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Original article

Prevalence and distributions of severely elevated low-density lipoprotein cholesterol (LDL-c) according to age, gender and clinic location among patients in the Malaysian primary care

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ABSTRACT

Background: Adults with severely elevated low-density lipoprotein cholesterol (LDL-c) may have familial hypercholesterolaemia (FH) and are at high risk of atherosclerotic cardiovascular disease (ASCVD). The prevalence of elevated LDL-c in primary care clinics in Malaysia is not known. Therefore, this study aimed to determine the prevalence and distributions of severely elevated LDL-c among adult patients attending public primary care clinics in Malaysia.

Methods: A cross-sectional study was conducted at 11 public primary care clinics in the central states of Malaysia, among adults ≥18 years old with LDL-c recorded in the electronic medical record. Sociodemographic and LDL-c data from 2018 to 2020 were extracted. Severely elevated LDL-c was defined as ≥4 mmol/L, which were further classified into: 4.0–4.9, 5.0–5.9, 6.0–6.9 and ≥ 7 mmol/L.

Results: Out of 139,702 patients, 44,374 (31.8 %) had severely elevated LDL-c of ≥4 mmol/L of which the majority were females (56.7 %). The mean (±SD) age of patients with severely elevated LDL-c was younger at 56.3 (±13.2) years compared to those with LDL-c of <4.0 mmol/L at 59.3 (±14.5) years. In terms of LDL-c levels, 30,751 (69.3 %), 10,412 (23.5 %), 2,499 (5.6 %) and 712 (1.6 %) were in the 4.0–4.9, 5.0–5.9, 6.0–6.9 and ≥ 7 mmol/L categories, respectively.

Conclusion: The prevalence of severely elevated LDL-c of ≥4.0 mmol/L among adult patients in public primary care clinics was high. These patients need to be further investigated for secondary and inherited causes such as FH. Therapeutic lifestyle modification and pharmacological management are pivotal to prevent ASCVD in these patients.

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1. Introduction

Atherosclerotic cardiovascular disease (ASCVD) namely coronary artery disease and ischaemic cerebrovascular disease are the leading causes of morbidity and mortality globally,[1] including in Malaysia.[2] Various risk factors have been associated with an increased risk of cardiovascular events.[1] Among these risk factors, elevated small dense low-density lipoprotein (LDL) has consistently been shown to cause ASCVD.[3–5] Elevated small dense LDL particles efficiently enter the arterial intima causing intimal retention leading to the progressive development of atherosclerotic plaque and subsequently causing ASCVD.[6] The increased atherogenic potential of small dense LDL is thought to be due to the greater propensity for transport into the subendothelial space, increased binding to arterial proteoglycans and susceptibility to oxidative modification.[6] In clinical practice, the plasma's small dense LDL level is not directly measured. Instead, it is estimated from the total amount of cholesterol contained in the LDL particles i.e., LDL cholesterol (LDL-c). Therefore, the calculated plasma LDL-c has become the focus for assessing the risk of ASCVD.[3,6]

Globally, 4.4 million people have died from elevated LDL-c in 2019 with ASCVD being the major cause of death.[4] Coronary artery disease and ischaemic cerebrovascular disease accounted for 86.1 % and 13.9 % of deaths attributed to elevated LDL-c, respectively.[4] In the Asia-Pacific regions, the prevalence of elevated LDL-c ranged from 7.8 % to 47.2 %.[7] A more recent study showed that the prevalence of elevated LDL-c in Australia, Indonesia and the Philippines were 33.2 %, 41.9 % and 47.5 %, respectively.[8] In Malaysia, the prevalence of elevated LDL-c among adults was 56.7 %,[9] which was among the highest in the Asia-Pacific region. A combination of high-fat and high-carbohydrate diet in the Malaysian population has been associated with higher plasma levels of small dense LDL particles.[10] High fat and high carbohydrate diet combination is also thought to play a significant role in modulating small dense LDL and subsequently the overall ASCVD risk in the Malaysian population.[10]

In Malaysia, a majority of individuals with dyslipidaemia are being managed in the primary care setting,[11] however, the prevalence and sociodemographic distribution are not known. Therefore, this study aimed to determine the prevalence and distribution of elevated LDL-c according to age, gender and clinic location among patients attending public primary care clinics in Malaysia.

