Pediatric Familial Hypercholesterolemia: Children and Adolescents Enrolled in the CAscade SCreening for Awareness and DEtection FH Registry

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BACKGROUND

- Patients with familial hypercholesterolemia (FH) have severe elevations in low density lipoprotein-cholesterol (LDL-C) from birth, leading to increased risk for atherosclerotic cardiovascular disease (ASCVD).
- FH is a common inherited disorder affecting 1 in every 250 individuals.

The CASCADE FH™ Patient Registry

In 2013, the FH Foundation (a patient-led nonprofit organization) created the **CAscade SCreening for Awareness and DEtection (CASCADE) FH Registry,** a national initiative to increase FH awareness, characterize trends in treatment, and monitor clinical and patient-reported outcomes over time. Children were included in the registry.

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Figure 1: Active clinical registry sites and sites in progress.

METHODS

We conducted a cross-sectional analysis of treatment patterns and cardiovascular risk factors in 383 children and adolescents <18 years (90 < 10 years of age) with heterozygous FH enrolled in CASCADE FH from 18 US lipid clinics between April 2014 and February 2017.

RESULTS

Median age at FH diagnosis was 10 yrs (interquartile range [IQR] 6,12); 50.1% were male, 68.1% white. In ~1/4rd of youth FH was diagnosed using formal criteria, e.g. MEDPED (15.7%), Simon Broome (6.5%), both (2.1%); the highest proportion of patients were diagnosed clinically (45.2%). Only 6 (1.6%) patients had a confirmed genetic mutation. Median LDL-C at enrollment was 175 mg/dl (IQR 140-225) While 32.6% had a family history of premature MI, no youth experienced cardiovascular events. Some youth with FH had additional cardiovascular risk factors, with low HDL-C (36%) and obesity (16.7%) being relatively common, followed by hypertension (2.3%) and diabetes (1.0%); 21.7% had ≥2 additional risk factors. Approximately half (52.5%) of the cohort was treated with a lipid-lowering therapy (LLT). (figure 2)

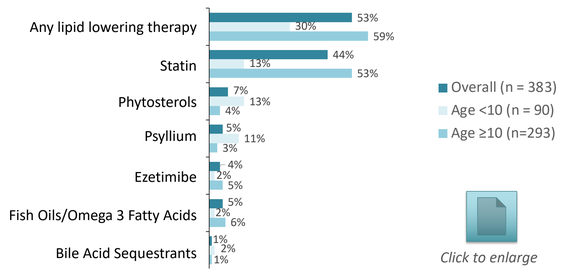

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Figure 2: Lipid lowering therapy between the ages <10 vs. ≥10 year-olds.

Children ≥10 years were more likely than younger patients to receive LLT (59.4% vs. 30.0%, p<0.0001); Young age was reported as a reason for non-treatment in 32.9% of those not on a statin. Median age at LLT initiation was 11 years (range 0-17). The median reported highest untreated LDL-C level was 229 mg/dL (IQR 193,269), n=364; while the average LDL-C on treatment was 167 mg/dL (132-210). Of patients on LLT, 22.4% had an LDL <130 mg/dL and 14.9% had an LDL-C ≥50% lower than their maximum untreated level; 26.4% met at least one of these LDL-C goals.

CONCLUSION

Among youth, at the time of enrollment, in the CASCADE FH registry, just over half reported being on LLT, with higher rates of LLT reported in older children. Despite this, less than a quarter of youth achieved sufficient LDL-C lowering. Opportunities exist to optimize the treatment of youth with FH to reduce their risk of cardiovascular disease.

Table 1: Characteristics of heterozygous FH CASCADE participants <18 years.
Data presented as n (%), mean (SD), or median (interquartile range [IQR]).

	All youth (n=383)	<10 years (n=90)	≥10 years old (n=293)
DEMOGRAPHICS			
Age at enrollment, years mean (SD)	12.2 (3.6)	7.1 (1.9)	13.8 (2.3)
Age at diagnosis, years mean (SD)	9.4 (4.0)	5.8 (2.4)	10.5 (3.8)
Gender			
Male (%)	192 (50.1%)	42 (46.7%)	150 (51.2%)
Female (%)	191 (49.9%)	48 (53.3%)	143 (48.8%)
Race/Ethnicity			
Hispanic	42 (11%)	17 (18.9%)	25 (8.5%)
Back/ African American	35 (9.1%)	12 (13.3%)	23 (7.8%)
Asian	19 (5.0%)	6 (6.7%)	13 (4.4%)
White	261 (68.1%)	49 (54.4%)	212 (72.4%)
Other	26 (6.8%)	6 (6.7%)	20 (6.8%)
BMI, kg/m²	23.5 (6.5)	23.1 (4.9)	23.6 (6.7)
LIPID PROFILE AT ENROLLMENT, md/dL mean (SD)			
Total Cholesterol	253 (73.0)	294 (91.6)	241 (61.2)
LDL-C	181 (59.6)	215 (54.0)	171 (57.5)
LDL-C>190 mg/dL n(%)	150 (39.4%)	52 (58.4%)	98 (33.6%)
HDL-C	51.0 (13.6)	53.4 (13.7)	50.3 (13.5)
Triglycerides	98.2 (65.3)	87.6 (45.5)	101 (70.0)
FH DIAGNOSIS			
Highest LDL-c, mg/ dL mean (SD)	237 (64.4)	243 (88.2)	235 (54.7)
Family history of premature MI (%)	125 (32.6%)	18 (20%)	107 (36.5%)
Reported previous cardiovascular events, n	0 (0%)	0 (0%)	0 (0%)

