Prevalence of familial hypercholesterolemia among the southern Thai population: A preliminary study

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Research Article

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Abstract

Background

Familial hypercholesterolemia (FH) is an autosomal dominant disease. The prevalence of FH among the Thai population has not been reported. This study investigated the prevalence of FH by using the low-density lipoprotein cholesterol (LDL-C) cutoff of the Dutch Lipid Clinic Network (DLCN), as well as the LDL-C cutoff of the US Make Early Diagnosis to Prevent Early Deaths (MEDPED) criteria.

Methods

This retrospective study used health checkup data from 2015 from the southern Thai population. A total of 1,480 participants (335 males and 1,145 females) aged 18–94-years-old from southern Thailand were enrolled in this study. Anthropometric, demographic, and biochemical data were measured. Additionally, FH was defined by using the DLCN and the US MEDPED criteria.

Results

With the use of the DLCN, 7 subjects were identified as having probable FH, and the estimated prevalence of FH was 0.47% (1:211). By using the US MEDPED, 6 subjects were identified as having definite FH, and the estimated prevalence of FH was 0.41% (1:247). Most of the subjects with probable FH (71.43%) and definite FH (83.33%), as defined by the DLCN and the US MEDPED, respectively, did not take the lipid-lowering drug.

Conclusions

The prevalence of FH among the population in southern Thailand was between 1:211-1:247. Most FH subjects in Thailand may be underdiagnosed and undertreated. Thus, the early detection and treatment of FH should be implemented to prevent the development of cardiovascular disease.

Background

Familial hypercholesterolemia (FH) is an autosomal dominant disease [1]. FH is characterized by severe hypercholesterolemia and premature cardiovascular disease (CVD) [1]. Moreover, FH results from mutations in the low-density lipoprotein receptor (*LDLR*), apolipoprotein B100 (*APOB100*), or proprotein convertase subtilisin/kexin type 9 (*PCSK9*) genes [2].

The prevalence of FH is approximately 1:200-1:250 in the general population [3]. It has been theorized that the number of FH patients is more than 30 million worldwide. However, most FH patients (80% of the cases) are undiagnosed [4]. In addition, the prevalence of FH varies widely among various populations [5]. There are numerous criteria for diagnosing FH. For example, the Dutch Lipid Clinic Network (DLCN) [6] and the Simon Broome criteria are commonly used [7]. These criteria include family history of CVD, patient history of CVD, physical examination, untreated low density lipoprotein cholesterol (LDL-C) levels,

and DNA analysis [6–7]. Individuals were classified into definite/probable/possible/unlikely FH categories for DLCN criteria or into definite/possible FH categories for Simon-Broome criteria. Another criterion for the diagnosis of FH was the use of the US MEDPED [8]. In contrast to the previously stated criteria, this criterion was based only on LDL-C or total cholesterol (TC) levels according to age [8]. The World Health Organization recommended early detection and treatment for FH [9]. Moreover, the high efficacy of LDL-C-lowering therapy in patients with FH could lead to a better prognosis and may decrease the risk of CVD [6, 10]. PCSK9 inhibitors, which are novel lipid-lowering drugs, have been found to reduce LDL-C by more than 50-60% and significantly decrease cardiovascular events in FH patients [11].

Although genetic mutations in Thai FH patients have been reported [12–13], the prevalence of FH among the Thai population is currently unknown. Consequently, this study aimed to investigate the prevalence of FH in communities in southern Thailand.

Methods

Study population

This was a retrospective study. We collected data from health checkups in 2015 among populations from Nakhon Si Thammarat and Patthalung Provinces in southern Thailand. The data from a total of 1,545 subjects were included in the analysis. After the exclusion of subjects with triglyceride (TG) ≥ 400 mg/dl, secondary hypercholesterolemia, thyroid disease, liver disease, chronic kidney disease (CKD), cancer, and pregnancy, 1,480 subjects were finally included in the analysis. The sample size in this study was calculated by using the Taro Yamane formula ($n = N/1 + Ne^2$) [14]. This calculation was considered based on $N = 9.454 \times 10^6$ and an allowable error (e) = 0.05. After the calculation, the minimum sample size was approximately 400 subjects. Moreover, from a total of 1,480 subjects, the statistical power for the t test, F test, and χ^2 test (with an effect size of 0.5, 0.25, and 0.3, respectively, and at a confidence level of 95%) was equal to 0.99. The statistical power was analyzed by using the G*power 3.1.9.4 program [15]. The study was approved by the Ethical Committee of Walailak University (Protocol No. WUEC-21-049-0). All of the participants signed informed consent forms before enrollment in the study.

