and malignancy registry.

Sociodemographic data of all children and adolescents younger than 19 years of age who were insured by Clalit Health Services were extracted from the database. Lipid profile analysis was performed on insured children and adolescents aged 2–17 years who had at least one measurement of their lipid status as well as records of their weight and height between 2007–2011. Additional retrieved information included diagnosis of chronic diseases and medication prescriptions as well as sociodemographic data and SES. The SES was categorized by the Clalit Health Services clinics as low, intermediate, or high according to geocoding techniques by linking the address of the primary care clinic serving the individual with the census area-level SES data, based on the ratings of Israel's Central Bureau of Statistics [10].

Excluded from the lipid profile analysis were children and adolescents with the following:

- Body mass index (BMI) > 85th percentile (overweight) or BMI < 5th percentile (underweight) according to U.S. Centers for Disease Control and Prevention growth charts, which were found adequate for assessing Israeli children [11]
- Hyperlipidemia and lipid-lowering medications
- Chronic disease including diabetes and thyroid disease (hyperthyroidism/ hypothyroidism), gastrointestinal disease affecting absorption, liver disease, kidney disease, malignancies, metabolic disease
- Genetic syndromes
- Chronic medication use, including steroids, anti-tumor agents, Eltroxin
- Recorded death

This study was approved by the institutional ethics committee and the Clalit Health Services community ethics committee. Informed consent by the parents was waived because the subjects whose data were retrieved were not identified.

SERUM LIPIDS AND LIPOPROTEINS

The collected data also included a standard serum lipid profile: total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-C), triglycerides, low-density lipoprotein-cholesterol (LDL-C), and non-high-density lipoprotein-cholesterol (non-HDL-C, after 2008). Biochemical analyses were performed on fresh samples of blood at Clalit Health Services laboratories with routine standardized methodologies. Serum measurements of TC, HDL-C, and triglycerides were performed by enzymatic spectrophotometry on an Olympus autoanalyzer AU640 and AU680 (Olympus Diagnostics, MA, USA). LDL-C was calculated using the Friedewald equation. Non-HDL-C concentration was computed as TC minus HDL-C. The Clalit Health Services laboratories are authorized to perform tests according to the international quality standard ISO 9001, and quality control is periodically assessed.

STATISTICAL ANALYSES

Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, Windows version 23 (SPSS, IBM Corp, Armonk, NY, USA). Descriptive statistics (means, standard deviations) were analyzed to summarize the following parameters: number of subjects tested in each age group, sex and ethnic distribution, TC, LDL-C, HDL-C, non-HDL-C, and triglycerides. The one-sample Kolmogorov–Smirnov test and histograms were used to test the null hypothesis that each of the continuous variables has a normal distribution. Variables with skewed distribution were log-transformed. Outliers of lipid values were excluded if the distance from mean value was more than 3 standard deviations (above or below the mean). Only one lipid evaluation was used for each subject. The median was used in cases of more than one lipid evaluation in a single year, and the first year was selected in cases of lipid testing that had been carried out in two or more years.

A direct method of adjustment to a reference population was used according to BMI values. The BMI-structured reference population was an existing population of children aged < 19 years with documented BMI who were insured by the Clalit Health Services during 2009–2011. The independent samples *t*-test was used to assess differences in the levels of each of the serum lipoproteins level parameters (TC, LDL-C, HDL-C, non-HDL-C, and triglycerides) according to sex and ethnicity. One-way analysis of variance was used to assess differences between the levels of SES, and post-hoc analysis (Tukey HSD test) was performed if differences were found. A multivariate logistic regression model was used to test the association between lipid testing and sociodemographic factors (age, sex, ethnicity, and SES). A linear regression model was used with adjustment for age, sex, and BMI to test independent associations of TC, LDL-C, HDL-C, non-HDL-C and triglycerides, and sociodemographic factors. *P* values and 95% confidence intervals (CI) were calculated for the analyses.