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Table Continued

	All youth (n=383)	<10 years (n=90)	≥10 years old (n=293)
FH Diagnostic Criteria			
Dutch Lipid Clinic	0 (0%)	0 (0%)	0 (0%)
Simon Broome	25 (6.5%)	6 (6.7%)	19 (6.5%)
MEDPED	60 (15.7%)	14 (15.6%)	46 (15.7%)
Clinical Diagnostics	173 (45.2%)	45 (50%)	128 (43.7%)
Other	2 (0.5%)	0 (0%)	2 (0.7%)
Multiple Methods	8 (2.1%)	0 (0%)	8 (2.7%)
Confirmed FH genetic mutation	6 (1.6%)	0 (0%)	6 (2.0%)
ADDITIONAL CARDIOVASCULAR RISK FACTORS			
Diabetes mellitus (%)	4 (1.0%)	1 (1.1%)	3 (1.0%)
Current or former smoker	1 (0.3%)	0 (0%)	1 (0.3%)
Hypertension (%)	9 (2.3%)	1 (1.1%)	8 (2.7%)
Obesity, BMI≥95th%ile (%)	64 (16.7%)	15 (16.7%)	49 (16.7%)
Low HDL cholesterol (<40mg/dL in males, <50 mg/dL females) n (%)	138 (36%)	30 (33.3%)	108 (36.9%)
Risk Factor Burden † n (%)			
No risk factor	148 (38.6%)	42 (46.7%)	106 (36.2%)
One risk factor	151 (39.5%)	33 (36.7%)	118 (40.3%)
Two risk factors	65 (17%)	13 (14.4%)	52 (17.7%)
Three risk factors	18 (4.7%)	2 (2.2%)	16 (5.5%)
TREATED WITH LIPID LOWERING THERAPY (LLT) n (%)			
Any LLT	201 (52.5%)	27 (30%)	174 (59.4%)
Statin	168 (43.9%)	12 (13.3%)	156 (53.2%)
Ezetimibe	17 (4.4%)	2 (2.2%)	15 (5.1%)
Bile acid sequestrants	5 (1.3%)	2 (2.2%)	3 (1%)
Niacin	1 (0.3%)	0 (0%)	1 (0.5%)
Phytosterols	25 (6.5%)	12 (13.3%)	13 (4.4%)
Fish oils/Omega 3 Fatty Acids	20 (5.2%)	2 (2.2%)	18 (6.1%)
Psyllium	19 (5%)	10 (11.1%)	9 (3.1%)
Other*	0 (0%)	0 (0)%	0 (0%)
TREATMENT RESULTS (n=201)			
% LDL reduction on LLT, mg/dL mean (SD)	27 (22.2)	10.6 (17.2)	29.7 (21.8)
LDL <130mg/dL	45 (22.4%)	1 (3.7%)	44 (25.3%)
LDL change (highest to enrollment) ≥50%	30 (14.9%)	1 (3.7%)	29 (16.7%)
LDL<130 mg/dL OR ≥50% reduction	53 (26.4%)	2 (7.4%)	51 (29.3%)

***Cardiovascular risk factors include smoking history, hypertension, low HDL, and family history of premature MI * no patients were treated with lomitapide, mipomersen, PCSK9 inhibitors or LDL apheresis † includes documented coronary artery disease, myocardial infarction, stroke, transient ischemic attack, heart failure, stenting or angioplasty, coronary artery bypass grafting, peripheral arterial revascularization, aortic valve replacement. MI – myocardial infarction; LLT – lipid-lowering therapy.*

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Acknowledgments and Funding/Disclosures

We would like to acknowledge the FH patients who participated in CASCADE FH™. The CASCADE FH™ Registry has been supported by Amgen, Astra Zeneca, Pfizer, Regeneron, and Sanofi.

S.D. de Ferranti: Research Grant; Modest; PCORI, Pediatric Heart Network, New England Children's Congenital HeartFoundation. Other; Modest; UpToDate. | **Z.S. Ahmad**: Research Grant; Modest; NIH, Regeneron. Honoraria; Modest; Genzyme, Sanofi. Consultant/Advisory Board; Modest; Genzyme. | **E.C. O'Brien**: Research Grant, modest: PCORI, NHLBI, Pfizer, Bristol Myers Squibb, Janssen Scientific, Novartis, Merck. Consultant/Advisory Board, modest: Portola Pharmaceuticals. | **D.J. Rader**: Consultant/Advisory Board; Modest; Aegerion,Alnylam, Sanofi. Other; Significant; Aegerion. | **C.M.Ballantyne**: Research Grant; Significant; Eli Lilly, Amarin, Amgen,Esperion, Novartis, Pfizer, Regeneron, Sanofi, Takeda, NIH, AHA, ADA.Consultant/Advisory Board; Modest; Amarin, Eli Lilly, Esperion, Genzyme,Matinas BioPharma, Novartis, Regeneron, Sanofi. Consultant/Advisory Board; Significant; Amgen, AstraZeneca, Merck, Pfizer. | **M.F. Linton**: ResearchGrant; Modest; Merck, ISIS, Genzyme, Sanofi, Regeneron.Consultant/Advisory Board; Modest; Merck, Retrophin, Amgen. | **M.D. Shapiro**: Research Grant; Modest; NIH, Amgen, Sanofi, Amarin, ISIS, Synageva, Merck. Consultant/Advisory Board; Modest; Synageva. | **J.W.Knowles**: Research Grant; Significant; AHA, Amgen, Leducq Foundation. | **I. Kindt:** None. | **S. Clauss:** None. | **A. A.L. Peterson:** None. | **I. Benuck:** None. | **L.C. Hudgins:** None. | **S.S. Gidding:** None. | **P.B. Duell:** None. | **M.T. Roe:** None. | **P. Shrader:** None. | **K. Wilemon:** None. | **W. Neal:** None.