Data Collection And Clinical Outcomes

Data including demographics, behavioral lifestyles, and the medication used were collected by using a questionnaire. Anthropometric data, including body mass index (BMI), systolic blood pressure (SBP), and diastolic blood pressure (DBP), were also measured. Hypertension was defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg. Diabetes mellitus was defined as fasting blood sugar (FBS) ≥ 126 mg/dl. Individuals with smoking habits were classified as being smokers or nonsmokers. Alcohol consumption was classified as current alcohol consumption and no history of alcohol consumption. Moreover, exercise was defined as strenuous physical activity for at least 30 minutes for three or more days per week. Obesity was defined as BMI ≥25 kg/m^2. Blood samples were

obtained from the subjects after 12 hours of fasting. Furthermore, the serum lipid profiles including total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), TG, and FBS were measured by using the enzymatic method (KONELAB 20, Tokyo, Japan). Low-density lipoprotein cholesterol (LDL-C) was measured by using the Friedewald equation.

Diagnosis Of Fh

The diagnosis of FH was based on the Dutch Lipid Clinic Network (DLCN) [6] and the US Make Early Diagnosis to Prevent Early Deaths (MEDPED) criteria [8]. For the DLCN score, the subjects were divided into four categories: unlikely FH (< 3 points), possible FH (3-5 points), probable FH (6-8 points), and definite FH (> 8 points). Tendon xanthomas, a personal history of CVD, family history, and genetic mutations were scored zero in this study because of the unavailability of these data. For the US-MEDPED score, FH was diagnosed on the basis of the following age-dependent threshold values for LDL-C: < 20 years, ≥ 200 mg/dl; 20 to 29 years, ≥ 220 mg/dl; 30 to 39 years, ≥ 240 mg/dl; and > 39 years, ≥ 260 mg/dl.

Statistical analysis

Continuous variables are expressed as the mean and standard deviation (SD). The data were tested for normality. Differences between the two groups and multiple comparisons of the means among the groups were tested by using the Mann–Whitney U test and the Kruskal–Wallis test, respectively. Differences in the percentages between the groups were compared by using the chi-square (χ^2) test. The associations of cardiovascular risk factors, sociodemographic data, and FH were modeled by using multivariate logistic regression analyses. Covariates including age, sex, diabetes mellitus, hypertension, smoking, physical activity, alcohol consumption, obesity, education, and area of residence were included in the multivariate model. A p value < 0.05 was considered to be statistically significant. All of the data were analyzed by using SPSS (SPSS Inc., Chicago, IL; Version 21).

Results

A total of 1,480 subjects were included in this study. According to the DLCN criteria, there were 7 (0.47%) and 91 (6.15%) subjects with probable FH and possible FH, respectively. No individual had definite FH (0%), and most of the individuals (93.38%) were defined as having unlikely FH. The prevalence of FH was 0.47% (1:211). However, with the use of the US MEDPED, 6 subjects (0.41%) were defined as having definite FH, and 1,474 subjects (99.59%) were defined as having unlikely FH (Fig. 1). The prevalence of FH was 0.41% (1:247) (Fig. 1).

The basic characteristics of the study subjects are shown in Table 1. According to the DLCN criteria, age, SBP, BMI, TC, TG, and LDL-C levels were significantly higher, but HDL-C levels were significantly lower, in possible FH individuals than in unlikely FH individuals (p < 0.05). In addition, TC and LDL-C levels were significantly higher in probable FH individuals than in possible FH and unlikely FH individuals (p < 0.05).