RESULTS

The overall mean rate of lipid testing among Israeli children and adolescents insured by the Clalit Health Services in 2007–2011 was 10.1%. A total of 162,035 of these children and adolescents had both blood lipid levels and documented BMI assessments,

Table 1. Lipid testing rate among Israeli children and adolescents aged 0–18 years (Clalit Health Services 2007–2011)

Characteristic	2007	2008	2009	2010	2011
Lipid testing rate					
Overall	8.7 (101,328 / 1,167,040)	9.8 (115,441 / 1,174,462)	10.4 (122,980 / 1,180,973)	10.8 (129,000 / 1,199,115)	10.9 (133,927 / 1,228,489)
Sex					
Male	7.9 (47,318 / 597,521)	8.9 (53,443 / 601,103)	9.5 (57,439 / 604,796)	9.9 (60,517 / 613,691)	9.9 (62,740 / 628,650)
Female	9.5 (54,010 / 569,508)	10.8 (61,998 / 573,359)	11.4 (65,541 / 576,151)	11.7 (68483 / 585,407)	11.9 (71,187 / 599,813)
Ethnicity					
Jewish	9.3 (68,736 / 735,978)	10.3 (75,941 / 739,663)	10.6 (78,722 / 744597)	10.8 (81,814 / 757,360)	10.7 (83,191 / 776,243)
Arab	7.6 (32,592 / 431,062)	9.1 (39,500 / 434,799)	10.1 (44,258 / 436,376)	10.7 (47,186 / 441,755)	11.2 (50,736 / 452,246)
Socioeconomic status					
Low	7.8 (48,246 / 620,437)	8.9 (55,649 / 623,688)	9.8 (61,023 / 624,759)	10.2 (64391 / 631,006)	10.5 (67549 / 645,359)
Intermediate	9.6 (37,944 / 395,898)	10.8 (42,751 / 397,093)	11.2 (44,872 / 399,053)	11.4 (46,430 / 405,779)	11.4 (47,340 / 414,678)
High	10.4 (15,121 / 145,843)	11.4 (17,007 / 149,358)	11.1 (17,038 / 152,988)	11.4 (18,123 / 158,875)	11.5 (18,985 / 165,584)

Rate was calculated by dividing the number of subjects who underwent lipid testing per year by the total number of subjects insured by Clalit Health Services for each specific year and category

The lipid testing rate is the percent of subjects tested

and 152,820 of them fulfilled all of the inclusion criteria of this study. There were 9215 individuals (5.7%) who were excluded from the analysis due to chronic diseases and/or chronic usage of medications.

The distribution of serum lipoprotein testing performed according to BMI categories revealed that 65.7% (n=100,375) were healthy normal-weight children and adolescents, 17% (n=26,028) were overweight and 17.3% (n=26,417) were obese. The sociodemographic characteristics of the children and adolescents who underwent lipid evaluation are presented in Table 1.

The associations between sociodemographic factors and lipid testing in pooled data across all five study years are presented in Table 2. Older children were more likely to undergo lipid testing (odds ratio [OR] = 1.132, 95%CI 1.132–1.133). Less likely to undergo lipid testing were boys (OR = 0.813, 95%CI 0.809–0.816), children from the Arab sector (OR = 0.952, 95%CI 0.941–0.963), and children in low and intermediate SES vs. high SES (OR = 0.740, 95%CI 0.728–0.752; OR = 0.894, 95%CI 0.880–0.908, respectively). As years progressed, more children and adolescents were likely to undergo lipid testing (OR = 1.050, 95%CI 1.045–1.056). Subjects belonging to the Arab sector were also more likely to undergo lipid testing over time (OR = 1.039, 95%CI 1.035–1.044). In addition, low or intermediate SES children were relatively more likely to be tested over time (OR = 1.010, 95%CI 1.004–1.017 and OR = 1.007, 95%CI 1.001–1.013, respectively). The interaction between sex and year of testing was not significant.

The serum lipoproteins levels (TC, LDL-C, HDL-C, non-HDL-C, and triglycerides) according to sex and age for the entire sample of healthy, normal-weight Israeli children and adolescents are presented in Table 3 and Table 4.

ASSOCIATIONS BETWEEN SOCIODEMOGRAPHIC FACTORS AND LIPOPROTEIN LEVELS

Age was positively associated with TC ($\beta = 2.717$, $P < 0.001$), LDL-C ($\beta = 0.426$, $P < 0.001$), HDL-C levels ($\beta = 2.544$, $P < 0.001$), non-HDL-C levels ($\beta = 0.638$, $P < 0.001$), and triglycerides levels ($\beta = 0.782$, $P < 0.001$).