2. Methods

2.1. Study design and population

This was a cross-sectional study conducted at 11 Ministry of Health (MOH) public primary care clinics in Selangor, Kuala Lumpur and Putrajaya from September 2020 to May 2021. The sampling frame was adult patients aged ≥18 years old with LDL-c results recorded in the electronic medical record (EMR). This study provided the baseline EMR data for a larger study to detect Familial Hypercholesterolaemia (FH) in the Malaysian population.[12]

2.2. Study setting and site selection

The public primary care clinics must be equipped with an EMR system, have minimum attendance of 500 patients per day, and were led by a family medicine specialist (FMS) in order to be eligible for selection. Overall, there were 21 MOH primary care clinics in Selangor, Kuala Lumpur and Putrajaya which were equipped with EMR. The FMS leading these 21 clinics were invited for a briefing to introduce the study. Of the 21 clinics, 11 clinics were interested to participate and were therefore included in the study. Of the 11 clinics, six were located in Selangor and the remaining five were located in Kuala Lumpur and Putrajaya. Fig. 1 shows the location of the study sites.

The demographic description of the 11 study sites is presented in Table 1. All of the clinics were located in either the urban or sub-urban areas and were serving a population ranging from approximately 78,000 to 500,000. The majority of the treated households were from the low to middle-income groups.

2.3. Inclusion/exclusion criteria and data collection procedure

Sociodemographic data including gender, age at the time of

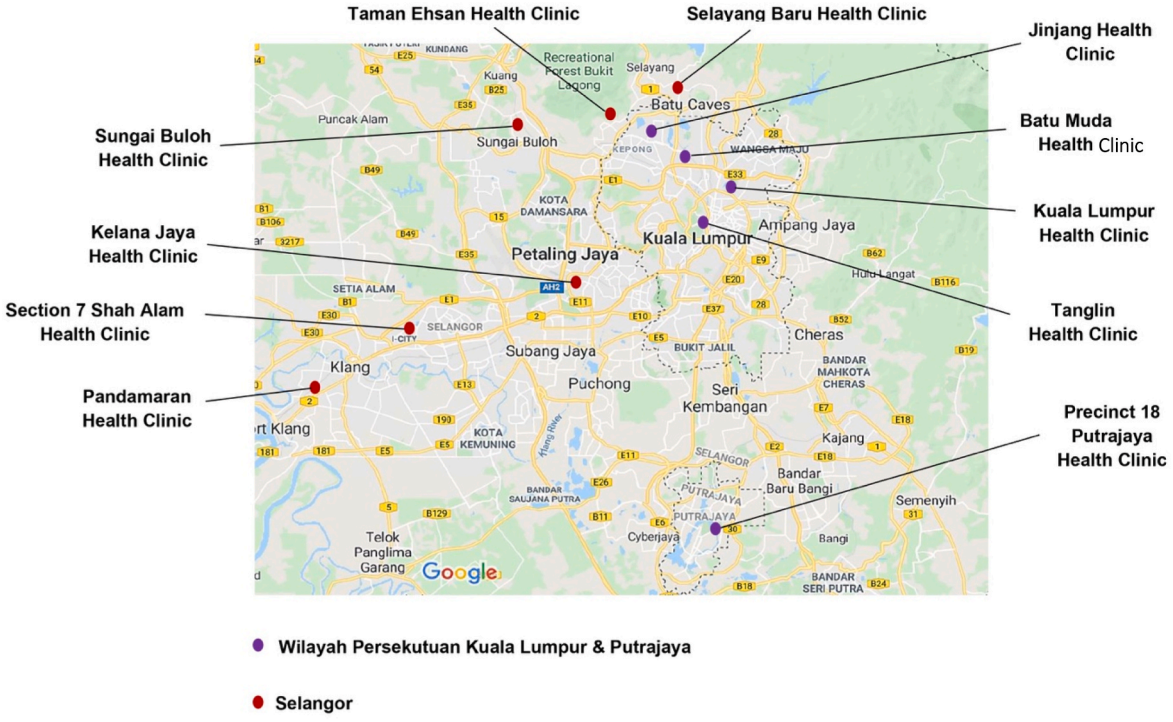

Fig. 1. The locations of study sites for prevalence and distributions of severely elevated LDL-c among adult patients.

Table 1
Demographic descriptions of the study sites, n = 139,702.

No.	Clinic name	Area	Total number of populations served	Description of population served
1	Precinct 18, Putrajaya	Sub-Urban	91, 900	• Middle to high income. • Majority are civil servants.
2	Section 7, Shah Alam	Urban	511, 153	• Low to middle income. • Majority are working in the private sector.
3	Sungai Buloh	Sub-Urban	466,163	• Low to middle income. • Majority are unemployed and self-employed.
4	Jinjang	Urban	132,272	• Low to middle income. • Majority are self-employed and unemployed.
5	Pandamaran	Urban	150,000	• Low to middle income. • A mixture of private sector workers and civil servants.
6	Kelana Jaya	Sub-Urban	180,000	• Low to middle income. • A mixture of private sector workers and civil servants
7	Taman Ehsan	Sub-Urban	78,693	• Low to middle income. • A mixture of private sector workers and civil servants
8	Selayang Baru	Urban	212,164	• Low to middle income. • A mixture of private sector workers and civil servants.
9	Tanglin	Urban	400,000	• Low to middle income. • A mixture of private sector workers and civil servants.
10	Kuala Lumpur	Urban	105,000	• Middle income. • A mixture of private sector workers and civil servants.
11	Batu Muda	Sub-Urban	180,000	• Low to middle income. • A mixture of private sector workers and civil servants.

