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Familial hypercholesterolaemia in children and adolescents from 48 countries: a cross-sectional study

European Atherosclerosis Society Familial Hypercholesterolaemia Studies Collaboration

Collaborators

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Abstract

Background: Approximately 450 000 children are born with familial hypercholesterolaemia worldwide every year, yet only 2·1% of adults with familial hypercholesterolaemia were diagnosed before age 18 years via current diagnostic approaches, which are derived from observations in adults. We aimed to characterise children and adolescents with heterozygous familial hypercholesterolaemia (HeFH) and understand current approaches to the identification and management of familial hypercholesterolaemia to inform future public health strategies.

Methods: For this cross-sectional study, we assessed children and adolescents younger than 18 years with a clinical or genetic diagnosis of HeFH at the time of entry into the Familial Hypercholesterolaemia Studies Collaboration (FHSC) registry between Oct 1, 2015, and Jan 31, 2021. Data in the registry were collected from 55 regional or national registries in 48 countries. Diagnoses relying on self-reported history of familial hypercholesterolaemia and suspected secondary hypercholesterolaemia were excluded from the registry; people with untreated LDL cholesterol (LDL-C) of at least 13·0 mmol/L were excluded from this study. Data were assessed overall and by WHO region, World Bank country income status, age, diagnostic criteria, and index-case status. The main outcome of this study was to assess current identification and management of children and adolescents with familial hypercholesterolaemia.

Findings: Of 63 093 individuals in the FHSC registry, 11 848 (18·8%) were children or adolescents younger than 18 years with HeFH and were included in this study; 5756 (50·2%) of 11 476 included individuals were female and 5720 (49·8%) were male. Sex data were missing for 372 (3·1%) of 11 848 individuals. Median age at registry entry was 9·6 years (IQR 5·8–13·2). 10 099 (89·9%) of 11 235 included individuals had a final genetically confirmed diagnosis of familial hypercholesterolaemia and 1136 (10·1%) had a clinical diagnosis. Genetically confirmed diagnosis data or clinical diagnosis data were missing for 613 (5·2%) of 11 848 individuals. Genetic diagnosis was more common in children and adolescents from high-income countries (9427 [92·4%] of 10 202) than in children and adolescents from non-high-income countries (199 [48·0%] of 415). 3414 (31·6%) of 10 804 children or adolescents were index cases. Familial-hypercholesterolaemia-related physical signs, cardiovascular risk factors, and cardiovascular disease were uncommon, but were more common in non-high-income countries. 7557 (72·4%) of 10 428 included children or adolescents were not taking lipid-lowering medication (LLM) and had a median LDL-C of 5·00 mmol/L (IQR 4·05–6·08). Compared with genetic diagnosis, the use of unadapted clinical criteria intended for use in adults and reliant on more extreme phenotypes could result in 50–75% of children and adolescents with familial hypercholesterolaemia not being identified.

Interpretation: Clinical characteristics observed in adults with familial hypercholesterolaemia are uncommon in children and adolescents with familial hypercholesterolaemia, hence detection in this age group relies on measurement of LDL-C and genetic confirmation. Where genetic testing is unavailable, increased availability and use of LDL-C measurements in the first few years of life could

help reduce the current gap between prevalence and detection, enabling increased use of combination LLM to reach recommended LDL-C targets early in life.

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