Male sex was positively associated with TC levels ($\beta = 1.087$, $P = 0.001$). TC levels in boys decreased by 0.664 mg/dl

Table 2. Binary logistic regression model for the association between sociodemographic factors and lipid testing (Clalit Health Services, 2007–2011)

	β	*P* value	Odds ratio	95% confidence interval	
				Lower	Upper
Constant	-3.303	< 0.001	0.037	0.036	0.037
Age	0.124	< 0.001	1.132	1.132	1.133
Sex (male)*	-0.207	< 0.001	0.813	0.809	0.816
Ethnicity (Arab)**	-0.049	< 0.001	0.952	0.941	0.963
Low SES***	-0.301	< 0.001	0.740	0.728	0.752
Intermediate SES***	-0.112	< 0.001	0.894	0.880	0.908
Year of test	0.049	< 0.001	1.050	1.045	1.056
Ethnicity (Arab)§ year of test	0.039	< 0.001	1.039	1.035	1.044
Low SES§ year of test	0.010	0.002	1.010	1.004	1.017
Intermediate SES§ year of test	0.007	0.028	1.007	1.001	1.013

*Girls comprised the reference group

**Jewish children comprised the reference group

***Children with a high SES comprised the reference group

§Independent variables were age, sex, ethnicity, SES, year of test, and first order interactions between independent variables

CHS = Clalit Health Services, SES = socioeconomic status, 95%CI = 95% confidence interval, OR = odds ratio

Table 3. Serum lipids among healthy, normal-weight Israeli children and adolescents by sex and age (Clalit Health Services 2007–2011)

Sex	Age, years	Total cholesterol (mg/dl)		LDL-C (mg/dl)		HDL-C (mg/dl)		non-HDL-C (mg/dl)		Triglycerides (mg/dl)	
		n	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)
Boys	2	829	144 (26)	545	86 (22)	555	41 (10)	356	105 (23)	734	91 (43)
	3	1267	148 (26)	865	89 (22)	896	44 (10)	570	105 (23)	1166	80 (38)
	4	1560	151 (25)	1066	89 (22)	1101	47 (11)	682	103 (22)	1439	72 (32)
	5	2531	154 (26)	1784	90 (22)	1826	50 (11)	1260	104 (23)	2347	70 (32)
	6	3374	154 (26)	2462	89 (22)	2510	51 (11)	1593	103 (23)	3129	68 (30)
	7	2622	154 (26)	1880	88 (21)	1929	53 (12)	1136	101 (23)	2441	66 (27)
	8	2043	157 (26)	1512	89 (20)	1553	55 (12)	972	102 (21)	1928	66 (28)
	9	1955	156 (26)	1462	87 (21)	1482	55 (12)	930	101 (22)	1845	66 (28)
	10	2078	157 (25)	1579	87 (20)	1602	56 (13)	976	100 (22)	1974	68 (31)
	11	2302	157 (25)	1778	89 (21)	1801	55 (12)	1115	104 (23)	2184	71 (31)
	12	2590	156 (26)	2044	87 (21)	2073	54 (12)	1262	101 (22)	2477	72 (32)
	13	3986	150 (26)	3114	84 (21)	3157	52 (12)	2055	99 (23)	3793	75 (35)
	14	4232	144 (25)	3384	80 (21)	3436	49 (11)	2201	95 (23)	4065	75 (32)
	15	4130	139 (24)	3320	77 (20)	3374	47 (10)	2096	92 (21)	4003	76 (33)
	16	4185	138 (24)	3396	77 (20)	3441	46 (10)	2105	93 (22)	4059	79 (34)
	17	5100	139 (25)	4197	78 (21)	4253	45 (9)	2454	94 (23)	4952	81 (36)
Girls	2	683	148 (28)	428	90 (24)	447	40 (10)	277	107 (26)	599	95 (46)
	3	954	152 (26)	663	91 (22)	686	43 (11)	419	108 (25)	886	84 (39)
	4	1212	154 (26)	855	93 (22)	875	46 (11)	561	108 (24)	1123	77 (33)
	5	2153	156 (27)	1510	93 (22)	1546	49 (11)	1076	108 (23)	2002	74 (31)
	6	3443	158 (26)	2493	93 (22)	2558	51 (11)	1638	107 (23)	3205	73 (30)
	7	2751	157 (26)	1969	91 (22)	2006	52 (12)	1226	106 (23)	2566	72 (29)
	8	2259	159 (26)	1672	91 (22)	1699	53 (12)	1083	106 (22)	2119	72 (29)
	9	2525	160 (27)	1910	92 (22)	1948	54 (12)	1160	106 (23)	2373	75 (31)
	10	2587	161 (27)	1963	92 (22)	1992	54 (12)	1210	107 (23)	2454	77 (32)
	11	2799	159 (26)	2196	89 (21)	2227	53 (12)	1359	106 (23)	2679	83 (36)
	12	3050	157 (26)	2464	88 (22)	2497	52 (11)	1499	105 (23)	2937	86 (37)
	13	5176	154 (25)	4134	86 (21)	4201	51 (11)	2827	104 (23)	4939	88 (38)
	14	5712	153 (25)	4615	85 (21)	4661	51 (11)	3020	102 (23)	5503	84 (34)
	15	6370	151 (25)	5189	85 (21)	5253	50 (10)	3195	101 (23)	6191	81 (33)
	16	6685	152 (26)	5516	85 (22)	5580	51 (11)	3296	101 (24)	6473	79 (32)
	17	6992	152 (26)	5817	85 (21)	5880	51 (11)	3261	101 (23)	6791	77 (31)

HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, SD = standard deviation

(β = -0.664, $P < 0.001$) for every 1-year increase in age. Levels were positively associated with HDL-C levels (β = 3.700, $P < 0.001$) and negatively associated with LDL-C levels (β = -0.994, $P = 0.002$), non-HDL-C levels (β = -3.224, $P < 0.001$), and triglycerides levels (β = -9.220, $P < 0.001$).

Jewish ethnicity was positively associated with TC levels (β = 5.263, $P < 0.001$), LDL-C levels (β = 3.796, $P < 0.001$), non-HDL-C levels (β = 3.876, P 0.001), and with triglycerides levels (β = 1.610, $P = 0.001$). These associations decreased as age increased (β = -0.253, $P < 0.001$), (β = -0.277, $P < 0.001$), (β = -0.333, $P < 0.001$), and (β = -0.290, $P < 0.001$), respectively. Jewish ethnicity was positively associated with HDL-C levels (β = 1.690, $P < 0.001$). The difference increased with age (β = 0.061, $P < 0.001$).

BMI was positively associated with TC levels (β = 1.699, $P < 0.001$). Associations with LDL-C levels (β = 1.262, $P < 0.001$), HDL-C levels (β = 0.405, $P < 0.001$), non-HDL-C levels (β = 1.825, $P < 0.001$), and triglycerides levels (β = 3.493, $P < 0.001$) decreased with age.

Lower SES was positively associated with higher TC levels (β = 2.652, $P < 0.001$). This difference decreased with age (β = -0.431, $P < 0.001$). A similar interaction was found between intermediate SES and age, but to a lesser extent (β = -0.174, $P < 0.001$). Intermediate SES was positively associated with higher LDL-C levels (β = 0.947, $P = 0.038$), which decreased with age. Low/intermediate SES levels were associated with higher HDL-C levels (β = 0.650, $P = 0.008$ vs. β = 0.630, $P = 0.007$, respectively), which decreased with age (β = -0.140, $P < 0.001$ vs. β = -0.064, $P = 0.001$, respectively). No significant associations between SES and non-HDL-C levels were found at baseline, but the non-HDL-C levels in children belonging to intermediate SES became lower than that in a high SES as age increased (β = -0.115, $P = 0.021$). A low SES was not associated with triglycerides levels, but intermediate SES was negatively associated with triglycerides levels (β = -3.843, $P < 0.001$), a gap that decreased with age (β = 0.256, $P < 0.001$).

DISCUSSION

Preventive medicine allows medical professionals to anticipate the natural history of the diseases and to define points where intervention may act to change future events. This cross-sectional study was designed to assess the effects of sociodemographic factors on lipid profile testing and lipoprotein levels in a large representative sample of the Israeli pediatric population who were members in the nation's largest HMO. The findings suggest that sex, ethnicity, and SES impact the extent to which children and adolescents undergo those evaluations.

The overall lipid testing rate in 2007–2011 was about 10% (approximately 120,000 individuals insured by Clalit Health Services per year). This rate was higher than the rate reported in the United States [12,13]. A plausible explanation for this difference is the fact that Israeli healthcare is universal and medical insurance is compulsory. The frequency of lipid testing in the Israeli pediatric population, however, appears to be lower than expected based on the reported percentage of children and adolescents with overweight/obesity being higher than the percentage of subjects insured by the HMO undergoing lipid evaluation.