cholesterol measurement, and LDL-c records from 2018 to 2020 were extracted from the EMR. The inclusion criteria were Malaysian citizens aged 18 years or older and who had an LDL-c level of 4.0 mmol/L or more recorded in their EMR. When multiple cholesterol measurements were recorded in the EMR for a patient, the highest LDL-c level recorded was selected to be used in this study.

2.4. Definition of variables

In this study, severely elevated LDL-c was defined as ≥4 mmol/L. This LDL-c cut-off value was defined lower than the guidelines' recommendation for patients with severe primary hypercholesterolaemia (≥4.9 mmol/L)[13] as the majority of patients in this study were believed to be on statin therapy. Subsequently, the severely elevated LDL-c levels were further classified into four categories: ≥7.0 mmol/L; 6.0–6.9 mmol/L; 5.0–5.9 mmol/L and 4.0–4.9 mmol/L.

2.5. Statistical analysis

Continuous variables were summarised as mean with standard deviation (±SD) or median with interquartile range (IQR); nominal variables were presented as counts with valid percentages. Normal distribution was graphically assessed by histograms. The independent T-test and one-way ANOVA were used for comparison of continuous variables and Chi-squared test was used for the comparison of categorical variables. All statistical analyses were performed using SPSS version 28. An α level of 0.05 was used for all analyses and all tests were two-tailed. A *P* value of <0.05 was considered significant.

3. Results

3.1. Characteristics of the study population

A total of 139,702 patients' data were extracted from the EMR and included in the analysis. Table 2 shows the sociodemographic and clinical characteristics of the study population. Out of 139,702 patients, 44,374 (31.8 %) had severely elevated LDL-c of ≥4 mmol/L. The mean (±SD) age of patients with severely elevated LDL-c was significantly lower at 56.3 (±13.2) years compared to those with LDL-c of <4.0 mmol/L at 59.3 (±14.5) years, *P* value < 0.001. The proportions of patients with severely elevated LDL-c were significantly higher in the younger age groups of 18–60 years old (59.8 %) compared to those with LDL-c of <4.0 mmol/L (48.3 %), *P* value < 0.001. The proportion of female patients with severely elevated LDL-c was significantly higher (56.7 %) compared to those with LDL-c <4 mmol/L (53.4 %), *P* value < 0.001. The proportion of patients from sub-urban areas with severely elevated LDL-c (40.4 %) was significantly higher compared to those with LDL-c <4 mmol/L (34.8 %), *P* value < 0.001.

The mean (±SD) LDL-c level among the study population was 3.51 (±1.1) mmol/L as shown in Fig. 2. The mean (±SD) LDL-c among female and male participants were 3.56 (±1.1) mmol/L and 3.44 (±1.1) mmol/L, respectively.

Fig. 3 shows the distributions of LDL-c levels among the study population. Among those with severely elevated LDL-c, the majority of individuals were in the LDL-c category of 4.0–4.9 mmol/L (69.3 %), while 1.6 % were in the LDL-c category of ≥7.0 mmol/L.

Table 3 shows the socio-demographic distribution of individuals with severely elevated LDL-c according to the LDL-c categories. With

Table 2
Sociodemographic characteristics of the study population for prevalence and distributions of severely elevated LDL-c among adult patients, n = 139,702.

Variables	Total	LDL-c <4 mmol/L	LDL-c ≥4 mmol/L	*P* value
n (%)	139,702 (100 %)	95,328 (68.2 %)	44,374 (31.8 %)	
Age (year), mean (±SD)	58.4 (±14.2)	59.3 (±14.5)	56.3 (±13.2)	<0.001[a,c]
Age (year), n (%)				
18-30	4,730 (3.4 %)	3,472 (3.7 %)	1,258 (2.8 %)	<0.001[b,c]
31-40	13,307 (9.5 %)	8,419 (8.8 %)	4,888 (11.0 %)	
41-50	20,637 (14.8 %)	12,866 (13.5 %)	7,771 (17.5 %)	
51-60	33,930 (24.3 %)	21,294 (22.3 %)	12,636 (28.5 %)	
>60	67,098 (48.0 %)	49,277 (51.7 %)	17,821 (40.2 %)	
Gender, n (%)				
Male	63,672 (45.6 %)	44,449 (46.6 %)	19,223 (43.3 %)	<0.001[b,c]
Female	76,026 (54.4 %)	50,876 (53.4 %)	25,150 (56.7 %)	
Clinic location, n (%)				
Urban	88,641 (63.5 %)	62,177 (65.2 %)	26,464 (59.6 %)	<0.001[b,c]
Sub-Urban	51,061 (36.5 %)	33,151 (34.8 %)	17,910 (40.4 %)	

LDL-c: Low-density lipoprotein cholesterol.
SD: Standard deviation.
[a] Independent T-test.
[b] Chi-squared test.
[c] Statistically significant.