Similarly, according to the US MEDPED criteria, TC and LDL-C levels were significantly higher in definite FH individuals than in unlikely FH individuals ($p < 0.05$). The prevalence of FH according to the DLCN and the US-MEDPED did not change with age. Furthermore, most of the probable/possible FH individuals (71.43%) identified by the DLCN and definite FH individuals (83.33%) identified by the US-MEDPED never received the lipid-lowering drug.

The prevalence of cardiovascular risk factors and sociodemographic data among the study subjects who were categorized according to the DLCN and the US MEDPED criteria are shown in Table 2. The association between cardiovascular risk factors and sociodemographic data and FH is shown in Table S1. Probable FH individuals (as identified by the DLCN) and definite FH individuals (as identified by the US MEDPED) had a higher frequency of receiving Bachelor's degrees in education than possible/unlikely FH individuals. Most of the individuals resided in urban areas (Table 2). Nevertheless, there was no association between cardiovascular risk factors and sociodemographic data or FH (Table S1.)

The FH prevalence based on the DLCN score and the US-MEDPED score is shown in Table 3. With the use of LDL-C > 190-249 mg/dl, LDL-C > 250-329 mg/dl, and LDL-C > 330 mg/dl via the DLCN, the prevalence of FH was 6.15%, 0.41%, and 0.07%, respectively. By using the US MEDPED, the prevalence of FH was higher in subjects aged > 40 years and LDL-C > 260 mg/dl (0.34%) than in subjects aged 20-29 years and LDL-C > 220 mg/dl (0.07%).

Altogether, 7 study subjects had probable FH according to the DLCN, and 6 study subjects had definite FH according to the US-MEDPED criteria. Six patients with definite FH according to the US-MEDPED were also diagnosed with probable FH according to the DLCN. Only one subject who was classified as having probable FH according to the DLCN criteria was not assessed as having definite FH according to the US MEDPED criteria.

Table 1
Basic characteristics according to the clinical FH diagnosis.

Characteristics	DLCN				US-MEDPED		
	Probable/ Definite FH	Possible FH	Unlikely FH	p-value	Definite FH	Unlikely FH	p-value
n	7/0 (0.47%)	91 (6.15%)	1,382 (93.38%)		6 (0.41%)	1,474 (99.59%)	
Male/Female	2/5	21/70	312/1,070	0.926 (χ^2 = 0.154)	2/4	333/1,141	0.530 (χ^2 = 0.394)
Age (years)	54.71 ± 19.13	54.81 ± 10.10**	52.12 ± 13.00	0.055	55.83 ± 20.70	52.28 ± 12.85	0.548
<40 years	1 (14.29%)	4 (4.40%)	215 (15.56%)	0.144 (χ^2 = 9.578)	1 (16.67%)	219 (14.86%)	0.928 (χ^2 = 0.458)
40-49 years	2 (28.57%)	26 (28.57%)	401 (29.02%)		1 (16.67%)	428 (29.04%)	
50-59 years	2 (28.57%)	34 (37.36%)	399 (28.87%)		2 (33.33%)	433 (29.38%)	
>59 years	2 (28.57%)	27 (29.67%)	367 (26.56%)		2 (33.33%)	394 (26.73%)	
SBP (mmHg)	133.14 ± 23.91	136.56 ± 18.84**	130.65 ± 18.88	0.007	134.67 ± 25.82	131.01 ± 18.92	0.669
DBP (mmHg)	83.00 ± 17.75	83.12 ± 12.61**	80.07 ± 11.74	0.076	84.33 ± 19.05	80.26 ± 11.81	0.859
BMI (kg/m^2)	22.72 ± 2.35	25.25 ± 3.78**	24.32 ± 4.09	0.032	22.90 ± 2.52	24.38 ± 4.07	0.419
Total cholesterol (mg/dl)	371.71 ± 50.24*	290.38 ± 23.36**	205.85 ± 35.75***	0.000	379.83 ± 49.80	211.15 ± 40.67	0.000
Triglyceride (mg/dl)	126.29 ± 47.19	142.78 ± 60.22**	117.42 ± 61.67	0.000	135.50 ± 44.27	118.96 ± 61.86	0.243
HDL-C (mg/dl)	57.43 ± 18.25	55.19 ± 12.83**	59.61 ± 16.44	0.058	57.17 ± 19.97	59.34 ± 16.27	0.474