Table 4. Linear models for lipoproteins according to sociodemographic variables

	β	Standard error	*t*	*P* value	95% confidence interval for β	
					Lower	Upper
Total cholesterol						
Constant	124.773	1.629	76.572	< 0.001	121.579	127.966
Age	2.717	0.122	22.268	< 0.001	2.477	2.956
Sex (male)*	1.087	0.318	3.420	0.001	0.464	1.711
Ethnicity (Jewish)**	5.263	0.375	14.026	< 0.001	4.527	5.998
BMI	1.699	0.096	17.718	< 0.001	1.511	1.887
SES low***	2.652	0.487	5.449	< 0.001	1.698	3.605
SES intermediate***	0.643	0.459	1.402	0.161	-0.256	1.542
Age × sex (male)	-0.664	0.026	-25.152	< 0.001	-0.715	-0.612
Age × ethnicity (Jewish)	-0.253	0.031	-8.216	< 0.001	-0.313	-0.193
Age × BMI	-0.146	0.007	-21.780	< 0.001	-0.159	-0.133
Age × SES low	-0.431	0.041	-10.561	< 0.001	-0.511	-0.351
Age × SES intermediate	-0.174	0.039	-4.492	< 0.001	-0.250	-0.098
Low density lipoprotein cholesterol						
Constant	73.972	1.548	47.780	< 0.001	70.938	77.007
Age	0.426	0.115	3.711	< 0.001	0.201	0.651
Sex (male)*	-0.944	0.310	-3.047	0.002	-1.551	-0.337
Ethnicity (Jewish)**	3.796	0.354	10.737	< 0.001	3.103	4.488
BMI	1.262	0.091	13.901	< 0.001	1.084	1.440
SES low***	-0.079	0.477	-0.166	0.868	-1.014	0.855
SES intermediate***	0.947	0.456	2.077	0.038	0.053	1.840
Age × sex (male)	-0.285	0.025	-11.316	< 0.001	-0.335	-0.236
Age × Ethnicity (Jewish)	-0.277	0.029	-9.676	< 0.001	-0.333	-0.221
BMI × Age	-0.059	0.006	-9.365	< 0.001	-0.072	-0.047
Age × SES low	-0.125	0.039	-3.192	0.001	-0.201	-0.048
Age × SES intermediate	-0.156	0.038	-4.153	< 0.001	-0.230	-0.082
High density lipoprotein cholesterol						
Constant	36.286	0.797	45.532	< 0.001	34.724	37.848
Age	2.544	0.059	42.972	< 0.001	2.428	2.660
Sex (male)*	3.700	0.160	23.172	< 0.001	3.387	4.013
Ethnicity (Jewish)**	1.690	0.183	9.250	< 0.001	1.332	2.048
BMI	0.405	0.047	8.631	< 0.001	0.313	0.497
SES low***	0.650	0.244	2.662	0.008	0.171	1.128
SES intermediate***	0.630	0.234	2.690	0.007	0.171	1.088
Age × sex (male)	-0.434	0.013	-33.309	< 0.001	-0.459	-0.408
Age × ethnicity (Jewish)	0.061	0.015	4.092	< 0.001	0.032	0.090
BMI × age	-0.105	0.003	-32.238	< 0.001	-0.112	-0.099
Age × SES low	-0.140	0.020	-6.971	< 0.001	-0.179	-0.101
Age × SES intermediate	-0.064	0.019	-3.315	0.001	-0.102	-0.026
Non-high density lipoprotein cholesterol						
Constant	81.977	2.076	39.487	< 0.001	77.908	86.046
Age	0.638	0.156	4.095	< 0.001	0.333	0.943
Sex (male)*	-3.224	0.413	-7.812	< 0.001	-4.032	-2.415
Ethnicity (Jewish)**	3.876	0.481	8.065	< 0.001	2.934	4.819
BMI	1.825	0.122	14.925	< 0.001	1.585	2.065
SES low***	-1.085	0.624	-1.738	0.082	-2.308	0.139
SES intermediate***	0.266	0.597	0.446	0.656	-0.904	1.437
Age × sex (male)	-0.187	0.034	-5.520	< 0.001	-0.254	-0.121
Age × ethnicity (Jewish)	-0.333	0.039	-8.519	< 0.001	-0.409	-0.256
Age × BMI	-0.078	0.009	-9.017	< 0.001	-0.094	-0.061
Age × SES low	-0.081	0.052	-1.570	0.117	-0.183	0.020
Age × SES intermediate	-0.115	0.050	-2.313	0.021	-0.213	-0.018
Triglycerides						
Constant	30.263	2.151	14.070	< 0.001	26.047	34.479
Age	0.782	0.161	4.862	< 0.001	0.467	1.097
Sex (male)*	-9.220	0.423	-21.797	< 0.001	-10.049	-8.391
Ethnicity (Jewish)**	1.610	0.492	3.276	0.001	0.647	2.574
BMI	3.493	0.126	27.673	< 0.001	3.246	3.741
SES low***	-0.992	0.654	-1.517	0.129	-2.273	0.290
SES intermediate***	-3.843	0.622	-6.182	< 0.001	-5.061	-2.624
Age × sex (male)	0.364	0.035	10.435	< 0.001	0.296	0.433
Age × ethnicity (Jewish)	-0.290	0.040	-7.214	< 0.001	-0.369	-0.211
Age × BMI	-0.098	0.009	-11.045	< 0.001	-0.115	-0.080
Age × SES low	0.053	0.054	0.981	0.327	-0.053	0.160
Age × SES intermediate	0.256	0.052	4.915	< 0.001	0.154	0.358