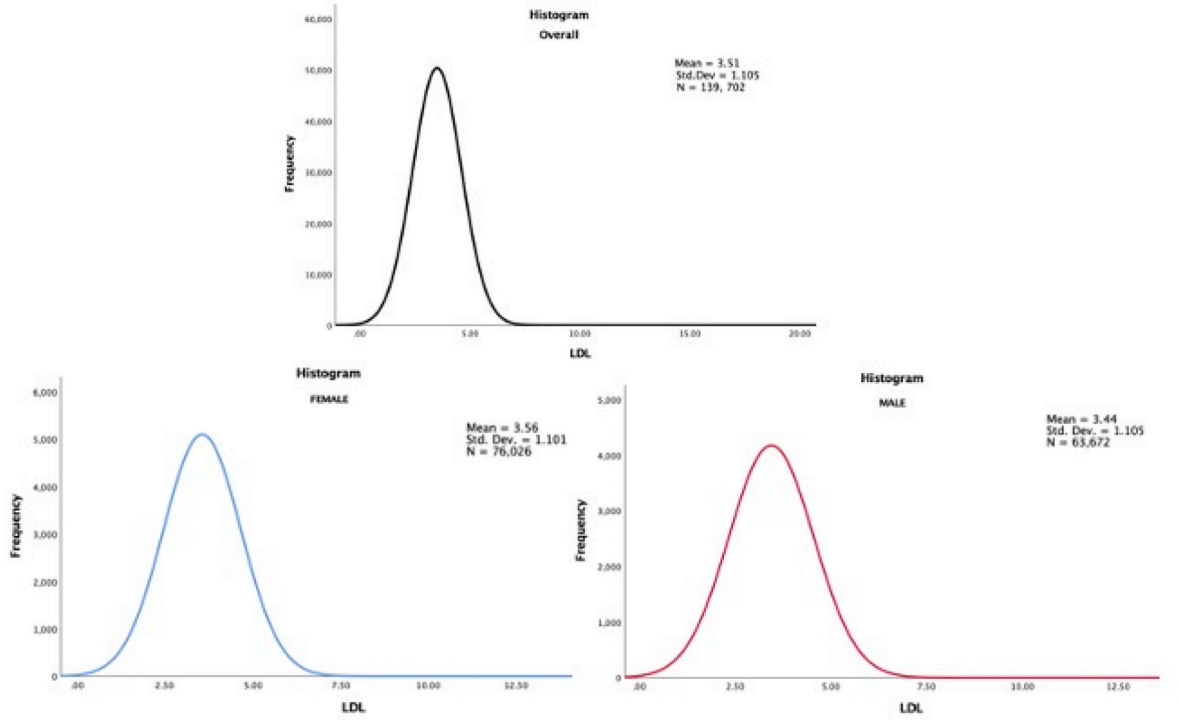

Fig. 2. The mean LDL-c distributions of the overall study population and according to gender.

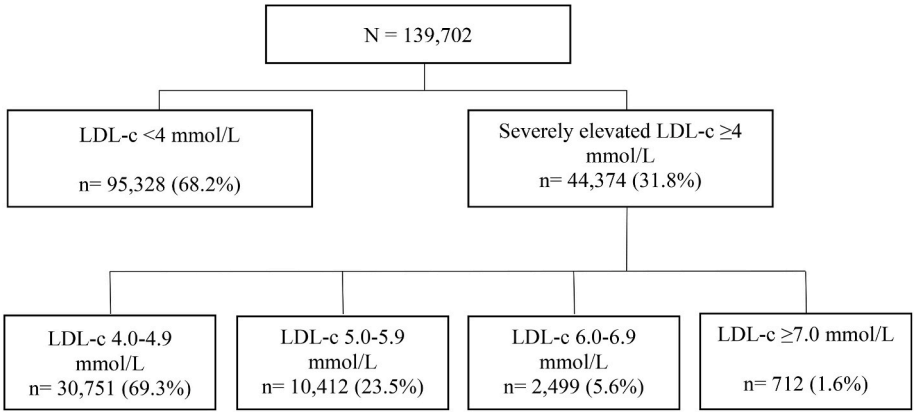

Fig. 3. Distribution of LDL-c levels among the study population.

regards to age distribution, those in the age groups of 41–50 and 51–60 had significantly higher proportions of individuals with LDL-c ≥7.0 mmol/L (18.8 % and 31.7 %, respectively) compared to the other LDL-c categories. The proportions of female participants were significantly higher in all the LDL-c categories compared to males. Among females, the highest proportion (63.1 %) was found in the LDL-c category of ≥7.0 mmol/L. Regarding the clinic location, those in the urban areas had significantly higher individuals with severely elevated LDL-c in all the categories compared to clinics that were located in the sub-urban areas.

