

Assessment of family physicians' awareness and knowledge of familial hypercholesterolemia in governmental hospitals in Riyadh, Saudi Arabia

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ABSTRACT

Background: Familial Hypercholesterolemia (FH) is an inherited and complex multifactorial disease that can lead to early onset of coronary artery disease (CAD). Diagnosis, treatment, and management of FH require a well-trained physician with high awareness of the disease and different risk factors to avoid complications. **Materials and Methods:** This cross-sectional study evaluated family physicians' awareness and knowledge of FH using self-administered questionnaires in governmental hospitals in Riyadh, Saudi Arabia, during 2018. **Results:** A total of 225 family physicians completed the questionnaire, with a response rate of 58.4%. The mean age of respondents was 31.3 years and more than 59.1% were men. Although 72.4% of physicians rated their familiarity with FH as average and above, 48.4% of all participants had poor FH knowledge, while only 51.6% had acceptable FH knowledge. About 65.8% of physicians reported that they routinely take a detailed family history, perform a physical examination, and screen close relatives. Awareness of various clinical algorithms for diagnosis of patients with FH was very low at 52.0%. The mean FH knowledge and familiarity scores were significantly higher ($P < 0.001$) among participants who were older, had higher training levels, or longer years in practice. **Conclusions:** The current study revealed significant deficits in FH familiarity, awareness, knowledge, and practice among Saudi physicians. FH educational programs directed at all physicians involved in FH patients' management are necessary to improve physicians' knowledge of all aspects of FH management, including the importance of a mechanism for identifying people at risk for a genetic condition by a process of systematic family tracing.

Keywords: Cholesterol, coronary artery disease, familial hypercholesterolemia, genetic, questionnaire

Introduction

Familial Hypercholesterolemia (FH) is a complex, inherited, multifactorial disease characterized by elevated levels of serum low-density lipoprotein cholesterol (LDL-C), which results in excess deposition of cholesterol, and is one of the most common dominant autosomal diseases encountered in clinical medicine.^[1,2] The estimated global prevalence of heterozygous FH (HeFH) is 1 in 500,^[3] although prevalence is considerably higher in some populations because of founder effects.^[4] Although homozygous

FH is uncommon (general prevalence $< 1/1000000$), it is a critical condition that commences in infancy.^[5]

The magnitude of the problem in the Middle East, including Saudi Arabia, is largely unknown.^[6] FH is caused by mutations in the genes coding for low-density lipoprotein receptors, apolipoprotein B, or Proprotein Convertase Subtilase/Kexin type 9 (PCSK9).^[7] Untreated FH increases risk of early-onset coronary artery disease (CAD) by 10–20 times,^[8,9] while early diagnosis and treatment can improve morbidity and mortality from CAD.^[10] Worldwide, at least 20 million people have FH; the majority remain undetected because of lack of

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country-specific FH guidelines^[3] and of physicians specifically trained and practicing as lipid experts. Additionally, primary care physicians (PCPs) practicing in suburban and rural regions may not have access to specialist services. Hence, current treatment is suboptimal.^[11]

Several tools are available for diagnosis of adults with FH, including the Make Early Diagnosis to Prevent Early Death,^[12] Simon Broome,^[13] and Dutch Lipid Clinic Network (DLCN) criteria;^[14] however, the DLCN criteria are widely used because of their higher sensitivity.^[15,16]

Opportunistic screening by GPs could address the low reporting of FH and subsequently improve patient outcomes.^[16-18] Around 92% of lipid profiles in the community were requested by GPs, confirming that they play an essential role in detecting individuals with FH.^[19] However, physicians' FH knowledge and awareness is suboptimal.^[20-23] Additionally, varying specialties (PCPs versus specialists) do not differ significantly in their FH knowledge and awareness.^[22]

The current study aimed to assess FH awareness and knowledge among family physicians in Riyadh, Saudi Arabia, and to compare FH familiarity with physician characteristics, including age, gender, years of practice, and level of training.

Materials and Methods

Setting and IRB approval

This multi-center cross-sectional study was conducted among family physicians working at five governmental hospitals at Security Forces Hospital, Prince Sultan Military Medical City, King Fahad Medical City, King Abdulaziz Medical City and King Khalid University Hospital in Riyadh, Saudi Arabia between November and December 2018 using an anonymous self-administered electronic questionnaire in English distributed among family physicians working in the above-mentioned medical centers in all different professional levels aged below 60 years and any physicians from other specialties than family medicine and other healthcare professionals were excluded.