Regression coefficients are unstandardized. Independent variables were age, sex, ethnicity, BMI, SES, and first order interactions between independent variables

*Girls comprised the reference group (0)

**Arab children comprised the reference group (0)

***Children in a high SES comprised the reference group (0)

Age is measured in years

BMI = body mass index, SES = socioeconomic status

SEXUAL DIMORPHISM

More girls underwent lipid testing than boys. The last decade has witnessed a considerable amount of research in sex and health, including sex differences in vulnerability to specific health conditions and illness impact. Sex distribution was also reported to influence the consolidation and implementation of health policies [14].The higher frequency of lipid testing in girls may stem from differences in healthcare-seeking behavior. Adolescent girls reportedly have higher overall primary care consultation rates compared to adolescent boys [15]. Among the explanations for this disparity were differences in health knowledge, health status, sensitivity to symptoms, willingness to report health problems and seek help, and compliance with treatment in adult populations.

As expected, the lipoprotein levels in serum changed with age, and adolescent girls had a less favorable lipid profile than adolescent boys (i.e., higher levels of TC, LDL-C, non-HDL-C, and triglycerides). This finding is in line with other reports of TC, HDL-C, LDL-C and non-HDL-C declining and HDL-C increasing more among boys than girls [16.17].

SOCIOECONOMIC STATUS

Children and adolescents with low/intermediate SES were significantly less likely to undergo lipid profile evaluation than

those with a high SES. This finding may stem from a greater awareness of adverse health outcomes of elevated serum lipoproteins in families belonging to a high SES. A lower SES has been reported as being associated with poorer health conditions, a higher prevalence of illness with a more severe course, and a higher likelihood of mortality across the lifespan from childhood to old age in many countries worldwide [18,19]. Thus, families belonging to a lower SES may be less inclined to visit the primary care physician for screening tests. It is reassuring, therefore, that the rate of lipid testing in our study population with an intermediate/lower SES increased over time. SES also influenced serum lipoprotein levels. As observed by others [20,21], our study children and adolescents with a low SES had a more favorable serum lipoprotein distribution compared to children and adolescents with a high SES. Interestingly, the triglycerides levels were similar for all three SES categories, in contrast to a 2016 Lebanese study on school children that reported an association between high triglycerides levels and a low SES [21].

ETHNICITY

In 2007, children and adolescents belonging to the Arab sector were less likely to undergo lipid profile testing, but the difference between the sectors narrowed and the ethnic gap disappeared by 2011. This trend may stem from the Israeli government's awareness of unequal treatment of the Arab minority in the early 1990s and the adoption of a social support ideology accompanied by policies aimed at narrowing the gaps since 1998 [22]. There was ethnic dimorphism in lipid levels evidenced by the Jewish children and adolescents having higher TC, LDL-C, HDL-C, and lower triglycerides levels compared to their Arab counterparts. Our findings are in line with previous reports published in the late 1980s and early 1990s, which described ethnic variability in Israeli children and adolescents [23,24]. Unlike our current work those studies had relatively small sample sizes that were not representative for the entire country.

Noteworthy, the mean serum TC and LDL-C levels in healthy, normal-weight Israeli children and adolescents were lower than those recently reported from the United States National Health and Nutrition Examination Survey, 1999–2006 [25]. Although our study was not designed to establish causality, plausible explanations for the discrepancy might be genetic, environmental, and/or epigenetic differences between the studied populations. Differences could be partially attributed to the Mediterranean diet of the Israeli population. Unfortunately, dietary recall questionnaires assessing the intake of foods were not conducted, nor was there any documentation in the medical files on supplementation of the diet with plant stanols, sterols, and omega-3 fatty acid (docosahexaenoic acid).