* Probable/definite FH vs. Possible FH, $p < 0.05$, Mann–Whitney U test

**Possible FH vs. Unlikely FH, $p < 0.05$, Mann–Whitney U test

*** Probable/definite FH vs. Unlikely FH, $p < 0.05$, Mann–Whitney U test

Characteristics	DLCN				US-MEDPED		
	Probable/ Definite FH	Possible FH	Unlikely FH	p-value	Definite FH	Unlikely FH	p-value
LDL-C (mg/dl)	288.77 ± 36.06*	206.61 ± 15.50**	122.84 ± 32.12***	0.000	295.40 ± 34.57	128.10 ± 37.40	0.000
FBS (mg/dl)	91.43 ± 12.63	101.38 ± 29.98	97.62 ± 23.20	0.484	92.83 ± 19.05	97.84 ± 23.67	0.540
Lipid-lowering therapy							
Ever statin used	2 (28.57%)	16 (17.58%)	199 (14.40%)	0.411 (χ^2 = 1.779)	1 (16.67%)	216 (14.65%)	0.889 (χ^2 = 0.019)
Never statin used	5 (71.43%)	75 (82.42%)	1,183 (85.60%)		5 (83.33%)	1,258 (85.35%)	
* Probable/definite FH vs. Possible FH, p < 0.05, Mann–Whitney U test							
**Possible FH vs. Unlikely FH, p < 0.05, Mann–Whitney U test							
*** Probable/definite FH vs. Unlikely FH, p < 0.05, Mann–Whitney U test							

Table 2
Prevalence of cardiovascular risk factors and sociodemographic data in subjects categorized according to the DLCN and the US MEDPED criteria.

Characteristics	DLCN			US-MEDPED		
	Probable/ Definite FH	Possible FH /Unlikely FH	p-value	Definite FH	Unlikely FH	p-value
Diabetes mellitus (%)						
Yes	0 (0%)	100 (6.79%)	0.475 (χ^2 = 0.510)	0 (0%)	100 (6.78%)	0.509 (χ^2 = 0.437)
No	7 (100%)	1,373 (93.21%)		6 (100%)	1,374 (93.22%)	
Hypertension (%)						
Yes	3 (42.86%)	501 (34.01%)	0.622 (χ^2 = 0.243)	3 (50%)	501 (33.99%)	0.409 (χ^2 = 0.682)
No	4 (57.14%)	972 (65.99%)		3 (50%)	973 (66.01%)	
Current Smoking (%)						
Yes	0 (0%)	145 (9.84%)	0.382 (χ^2 = 0.764)	0 (0%)	145 (9.84%)	0.419 (χ^2 = 0.654)
No	7 (100%)	1,328 (96.37%)		6 (100%)	1,329 (90.16%)	
Exercise (%)						
Yes	6 (85.71%)	816 (55.40%)	0.107 (χ^2 = 2.593)	5 (60%)	817 (55.53%)	0.170 (χ^2 = 1.885)
No	1 (14.29%)	657 (44.60%)		1 (40%)	657 (44.47%)	
Current alcohol (%)						
Yes	2 (28.57%)	171 (11.61%)	0.163 (χ^2 = 1.942)	2 (33.33%)	171 (11.60%)	0.098 (χ^2 = 2.734)
No	5 (71.43%)	1,302 (88.39%)		4 (66.67%)	1,303 (88.40%)	
Obesity (%)						
Yes	1 (14.29%)	575 (39.04%)	0.180 (χ^2 = 1.795)	1 (16.67%)	575 (39.01%)	0.263 (χ^2 = 1.255)
No	6 (85.71%)	898 (60.96%)		5 (83.33%)	899 (60.99%)	