4. Discussion

This was the first study which describes the prevalence and distribution of LDL-c levels among individuals attending public primary care clinics in Malaysia. Out of 139,702 patients, 44,374 (31.8 %) had severely elevated LDL-c of ≥4 mmol/L. Direct comparison with other studies are difficult as different thresholds were used to define elevated LDL-c. The prevalence was higher at 56.7 %[9] in the REDISCOVER study involving 11,288 Malaysian adults in the community, however they had used a lower threshold for elevated LDL-c (>3.4 mmol/L). Similarly, the prevalence of elevated LDL-c was also higher in the Philippines (47.2 %, LDL-c cut-off ≥4.1 mmol/L)[14] and Australia (33.2 %, LDL-c cut-off ≥3.5 mmol/L).[15] In contrast, the prevalence of elevated LDL-c (≥4.1 mmol/L) in several other Asian countries were lower i.e., Korea (19.2 %),[16] China (17.9 %),[17] Singapore (15.2 %),[18] and Thailand (26.9 %).[19] The UK longitudinal retrospective study using a primary care dataset from 2009 to 2019 reported that the prevalence of severely elevated LDL-c (≥4.3 mmol/L) was 23.5 %.[20] The lower elevated LDL-c prevalence in these countries may be explained by a lower saturated fat intake by their populations.[21]

In our study, the mean (±SD) age of individuals with severely elevated LDL-c was 56.3 (±13.2) years. This is similar to the mean age of those with severely elevated LDL-c in the UK (58 years, LDL-c cut-off ≥4.3 mmol/L).[20] In terms of age group, our study shows that the prevalence of severely elevated LDL-c was found to be the highest in those aged >50 years (68.7 %). This is comparable to the REDISCOVER

Table 3
Socio-demographic distributions of individuals with severely elevated LDL-c according to the LDL-c categories, n = 44,374.

Variables	Total	LDL-c 4.0–4.9 mmol/L	LDL-c 5.0–5.9 mmol/L	LDL-c 6.0–6.9 mmol/L	LDL-c ≥7.0 mmol/L	*P* value
n (%)	44,374 (100 %)	30,751 (69.3 %)	10,412 (23.5 %)	2,499 (5.6 %)	712 (1.6 %)	
Age (year), mean (±SD)	56.3 (±13.2)	56.4 (±13.4)	56.0 (±12.9)	56.6 (±12.4)	55.8(±12.3)	0.036[a],[c]
Age (year), n (%)						
18-30	1,258 (2.8 %)	916 (3.0 %)	266 (2.6 %)	59 (2.4 %)	17 (2.4 %)	<0.001[b],[c]
31-40	4,888 (11.0 %)	3,396 (11.0 %)	1,173 (11.3 %)	247 (9.9 %)	72 (10.1 %)	
41-50	7,771 (17.5 %)	5,389 (17.5 %)	1,843 (17.7 %)	405 (16.2 %)	134 (18.8 %)	
51-60	12,636 (28.5 %)	8,513 (27.7 %)	3,107 (29.8 %)	790 (31.6 %)	226 (31.7 %)	
>60	17,821 (40.2 %)	12,537 (40.8 %)	4,023 (38.6 %)	998 (39.9 %)	263 (36.9 %)	
Gender, n (%)						
Male	19,223 (43.3 %)	13,599 (44.2 %)	4,340 (41.7 %)	1,022 (40.9 %)	262 (36.8 %)	<0.001[b],[c]
Female	25,150 (56.7 %)	17,152 (55.8 %)	6,072 (58.3 %)	1,477 (59.1 %)	449 (63.1 %)	
Clinic location, n (%)						
Urban	26,464 (59.6 %)	18,846 (61.3 %)	5,855 (56.2 %)	1,361 (54.5 %)	402 (56.5 %)	<0.001[b],[c]
Sub-Urban	17,910 (40.4 %)	11,905 (38.7 %)	4,557 (43.8 %)	1,138 (45.5 %)	310 (43.5 %)	

LDL-c: Low-density lipoprotein cholesterol.
SD: Standard Deviation.
[a] One way ANOVA test. Post-hoc comparison using the Tukey HSD test indicated no significant difference in mean age between LDL-c categories.
[b] Chi-squared test.
[c] Statistically significant.