The major strength of our study is the accessibility to such a comprehensive database, which enabled us to analyze sociodemographic factors potentially associated with lipid profile testing in a large section of the Israeli pediatric population. The limitations of this study include a lack of pertinent information on the reason for referral for lipid testing and on family history of hyperlipidemia and/or premature cardiovascular disease. Anthropometric parameters were determined in only part of the study cohort. Subcategorization of the Jewish population by religious affiliation (secular/Orthodox/ultra-Orthodox) was not performed since the ultra-Orthodox population is underrepresented in Clalit Health Services, thus the power to distinguish this group from the general Jewish population is limited. This issue should be addressed in future studies that include individuals insured by other HMOs.

Lifestyle and nutritional habits were not available in the medical files. A survey of Israeli pediatricians reporting cholesterol screening approach and treatment practices would be of value to understand lipid profile testing decision-making processes.

CONCLUSIONS

Our finding, derived from a large representative national sample, suggest that sex, ethnicity, and SES impact the frequency of serum lipid testing and lipid levels among Israeli children and adolescents. These differences highlight the need for our primary care physicians to have increased awareness of lipoprotein distribution among divergent sectors nationwide. Those physicians should be surveyed on lipid screening and treatment practices in an attempt to discern whether they meet existing guidelines. Indeed, we propose that one explanation for narrowing the gap between socioeconomic groups over time might be due to increased physician awareness of health disparities and attempts to compensate for them, as well as a top-down initiative of standardized healthcare.

Acknowledgments

The authors thank Esther Eshkol for her editorial assistance. Appreciation is also expressed to Alona Hamou, our research coordinator

Correspondence

Dr. Y. Lebenthal

Pediatric Endocrinology and Diabetes Unit, Dana–Dwek Children's Hospital, Tel Aviv Sourasky Medical Center, Tel Aviv 6423906, Israel

Phone: (972-3) 697-2513

Fax: (972-3) 697-4306

email: yaelleb@tlvmc.gov.il

References

1. Raitakari OT, Juonala M, Kähönen M, et al. Cardiovascular risk factors in childhood and carotid artery intima-media thickness in adulthood: the Cardiovascular Risk in Young Finns Study. *JAMA* 2003; 290: 2277-83.
2. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents; National Heart, Lung, and Blood Institute. Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. *Pediatrics* 2011; 128 (Suppl 5): S213-56.
3. Psaty BM, Rivara FP. Universal screening and drug treatment of dyslipidemia in children and adolescents. *JAMA* 2012; 307: 257-8.