The study was approved by the Institutional Review Board College of Medicine, King Saudi University (no. E-16-1824) and ethical approval was taken from Security Forces Hospital Program Research Committee.

Questionnaire

A reliable and validated questionnaire was adopted from a previous similar study in Saudi Arabia.^[24] This questionnaire was basically developed by Bell *et al.*^[23] and Pang *et al.*^[22] with some additional questions by Batais *et al.*^[24] based on previous expert recommendations and international guidelines dealing with FH management.^[11,16,17] The questionnaire was initially tested by 20 physicians at King Khalid University Hospital in Riyadh, Saudi Arabia to ensure the questions were clear, understandable,

and logically ordered. A month later, the questionnaire was re-administered to the same group to ensure reliability and consistency. We used Kappa test agreement measures between test and retest; the average kappa value was 0.85 ($P < 0.001$). The questionnaire's reliability coefficient (Cronbach's alpha) in this pilot study was >0.7 .

The questionnaire consisted of two main sections. The first section assessed physician's demographic data including, gender, qualifications and training status, years of practice, and number of patients seen in clinic per month. The second section was questions about FH knowledge, practice, detection, and awareness, [see Table 1] Participants selected one correct answer to questions from a list of options provided. There were no open-ended questions.

Sample size

The sample size was calculated based on the results of the pilot study, where 68.7% of participants reported their familiarity with FH as average and above average. The appropriate sample size was calculated to be 331 participants based on a 5% margin of error, a confidence interval of 95%, and 68.7% average or above average familiarity with FH. Considering the nonresponse rate of 20%, the survey questionnaire was distributed to 385 participants.

Statistical analysis

You should write first how you calculated your sample size Data were analyzed using SPSS 22 (IBM Corp., New York). Continuous variables were expressed as mean \pm standard deviation; categorical variables were expressed as percentages. Chi-square tests were used for categorical variables. T-tests and one-way ANOVA were used for continuous variables. Logistic regression was used to assess risk factors. A P value < 0.05 was considered statistically significant.

Results

Descriptive statistics

Table 2 shows the participants characteristics. The questionnaire was distributed to 385 family physicians; 225 returned completed questionnaires, for a response rate of 58.4%. Respondents' mean age (\pm SD) was 31.32 (\pm 7.63) years, with 6.69 (\pm 8.81) mean years of practice; more than half (59.11%) were men, and more than two-thirds (70.22%) were general practitioners (GPs), and one third (29.78%) were cardiologists, endocrinologists, gynecologists, internists, and pediatricians.

Knowledge of FH management

Most family physicians (72.40%) rated their familiarity with FH as average and above [see Table 2]. The mean (\pm SD) overall FH knowledge score was 5.65 (\pm 2.15). Table 1 summarizes participants' overall FH knowledge. The clinical description of FH was underestimated by 56.4% of participants. Only 19.6% of physicians correctly identified the general prevalence of HeFH as 1:500, and only a third (33.8%) recognized its

Table 1: Summary of physicians' responses to questions about FH knowledge, practice, detection, and awareness

	n	Percentage
Knowledge		
Correctly described FH	127	56.4
Correctly identified the prevalence of heterozygous FH in the general population	44	19.6
Correctly identified the transmission rate to first degree relatives	76	33.8
Correctly identified the CVD risk in untreated FH	13	5.8
Correctly identified the age threshold for premature CVD in males	133	59.1
Correctly identified the age threshold for premature CVD in females	133	59.1
Correctly identified that genetic testing was not required to accurately diagnosis FH	90	40.0
Correctly identified LDL-C target for adult with FH	72	32.0
Correctly identified LDL-C target for FH adults with known CAD or diabetes	96	42.7
Selected statins to treat familial hypercholesterolemia	134	59.6
Selected a combination of statin and ezetimibe to treat severe hypercholesterolemia	84	37.3
Practice		
Routinely take a detailed family history, perform physical examination and screen close relatives for all patients with premature CAD	148	65.8
Had diagnosed patient with FH	68	30.2
Had managed FH patients under their care	72	32.0
Performed routine close relative screening with lipid profile of patients with FH	97	43.1
The most prevalent age for screening young people in kindred with FH was 13-18 years	71	31.6
Opinions and detection		
Selected family physicians as the most effective health care provider for the early detection of FH	189	84.0
Selected laboratory comment on lipid profiles, alert by the clinical software system, and direct telephone call from the laboratory to highlight patients at risk of FH	86	38.2
Awareness		
Aware of the clinical algorithms to diagnose patients with FH		
·The Simon Broome criteria	33	14.7
·The DLCN criteria	33	14.7
·The US MedPed Program	39	17.3
Aware of the cascade screening for patients with FH	60	26.7
Aware of any specialist clinical services for lipid disorders to whom patients can be referred	107	47.6
Aware of the new medications for FH patients beside statins		
·PCSK9 inhibitors	59	26.2
·MTP inhibitors	36	16.0
·Mipomersen (an antisense oligonucleotide inhibitors)	22	9.8