study which showed that the prevalence of elevated LDL-c among Malaysian adults was the highest in those aged >50 years (60.4 %).[9] Similarly, the prevalence of elevated LDL-c also appeared to be the highest in the age bracket between 50 and 69 years in Korea (62.3 %)[16] and Singapore (42.3 %).[18] In Australia, the prevalence of elevated LDL-c was also the highest (45.7 %) in the age group of 55–64 years.[15]

Our study also shows that approximately one-third of the patients aged ≤50 years had severely elevated LDL-c in all of the categories i.e., ≥7 mmol/L (31.3 %), 6–6.9 mmol/L (28.5 %), 5–5.9 mmol/L (31.6 %), and 4–4.9 mmol/L (31.5 %). While this could be explained by a high saturated fat intake in the Malaysian population in general, genetic causes of elevated LDL-c must be excluded in these younger age groups. One of the commonest genetic causes of severely elevated LDL-c is FH which is predominantly caused by mutations in the low-density lipoprotein receptor (*LDLR*), apolipoprotein B (*APOB*), and/or proprotein convertase subtilisin/kexin type 9 (*PCSK9*) genes.[22] In Malaysia, the prevalence of clinically diagnosed FH was 1 in 100,[23] while the prevalence of genetically confirmed FH was 1 in 427.[24] A majority of these cases were previously undiagnosed resulting in a lost opportunity to prevent premature ASCVD.[25] Therefore, FH must be excluded in those presenting with elevated LDL-c, especially at higher levels. Identifying FH in the younger population is a particular priority, to prevent development of premature atherosclerosis.

With regards to gender distribution, our study shows that the proportion of female patients (56.7 %) with severely elevated LDL-c was higher than males, and their mean (±SD) LDL-c was also higher at 3.56 (±1.1) mmol/L, compared to males at 3.44 (±1.1) mmol/L. Several other studies have also shown that women have higher LDL-c levels than men. The REDISCOVER study showed that the prevalence of elevated LDL-c among Malaysian women was 56.1 %.[9] In Australia, the prevalence of elevated LDL-c (>3.5 mmol/L) was also higher in women (40.4 %) versus men (36.5 %).[26] In Iran, the prevalence of elevated LDL-c (≥3.4 mmol/L) was also higher among women (46 %) compared to men (41 %).[27] This is likely due to a combination of factors, including differences in body fat distribution due to oestrogen hormone or women being more physically inactive than men which can contribute towards a higher LDL-c level.[28]

Regarding clinic location, this study showed that a higher proportion of patients (59.6 %) with severely elevated LDL-c were from clinics located in urban areas. These findings are consistent with previous studies. In the REDISCOVER study, the prevalence of elevated LDL-c was also higher among urban(61.2 %) compared to rural participants (52.2 %).[9] In Poland, the prevalence of elevated LDL-c was also higher in the urban areas (51.2 %) than in the rural areas (48.8 %).[29] The reasons for the higher prevalence of elevated LDL-c among urban participants are not fully understood. However, this could be explained by a number of factors, including increased consumption of processed and fast food which is high in saturated and trans fats.[21] Urban participants may also be less physically active and may have an increased stress level contributing to the higher prevalence of elevated LDL-c.[29]

4.1. Strengths and limitations

The strength of this study includes the large sample size which strengthened the external validity of the findings. However, this study has several limitations. The data was extracted from routine health records rather than a prospective cohort data collection, therefore some of the socio-demographic variables were missing. Data on lipid-lowering medications (LLM) were not extracted from the EMR in this baseline study. Therefore, the analysis was not adjusted for this variable. Our study used ≥4.0 mmol/L as the cut-off point for severely elevated LDL-c and this may limit comparison with other studies.

4.2. Implications for further research and clinical practice

The high prevalence of elevated LDL-c especially among the younger age groups in this study population has important implications for further research and clinical practice. Further research needs to include the prevalence of LLM use in the younger age groups, which may be lower compared to those aged above 60 years old. In terms of clinical practice, primary care physicians need to be aware that individuals with elevated LDL-c have a high risk of ASCVD. Therefore, in the Malaysian population, patients aged ≥30 years should be screened for ASCVD risk factors which include elevated LDL-c.[30] Patients with severely elevated LDL-c should be treated with lifestyle interventions, such as low-fat diet and exercise, and started early on LLM. Additionally, FH must also be excluded in those presenting with severely elevated LDL-c, especially in the younger age groups as this condition requires intensive lipid-lowering treatment from lipid specialists.[23] Public health campaigns should be launched to raise awareness and educate the general public regarding the importance of screening, detection and treatment of hypercholesterolaemia, in particular elevated LDL-c, to prevent ASCVD.