Characteristics	DLCN			US-MEDPED		
	Probable/ Definite FH	Possible FH /Unlikely FH	p-value	Definite FH	Unlikely FH	p-value
Education						
Bachelor degree	5 (71.43%)	379 (25.73%)	0.006 (χ^2 = 7.572)	4 (66.67%)	380 (25.78%)	0.023 (χ^2 = 5.199)
High school/Elementary school	2 (28.57%)	1,094 (74.27%)		2 (33.33%)	1,094 (74.22%)	
Area						
Urban	5 (71.43%)	301 (20.43%)	0.001 (χ^2 = 11.046)	4 (66.67%)	302 (20.49%)	0.005 (χ^2 = 7.770)
Rural	2 (28.57%)	1,172 (79.57%)		2 (33.33%)	1,172 (79.51%)	

Table 3
Potential FH prevalence based on the DLCN score and the US-MEDPED score.

	Number of people meeting the criteria	Prevalence
the DLCN		
LDL-C ≥ 190-249 mg/dl	91 (6.15%)	1:16
LDL-C ≥ 250-329 mg/dl	6 (0.41%)	1:247
LDL-C ≥ 330 mg/dl	1 (0.07%)	1:1,480
the US-MEDPED		
Age < 20 years, LDL-C ≥ 200 mg/dl	0 (0%)	0
Age 20-29 years, LDL-C ≥ 220 mg/dl	1 (0.07%)	1:1,480
Age 30-39 years, LDL-C ≥ 240 mg/dl	0 (0%)	0
Age >40 years, LDL-C ≥ 260 mg/dl	5 (0.34%)	1:296

Discussion

This was the first preliminary study in which we demonstrated the prevalence of FH among a population in southern Thailand. The FH prevalence according to the DLCN and the US-MEDPED criteria were 0.47% (1:211) and 0.41% (1:247), respectively. Currently, there are 69.93 million people in Thailand [16]. We assumed that the number of FH cases in Thai subjects may be approximately 286,713 to 328,671. Our

results were similar to a previous report that the overall prevalence of FH was 1:200-1:250 in the general population worldwide [3]. However, variations in the prevalence of FH have been observed among various populations. For example, previous prevalence data has demonstrated rates of 1:208 in Japan, 1:323 in China, 1:353 in Australia, 1:250 in the USA, 1:295 in Germany, 1:319 in the Netherlands, and 1:300 in Spain [5]. These differences may be due to the different ethnicities, as well as due to the different criteria applied among various studies. However, in some populations, including Tunisia (1:165), Denmark (1:137), Christian Lebanon (1:85), South Africans Afrikaners (1:72), and Ashkenazi Jews (1:67), the prevalence of FH was higher because of the “founder effect” [3, 17–19].

In this study, subjects with probable FH and definite FH had a Bachelor's degree in education. Most of the subjects also resided in the urban area. A previous study in a Thai population also demonstrated that subjects in urban areas had higher levels of TC and LDL-C than subjects in rural areas [20]. This may be due to the different behavioral lifestyles and sociodemographic data among subjects who resided in urban and rural areas. Nevertheless, education, area of residence, and other cardiovascular risk factors, such as age, sex, diabetes mellitus, hypertension, smoking, physical activity, alcohol consumption, and obesity, were not associated with FH in this study.

In this study, only 1 in 3 to 1 in 5 patients received lipid-lowering therapies. However, most of the individuals never received lipid-lowering therapies. This may be due to the fact that they lost self-awareness for their lipid control. Our results were consistent with those of previous studies [21–22]. In Thailand, 78% and 61.7% of hypercholesterolemic subjects were undiagnosed in 2004 and 2014 national health examination surveys, respectively [21–22]. This may be due to the low number of treatments and controls among Thai subjects. In addition, a previous study showed that only 9.7-19.8% of Thai adults aged ≥ 20 years with high LDL-C were treated [20]. Moreover, data on the prevalence of FH in Thai subjects have not been reported. Although two mutations of *LDLR* (D151Y and M391T) have been reported in Thai FH patients [12–13], other genetic mutations in Thai FH patients have not yet been elucidated. This suggests that FH subjects in Thailand may be underdiagnosed and undertreated. Similarly, a previous report in the USA, European, and Asian populations among 22 countries showed that most FH patients were underdiagnosed and undertreated in the general population [4]. Moreover, it was found that less than 1% of FH cases were diagnosed in most countries. However, a higher diagnosis rate of FH was observed in some countries (71% in the Netherlands, 43% in Norway, 19% in Iceland, 13% in Switzerland, 12% in the UK, and 6% in Spain) [4].