4. Kark JD, Gordon ES, Haklai Z. Coronary heart disease mortality among Arab and Jewish residents of Jerusalem. *Lancet* 2000; 21; 356 (9239): 1410-1.
5. Kark JD, Fink R, Adler B, Goldberger N, Goldman S. The incidence of coronary heart disease among Palestinians and Israelis in Jerusalem. *Int J Epidemiol* 2006; 35 (2): 448-57.
6. Cheng TL, Goodman E. Committee on Pediatric Research. Race, ethnicity, and socioeconomic status in research on child health. *Pediatrics* 2015; 135: e225-37.
7. Larson K, Cull WL, Racine AD, Olson LM. Trends in access to health care services for US children: 2000-2014. *Pediatrics* 2016; 138: e20162176.
8. Clarfield AM, Manor O, Nun GB, et al. Health and health care in Israel: an introduction. *Lancet* 2017; 389: 2503-13.
9. Andria N, Nassar A, Kusniec F, et al. Ethnicity of symptomatic coronary artery disease referred for coronary angiography in the Galilee: prevalence, risk factors, and a case for screening and modification. *IMAJ* 2018; 20 (3): 182-5.
10. Filc D, Davidovich N, Novack L, Balicer RD. Is socioeconomic status associated with utilization of health care services in a single-payer universal health care system? *Int J Equity Health* 2014; 13: 115.
11. Goldstein A, Haelyon U, Krolik E, Sack J. Comparison of body weight and height of Israeli schoolchildren with the Tanner and Centers for Disease Control and Prevention growth charts. *Pediatrics* 2001; 108 (6): E108.
12. Margolis KL, Greenspan LC, Trower NK, et al. Lipid screening in children and adolescents in community practice: 2007 to 2010. *Circ Cardiovasc Qual Outcomes* 2014; 7: 718-26.
13. Vinci SR, Rifas-Shiman SL, Cheng JK, Mannix RC, Gillman MW, de Ferranti SD. Cholesterol testing among children and adolescents during health visits. *JAMA* 2014; 311: 1804-7.
14. Vlassoff C. Gender differences in determinants and consequences of health and illness. *J Health Popul Nutr* 2007; 25: 47-61.
15. Wang Y, Hunt K, Nazareth I, Freemantle N, Petersen I. Do men consult less than women? An analysis of routinely collected UK general practice data. *BMJ Open* 2013; 3: e003320.
16. Skinner AC, Steiner MJ, Chung AE, Perrin EM. Cholesterol curves to identify population norms by age and sex in healthy weight children. *Clin Pediatr (Phila)* 2012; 51: 233-7.
17. Interator H, Lebenthal Y, Hoshen M, et al. Distinct lipoprotein curves in normal weight, overweight and obese children and adolescents. *J Pediatr Gastroenterol Nutr* 2017; 65: 673-80.
18. Puolakka E, Pahkala K, Laitinen TT, et al. Childhood socioeconomic status in predicting metabolic syndrome and glucose abnormalities in adulthood: the Cardiovascular Risk in Young Finns Study. *Diabetes Care* 2016; 39: 2311-7.
19. Truesdale BC, Jencks C. The health effects of income inequality: averages and disparities. *Annu Rev Public Health* 2016; 37: 413-30.
20. Dathan-Stumpf A, Vogel M, Rieger K, Thiery J, Hiemisch A, Kiess W. Serum lipid levels were related to socio-demographic characteristics in a German population-based child cohort. *Acta Paediatr* 2016; 105: e360-7.
21. Gannagé-Yared MH, Farah V, Chahine E, et al. Distribution and correlates of non-high-density lipoprotein cholesterol and triglycerides in Lebanese school children. *J Clin Lipidol* 2016; 10: 378-85.
22. Barnes AJ, Hanoch Y. Knowledge and understanding of health insurance: challenges and remedies. *Isr J Health Policy Res* 2017; 6: 40.
23. Tamir D, Edelstein P, Reshef A, Halfon ST, Palti H. Serum cholesterol (total, low-density lipoprotein, and high-density lipoprotein cholesterol), triglyceride levels, and fat consumption among Jerusalem Arab and Jewish schoolchildren. *Prev Med* 1987; 16: 752-60.
24. Greenland P, Goldbourt U, Yaari S, et al. Divergent age-associated patterns of high density lipoprotein cholesterol and its percentage in Jewish and Moslem Arab Israeli children and adolescents: the Petach Tikva Project. *Am J Epidemiol* 1993; 137: 549-58.
25. Ford ES, Li C, Zhao G, Mokdad AH. Concentrations of low-density lipoprotein cholesterol and total cholesterol among children and adolescents in the United States. *Circulation* 2009; 119: 1108-15.

Capsule

American College of Rheumatology provisional criteria for clinically relevant improvement in children and adolescents with childhood-onset-systemic lupus erythematosus

Brunner and colleagues tried to develop a Childhood Lupus Improvement Index (CHILI) as a tool to measure response to therapy in childhood-onset systemic lupus erythematosus (cSLE), with a focus on clinically relevant improvement (CRIcSLE). Pediatric nephrology and rheumatology subspecialists (n=213) experienced in cSLE management were invited to define CRIcSLE and rate a total of 433 unique patient profiles for the presence/absence of CRIcSLE. Patient profiles included the following cSLE core response variables (CRVs): global assessment of patient well-being (patient-global), physician assessment of cSLE activity (MD-global), disease activity index, urine protein-to-creatinine ratio, and Child Health Questionnaire physical summary score. Percentage and absolute changes in these cSLE-CRVs (baseline vs. follow-up) were considered to develop candidate algorithms and validate their performance (sensitivity, specificity, area under the receiver operating characteristic curve [AUC]; range 0–1). During an international consensus conference, unanimous agreement on a definition of CRIcSLE was achieved; cSLE experts (n=13) concurred (100%) that the preferred CHILI algorithm considers absolute changes in the cSLE-CRVs. After transformation to a range of 0–100, a CHILI score of ≥ 54 had outstanding accuracy for identifying CRIcSLE (AUC 0.93, sensitivity 81.1%, and specificity 84.2%). CHILI scores also reflect minor, moderate, and major improvement for values exceeding 15, 68, and 92, respectively (all AUC ≥ 0.92, sensitivity ≥ 93.1%, and specificity ≥ 73.4%).

Arthritis Care Res 2019; 71: 579

Eitan Israeli

"You have to hold your audience in writing to the very end – much more than in talking, when people have to be polite and listen to you"

Brenda Ueland (1891–1985), writer

"If you are not prepared to be wrong, you'll never come up with anything original"

Sir Ken Robinson (born 1950), English expert on innovation in education