inheritance pattern. CVD risk in untreated FH patients was correctly scored by 5.8% of respondents as 20 times that of the general population; less than half (40.9%) of physicians could not identify the age threshold for premature CVD in males and the same percentage could not identify it in females. Only 40% of physicians knew that genetic testing was not required

Table 2: Physicians' demographics (n=225)

Characteristics	n (%)	Mean (SD)
Age (mean±SD)	31.32	7.63
Gender		
Male	133	59.11
Female	92	40.89
Level of training		
General practice	158	70.22
Senior registrar	20	8.89
Resident	24	10.67
Registrar	13	5.78
Consultant	10	4.44
Years of Practice (mean±SD)	6.69	8.81
Familiarity with FH *		
Below average	62	27.6
Average and above	163	72.40
Overall knowledge of FH [†] (mean±SD)	5.65	2.15

*The responses were classified into "below average" and "average and above" familiarity, where average and above familiarity with FH was defined for responses of 4 and above on the 7-point scale.[†] A mean knowledge score was computed by summing correct answers to all 11 knowledge questions.

to accurately diagnose FH. Only 32% of physicians selected LDL-C < 2.5 mmol/L as the target for adults with FH, while 42.7% selected LDL-C < 1.8 mmol/L as the target for FH adults with known CAD or diabetes. Statins, as the first-line medication for treating FH patients, were selected by 59.6% of physicians. The preferred combination to treat severe hypercholesterolemia is statins plus ezetimibe, which was selected by 37.3% of physicians. Data are shown in Table 1.

Practices

About two-thirds (65.8%) of physicians reported that they routinely take a detailed family history, perform a physical examination, and screen close relatives of all patients with premature CAD. The screening for lipid profile for adults with FH was 32.0% and for FH adults with known CAD or diabetes was 42.7%. Of the respondents, 30.2% diagnosed patients with FH, and 32% managed FH patients under their care. The most prevalent age for screening young people for FH is 13–18 years, which was selected by 31.6% of physicians [Table 1].

Opinions and FH detection

Most participants (84%) selected family physicians as the most effective in detecting early FH and screening first-degree relatives. Laboratory comments on lipid profile alerting to possible FH, a direct telephone call from the laboratory, and alerts by the clinical software system, were all selected as the preferred choice in helping physicians detect FH by only (38.2%) of respondents [Table 1].

Awareness of FH management

The results showed that awareness of various clinical algorithms for FH diagnosis was very low; 14.7% identified the DLCN criteria, 14.7% the Simon Broome criteria, and 17.3% the US MedPed Program. A high percentage (73.3%) were unaware of cascade screening for patients with FH, and 52.4% were unaware of specialized clinical services for lipid disorders to which patients can be referred. A clear majority were unaware of new FH

medications besides statins, including PCSK9 inhibitors (73.8%), Mipomersen (an antisense oligonucleotide inhibitor) (90.2%), and Lomitapide (MTP) inhibitors (84%) [Table 1].

Regarding relationships between FH familiarity and mean knowledge scores and physician demographics overall, 48.4% of participants had poor FH knowledge, while only 51.6% had acceptable knowledge. Of the 51.6% of physicians with acceptable knowledge, 55.2% rated their FH familiarity as average and above. There were no significant associations between FH familiarity and physicians' demographics except for years of practice ($P < 0.05$) [Table 3].

Logistic regression analysis showed that participants with > 15 years' experience were 88% less likely to be familiar with FH compared to those with ≤5 years' experience (OR = 0.129, 95% CI = 0.017–0.997, $P < 0.049$) [Table 4].