5. Conclusion

This study found that the prevalence of severely elevated LDL-c among individuals attending public primary care clinics in Malaysia is worryingly high. More importantly, one-third of the patients aged ≤50 years already had severely elevated LDL-c. These patients have a high ASCVD risk if they are not treated with lifestyle interventions and lipid-lowering therapy. Patients who attend public primary care clinics have to be regularly screened for hypercholesterolaemia from the age of 30 years old, while patients with confirmed FH should be referred to lipid specialists for specialised treatment.

Ethical approval

This study was approved by the respective research ethics committees in Malaysia, namely, the UiTM Research Ethics Committee [(REC/03/2020) (FB/48)] and the Medical Research Ethics Committee of the Ministry of Health Malaysia [NMRR-20-272-52797 (IIR)].

Authors' contributions

ASR: Conceptualization, Methodology, Validation, Writing - Original Draft, Visualization, Supervision, Project administration, Funding acquisition. **NQ**: Conceptualization, Methodology, Validation, Writing - Review & Editing, Visualization, Supervision, Project administration, Funding acquisition. **JDK**: Formal analysis, Investigation, Data Curation, Writing - Original Draft, Visualization. **RKA**: Validation, Formal analysis, Data Curation, Investigation, Writing - Review & Editing. **NB**: Validation, Formal analysis, Data Curation, Writing - Original Draft, Visualization, Supervision. **MSMY**: Validation, Formal analysis, Data Curation, Writing - Original Draft, Visualization, Supervision. **AK**: Investigation, Data Curation, Writing - Review & Editing. **YAC**: Formal analysis, Writing - Review & Editing. **AZR**: Formal analysis, Writing - Review & Editing. **HAH**: Validation, Writing - Review & Editing, Project administration. **SAR**: Validation, Writing - Review & Editing. **SFBS**: Validation, Writing - Review & Editing. **AFAA**: Validation, Writing - Review & Editing.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Professor Dr. Anis Safura Ramli was the Principal Investigator for Malaysia and Professor Dr. Nadeem Qureshi was the Principal Investigator for the United Kingdom. Financial support for this study was provided by the UKRI Medical Research Council & the Newton-Ungku Omar Fund (NUOF): The UK-Malaysia Joint-Partnership Call on Non-Communicable Diseases.

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Abbreviation

LDL-c	Low-Density Lipoprotein cholesterol
FH	Familial Hypercholesterolaemia
ASCVD	Atherosclerotic Cardiovascular Disease
EMR	Electronic Medical Record
MOH	Ministry of Health
FMS	Family Medicine Specialists
LDLR	Low-density lipoprotein receptor
LLM	Lipid-lowering medications
APOB	Apolipoprotein B
PCSK9	Proprotein convertase subtilisin/kexin type 9

References

1. Vaduganathan M, Mensah GA, Turco JV, Fuster V, Roth GA. The global burden of cardiovascular diseases and risk: a compass for future health. *J Am Coll Cardiol*. 2022;80(25):2361–2371.
2. Wan Azman WA. *Annual Report of the NCVD-ACS Registry 2014-2015. National Cardiovascular Disease Database (NCVD)*. Kuala Lumpur, Malaysia: National Heart Association of Malaysia (NHAM) and the Ministry of Health Malaysia; 2017. URL: https://www.malaysianheart.org/?p=ncvd&a=1250. Accessed January 1, 2020.
3. Ference BA, Ginsberg HN, Graham I, et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. *Eur Heart J*. 2017;38(32):2459–2472.
4. Du H, Shi Q, Song P, et al. Global burden attributable to high low-density lipoprotein-cholesterol from 1990 to 2019. *Front Cardiovasc Med*. 2022:1–10.
5. Mora S, Szklo M, Otvos JD, et al. LDL particle subclasses, LDL particle size, and carotid atherosclerosis in the Multi-Ethnic Study of Atherosclerosis (MESA). *Atherosclerosis*. 2007;192(1):211–217.
6. Goldstein JL, Brown MS. A century of cholesterol and coronaries: from plaques to genes to statins. *Cell*. 2015;161(1):161–172.
7. Lin CF, Chang YH, Chien SC, Lin YH, Yeh HY. Epidemiology of dyslipidemia in the Asia-Pacific region. *Int J Gerontol*. 2018;12(1):2–6.
8. Lee ZV, Llanes EJ, Sukmawan R, Thongtang N, Ho HQT, Barter P. Prevalence of plasma lipid disorders with an emphasis on LDL cholesterol in selected countries in the Asia-Pacific region. *Lipids Health Dis*. 2021;20(1):1–12.
9. Mohamed-Yassin MS, Baharudin N, Daher AM, et al. High prevalence of dyslipidaemia subtypes and their associated personal and clinical attributes in Malaysian adults: the REDISCOVER study. *BMC Cardiovasc Disord*. 2021;21(1):1–13. https://doi.org/10.1186/s12872-021-01956-0.
10. Karupaiah T, Chuah KA, Chinna K, et al. A cross-sectional study on the dietary pattern impact on cardiovascular disease biomarkers in Malaysia. *Sci Rep*. 2019;9(1), 13666.
11. Ramli AS, Taher SW. Managing chronic diseases in the Malaysian primary health care - a need for change. *Malaysian Fam Physician*. 2008;3(1):7–13.
12. Ramli AS, Qureshi N, Abdul-Hamid H, et al. Reducing premature coronary artery disease in Malaysia by early Identification of familial hypercholesterolemia using the familial hypercholesterolemia case ascertainment tool (FAMCAT): protocol for a mixed methods evaluation study. *JMIR Res Protoc*. 2023;12, e47911. https://doi.org/10.2196/47911. PMID: 37137823; PMCID: PMC10276320.
13. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American college of cardiology/American heart association task force on clinical practice guidelines. *Circulation*. 2019;139(25):e1082–e1143.
14. Food and Nutrition Institute. Philippine Nutrition Facts and Figures 2013: 8th National Nutrition Survey Overview.
15. Australian Bureau of Statistics. Australian health survey: biomedical results for chronic diseases, 2011-12. *J Chem Inf Model*. 2013;4364(0.55):1–74.
16. Cho SMJ, Lee H, Lee HH, et al. Dyslipidemia fact sheets in Korea 2020: an analysis of nationwide population-based data. *J Lipid Atheroscler*. 2021;10(2):202–209.
17. Cai L, Zhang L, Liu A, Li S, Wang P. Prevalence, awareness, treatment, and control of dyslipidemia among adults in Beijing, China. *J Atherosclerosis Thromb*. 2012;19(2):159–168.
18. Vee ML. *National Health Survey 2010. Stat Singapore Needl*. 2010:25–27.
19. Aekplakorn W, Taneepanichskul S, Kessomboon P, et al. Prevalence of dyslipidemia and management in the Thai population, national health examination survey IV, 2009. *J Lipids*. 2014;2014:1–13.
20. Bilitou A, Were J, Farrer A, et al. Prevalence and patient outcomes of adult primary hypercholesterolemia and dyslipidemia in the UK: longitudinal retrospective study