Studies of FH in Thailand have been rarely conducted. Furthermore, the reasons for the underdiagnosis of FH among Thai subjects are still unknown. However, we hypothesized that this may result from the lack of lipid screening and monitoring among the Thai population. Although district health hospitals have been distributed in all provinces of Thailand, there were no laboratory facilities or manpower for lipid determination. Moreover, the genetic analysis for FH in Thailand was not performed in the routine laboratory tests because of costs. The detection of gene mutations in Thai FH patients is usually conducted under research projects funded by universities or the government. Furthermore, the FH screening program in Thailand has not been set up, and FH awareness and education among physicians

and other health care professionals should be considered. A previous study showed that Asian physicians had a lower awareness of FH guidelines than did UK physicians [23]. In addition, a study of the awareness and knowledge of FH among 230 physicians in Japan, Korea, and Taiwan also demonstrated that only 47% were aware of the heritability, 27% of the prevalence, and 13% of the risk of cardiovascular disease relating to FH [24]. However, a small number of Thai subjects had LDL-C > 250-329 mg/dl (0.47%) and LDL-C > 330 mg/dl (0.07%). Many subjects in this study had LDL-C > 190-249 mg/dl (6.15%). It has been found that 2% of the subjects with LDL-C > 190 mg/dl were diagnosed with FH [25]. Moreover, the prevalence rates of FH (as diagnosed by the DLCN and the US MEDPED) were likely similar in this study. The prevalence rates of FH according to the DLCN and the US MEDPED were higher in subjects aged > 40 years than in subjects aged < 40 years. We suggested that subjects who had LDL-C > 190 mg/dl should be referred to lipid specialists or expert physicians to screen for FH. Moreover, subjects aged > 40 years should pay more attention to lipid control.

Our study had some limitations. First, the study subjects were from Nakhon Si Thammarat and Patthalung Provinces in southern Thailand. Therefore, the results may not represent the data from all regions of Thailand. Even though the number of study subjects appeared to be small, the sample size was calculated, and it was representative of the southern Thai population. Moreover, the statistical power for the data analysis was high. Second, data on family history, personal history, tendon xanthomas, and genetic analysis were not collected. We suggest that the prevalence of FH according to the DLCN criteria among these study subjects may be underestimated. Nevertheless, the US MEDPED criteria for the diagnosis of FH used only LDL-C levels according to age in this study. The family history, genetic detection, xanthomas, and history of CVD were not used in the US MEDPED criteria. Therefore, we could imply that the prevalence of FH among southern Thai subjects was approximately 1:247 by using the US MEDPED criteria. This estimated prevalence was not considerably different from the estimated prevalence via the DLCN (1:211). Moreover, the DLCN and the US MEDPED criteria used for the diagnosis of FH were developed from European and US populations. In practice, the lower serum lipid levels among the Asian population [26] may lead to false negative results when using the same LDL-C cutoff. These results suggest that the modified criteria for FH diagnosis among the Thai population should be further developed. Furthermore, other diagnostic criteria for FH in some studies in Hong Kong [27], Cyprus [28], and India [29] have used only serum lipids. Overall, we suggest that the varying FH criteria used in the diagnosis of FH among various populations may lead to a different prevalence of FH and difficulty in determining the true prevalence of FH.

Finally, the exact dosage, duration, and compliance of the lipid-lowering therapies were not recorded. Future studies with larger sample sizes and data collection of all FH diagnosis criteria from all regions of Thailand should be implemented.

Conclusions

The prevalence of FH among the population in southern Thailand was between 1:211-1:247. Moreover, most FH subjects in Thailand may be underdiagnosed and undertreated. The early detection and

treatment of FH should be implemented to prevent the development of cardiovascular disease. In addition, further genetic analysis, which is the gold standard for the diagnosis of FH in Thai FH patients, should be investigated.