The mean knowledge scores by physicians' characteristics and FH familiarity were calculated [see Table 5]. The mean knowledge score increased significantly ($P < 0.001$) with age, being highest (7.13) among those aged >45 years. There was a significant difference ($P < 0.001$) in mean knowledge score by training level, being highest among residents at 6.92, and lowest among general practitioners at 5.23. The mean knowledge score of physicians who rated their familiarity with FH as "average and above" was significantly ($P < 0.002$) higher compared to those who rated it as "below average," at 5.92 versus 4.93, respectively.

Figure 1 shows a summary of physician responses to the most selected risk factors that further increase CVD risk in patients

with FH. In general, 59.6% of participants identified smoking as a risk factor, 50.7% selected type 2 diabetes, and 39.1% selected elevated Lp (a).

Table 3: The relationship between FH familiarity and physicians' demographics

Characteristics	Familiarity with FH				P
	Below average		Average and above		
	n (62)	Percentage	n (163)	Percentage	
Age					
≤30 years	45	72.6	108	66.3	0.104
31-45 years	16	25.8	41	25.2	
>45 years	1	1.6	14	8.6	
Gender					
Male	33	53.2	100	61.3	0.268
Female	29	46.8	63	38.7	
level of training					
General practice	48	77.4	110	67.5	0.608
Senior registrar	5	8.1	15	9.2	
Resident	4	6.5	20	12.3	
Registrar	3	4.8	10	6.1	
Consultant	2	3.2	8	4.9	
Years of Practice					
≤5 years	47	75.8	103	63.2	0.039*
6-10 years	11	17.7	27	16.6	
11-15 years	3	4.8	16	9.8	
> 15 years	1	1.6	17	10.4	
Overall knowledge of FH					
Acceptable knowledge	26	41.9	90	55.2	0.075
Poor knowledge	36	58.1	73	44.8	

*Significant P value, Chi Square Test

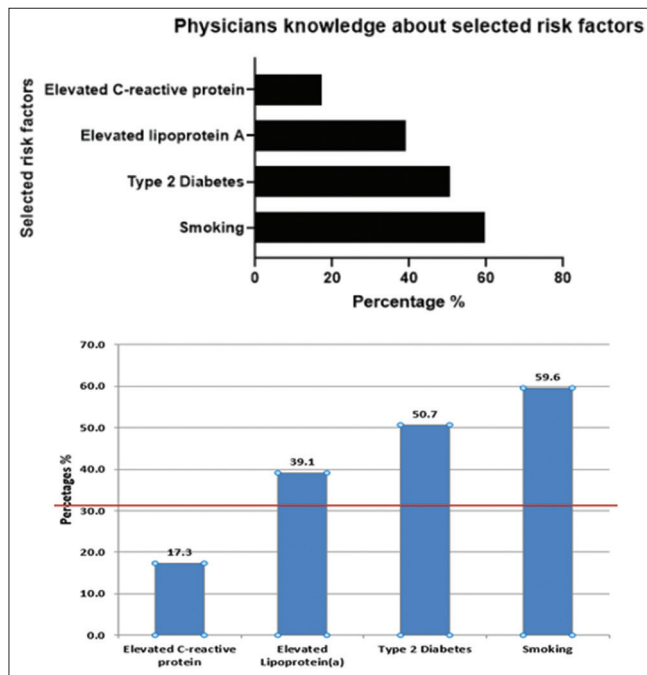


Figure 1: Physician responses to the most selected risk factors that further increase CVD risk in patients with FH

Table 4: Low familiarity with FH as predicted by physicians' characteristics

Characteristics	Odds Ratio	95% CI		P
		Lower	Upper	
Age				
≤30 years [†]	1			
31-45 years	0.937	0.477	1.838	0.849
>45 years	0.171	0.022	1.343	0.093
Gender				
Male [†]	1			
Female	1.395	0.773	2.517	0.269
Level of training				
General practice [†]	1			
Senior registrar	0.621	0.764	0.263	2.221
Resident	0.174	0.458	0.149	1.413
Registrar	0.582	0.688	0.181	2.610
Consultant	0.491	0.573	0.117	2.799
Years of Practice				
≤5 years [†]	1			
6-10 years	0.893	0.409	1.950	0.776
11-15 years	0.411	0.114	1.479	0.173
> 15 years	0.129	0.017	0.997	0.049*