using a primary care dataset from 2009 to 2019. *Clin Outcomes Res*. 2022;14:189–203.
21. Micha R, Khatibzadeh S, Shi P, et al. Global, regional, and national consumption levels of dietary fats and oils in 1990 and 2010: a systematic analysis including 266 country-specific nutrition surveys. *BMJ*. 2014;15:348.
22. Doi T, Hori M, Harada-Shiba M, et al. Patients with LDLR and PCSK9 gene variants experienced higher incidence of cardiovascular outcomes in heterozygous familial hypercholesterolemia. *J Am Heart Assoc*. 2021;10(4), e018263.
23. Chua YA, Razman AZ, Ramli AS, Mohd Kasim NA, Nawawi H. Familial hypercholesterolaemia in the Malaysian community: prevalence, under-detection and under-treatment. *J Atherosclerosis Thromb*. 2021;28(10):1095–1107.
24. Razman AZ, Chua YA, Mohd Kasim NA, et al. Genetic spectrum of familial hypercholesterolaemia in the Malaysian community: identification of pathogenic gene variants using targeted next-generation sequencing. *Int J Mol Sci*. 2022;23(23), 14971.
25. Vallejo-Vaz AJ, De Marco M, Stevens CA, et al. Overview of the current status of familial hypercholesterolaemia care in over 60 countries-The EAS Familial Hypercholesterolaemia Studies Collaboration (FHSC). *Atherosclerosis*. 2018;277:234–255.
26. Banks E, Welsh J, Joshy G, Martin M, Paige E, Korda RJ. Comparison of cardiovascular disease risk factors, assessment and management in men and women, including consideration of absolute risk: a nationally representative cross-sectional study. *BMJ Open*. 2020;10(12):1–10.
27. Toori MA, Kiani F, Sayehmiri F, et al. Prevalence of hypercholesterolemia, high LDL, and low HDL in Iran: a systematic review and meta-analysis. *Iran J Med Sci*. 2018;43(5):449–465.
28. Tappia PS, Dhalla NS. Modifiable factors for reducing the gender difference in lipid control. *Clin Lipidol*. 2012;7(4):379–387.
29. Studziński K, Tomasik T, Windak A, et al. The differences in the prevalence of cardiovascular disease, its risk factors, and achievement of therapeutic goals among urban and rural primary care patients in Poland: results from the LIPIDOGRAM 2015 study. *J Clin Med*. 2021;10(23):45–52.
30. Ministry of Health Malaysia. Clinical practice guidelines on primary and secondary prevention of cardiovascular disease 2017. Health Technology assessment unit, medical development division, Putrajaya, Malaysia.