Abbreviations

APOB100	Apolipoprotein B100
BMI	Body mass index
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
DLCN	Dutch Lipid Clinic Network
FBS	Fasting blood sugar
FH	Familial hypercholesterolemia
HDL-C	High-density lipoprotein cholesterol
LDL-C	Low-density lipoprotein cholesterol
LDLR	Low-density lipoprotein receptor
MEDPED	Make Early Diagnosis to Prevent Early Deaths
PCSK9	Proprotein convertase subtilisin/kexin type 9
SBP	Systolic blood pressure
SD	Standard deviation
TC	Total cholesterol
TG	Triglyceride

Declarations

Ethics approval and consent to participate

All of the participants provided written consent before entering the study. The study was approved by the Ethical Committee of Walailak University (Protocol No. WUEC-21-049-0).

Consent for publication

Not applicable.

Availability of data and material

All of the data generated or analyzed during this study are included in this published article and its supplementary information files.

Competing interests

The authors declare that they have no conflicts of interest.

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Authors' contributions

NJ was involved in the conception, design, data analysis and interpretation, preparation of the draft of the manuscript, and overall scientific management. MN performed the experiment, specimen collection, and data collection. CR participated in the discussion on the interpretation of the research content**.** All of the authors have read and approved the final manuscript.

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Figures

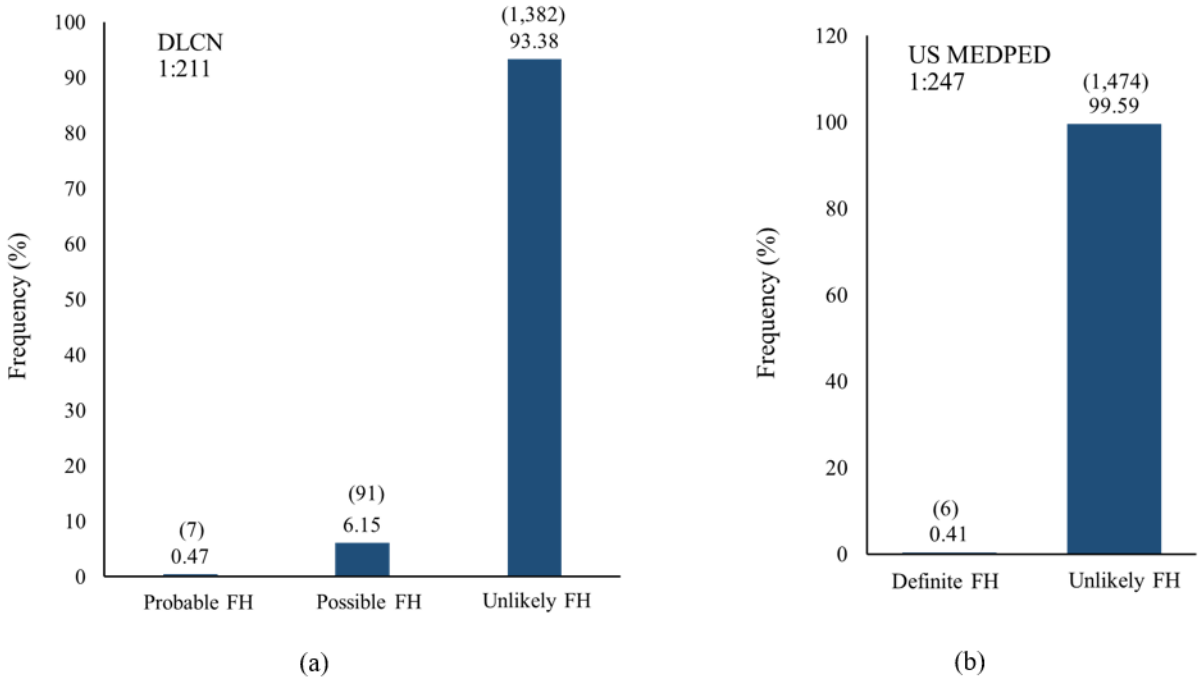

Figure 1

Prevalence of FH according to the DLCN (a) and the US MEDPED criteria (b).

Supplementary Files

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