*Significant P value, Chi Square Test

Table 5: Mean knowledge score by physicians' characteristics and FH familiarity

Characteristics	n	Mean Knowledge score	P
Age			
≤30 years	153	5.1307	< 0.001*
31-45 years	57	6.6667	
>45 years	15	7.1333	
Gender			
Male	133	5.6767	0.845
Female	92	5.6196	
Level of training			
General practice	158	5.2278	< 0.001*
Senior registrar	20	6.9000	
Resident	24	6.9167	
Registrar	13	6.2308	
Consultant	10	6.1000	
Years of Practice			
≤5 years	150	5.1200	< 0.001*
6-10 years	38	6.1842	
11-15 years	19	7.4737	
> 15 years	18	7.0556	
Familiarity with FH			
Below average	62	4.9355	0.002*
Average and above	163	5.9264	

* Significant P value, Chi Square Test

Discussion

We conducted this cross-sectional survey to determine FH knowledge, awareness, detection, and clinical practices of family medicine physicians in Riyadh, Saudi Arabia, a country well known for its high consanguinity rate and underreporting of FH mutations, indicating poor awareness of CVD genetic risks.^[25] Consistent with a previous study Batais in Saudi Arabia in 2017,^[24] most participants rated themselves as average and above average in FH familiarity, at 68.7%, and 72.4%, respectively. However, this contrasts with the results of Rangarajan study in 2016 in Tamil Nadu,^[21] where only 27.9% of participants rated their familiarity as average and above. Generally, overall FH knowledge among family physicians in Riyadh can be considered average, a result which is better compared to the previous Saudi study.^[24] The current study revealed significant deficits in FH familiarity among Saudi physicians even though most of them perceived their familiarity with FH as average and above average. A very low percentage (5.8%, and 19.6%) correctly identified the CVD risk in untreated FH and the general prevalence of HeFH. Additionally, a low percentage (<40%) correctly identified LDL-C targets for adults with FH, correctly identified the transmission rate to first-degree relatives, and selected a combination of statin and ezetimibe to treat severe hypercholesterolemia.

Similarly, the data highlighted substantial deficits in FH awareness, especially of various clinical algorithms for FH patients' diagnosis, cascade screening, and of new, non-statin medications for FH, such as Mipomersen. Such findings are consistent with A UK-based survey in 2016 in France, Rangarajan study in 2016 in Tamil Nadu, Asia-Pacific countries: a pilot

study in 2015 and Bell DA data in western Australia and Batais study in Saudi Arabia in 2017,^[20-24] and indicate significant gaps in knowledge and awareness of FH. Therefore, our study demonstrates the need and importance of conducting successful educational intervention and training programs for family physicians regarding FH.

Achieving the optimal target LDL-C levels of FH patients of <2.5 mmol/L or <1.8 mmol/L with known atherosclerotic cardiovascular disease is imperative to reducing lifetime CVD risk.^[11,26,27] In the current study, less than half of respondents correctly identified LDL-C targets for FH adults and for FH adults with known CAD or diabetes. This was consistent with Batais *et al.*'s results,^[24] with an even lower percentage of correct answers.

Being aware of potential therapeutic options for FH is critical for appropriate management. The current data revealed that most physicians were unaware of highly effective new medications for lowering LDL-C, illustrated by increased use of PCSK9 inhibitors.^[28] This finding resembles the findings of Batais *et al.*^[24] and Schofield *et al.*^[20]

Consistent with previous studies from Saudi Arabia, Asia, and the United Kingdom (UK),^[20,22,24] most respondents in the current study selected family physicians as the most effective health care provider for detecting FH early and screening first-degree relatives. A different finding was reported from Western Australia where most GPs described themselves as the most effective healthcare provider to detect FH, even though this study showed that GPs had suboptimal awareness and knowledge of FH.^[23]

Only 39% of family physicians in the current study recognized increased Lp (a) as an adjunctive risk factor in FH patients. This is considered a low percentage compared to what was reported in Japanese, Taiwanese, and Korean studies at 51%, 66%, and 83%, respectively.^[22]

In contrast to a similar previous Saudi study,^[24] the current study showed that more than half of participants had acceptable FH knowledge (7.1% versus 51.6%). Our findings highlighted that FH familiarity scores tended to be higher among physicians with more experience, indicating that experience improves their ability to effectively manage FH, which agrees with the previous study's results.^[24]

The current study findings highlighted the need for ongoing FH educational programs, that should be directed to all physicians involved in FH patients' management, since such education programs have been implemented in the UK and significantly improved physicians' knowledge in all aspects of FH management, including the importance of cascade screening.^[20]

The main limitations of this study were the small sample size and the cross-sectional design.

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Conflicts of interest

There are no conflicts of interest.

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