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Identification and Analysis of Dyslipidemia Risk Factors in a Population-Based Study: Data from the Fasa Persian Cohort

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Abstract

Background & Objectives: Dyslipidemia is a major public health issue worldwide characterized by changes in lipid index such as cholesterol, Low Density Lipoprotein (LDL), High Density Lipoprotein (HDL) and triglycerides (TG).This manuscript aimed to investigate the associated factors of dyslipidemia in Fasa Persian cohort study.

Materials & Methods: This cross-sectional study was conducted on the baseline data of Fasa Persian cohort with an initial sample size of 10129 subjects (35-70 years old) in 2021 in Iran. Univariate and multivariate logistic regression models were used to assess the relationship between covariates and dyslipidemia.

Results: The number of males in this study was 4572 and the number of females was 5557. The prevalence of dyslipidemia in them was 40.8% and 27.7%, respectively (p-value < 0.001), and the prevalence of dyslipidemia in the whole study population was 3407 (33.6%). Dyslipidemia was also more common in alcoholics, opium users, smokers, high glycemic index and higher body mass index (BMI). Men were 1.68 times more likely to have dyslipidemia than women. Opium and cigarette smokers were 1.15 and 1.36 times more likely to have dyslipidemia than non-smokers, respectively. Also, as BMI increases, the likelihood of dyslipidemia becomes higher than the reference group (below 18.5), and people with a BMI greater than 30 have the highest obesity range.

Conclusions: This study showed that the prevalence of dyslipidemia in the studied population was higher in men than in women and several risk factors such as gender differences, body mass index, smoking and opium use are effective in the prevalence of dyslipidemia.

Keywords: Dyslipidemia, Cholesterol, High Density Lipoprotein, Related Factors

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Introduction

Dyslipidemia, including hypercholesterolemia, hypertriglyceridemia, elevated low-density lipoprotein (LDL) cholesterol, and reduced high-density lipoprotein (HDL) cholesterol as a major modifiable risk factor, has become a major public health concern worldwide (1). Dyslipidemia can be broadly classified into two groups: primary (familial) or secondary (acquired) dyslipidemia. Primary dyslipidemia results from a variety of genetic conditions that a person may inherit at birth, whereas secondary dyslipidemia usually results from other underlying causes, such as unhealthy diet, medications (e.g., amiodarone, glucocorticoids), hypothyroidism, uncontrolled diabetes, and/or a sedentary lifestyle (2). Dyslipidemia, particularly high levels of LDL

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(hypercholesterolemia), is one of the most common risk factors for the progression of atherosclerosis and subsequent vascular disease. It is essentially characterized by elevated levels of lipids or fats in the bloodstream. The development of atherosclerosis is influenced by various factors such as endothelial damage, dyslipidemia, inflammatory and immunological factors, plaque erosion or rupture, hypertension and smoking (3). The most important laboratory test to perform is the fasting lipid profile, which typically assesses levels of LDL, HDL, triglycerides and total cholesterol. In addition, for a more comprehensive evaluation, v-LDL, total cholesterol:HDL, and LDL:HDL ratios may be included in the test (4).

According to the World Health Organization (WHO) regions in 2018, the global prevalence of dyslipidemia was estimated to be 39% in adults of both sexes (5). According to a study in Saudi Arabia, one in four people suffer from dyslipidemia (6). In Iran, according to studies conducted in 2014, the prevalence of dyslipidemia was 63.4% in Shahrood (7) and 40% in Ramsar (8), highlighting that the prevalence of dyslipidemia is quite high in different parts of Iran. Globally, the burden of dyslipidemia in various diseases is constantly increasing (9). According to WHO, in 2018, 17.9 million deaths occurred every year due to cardiovascular diseases, which is 31% of all deaths worldwide (10). Dyslipidemia is the primary and most important risk factor for atherosclerosis of the blood vessels of the heart and brain, which causes coronary heart disease and cerebrovascular disease (11, 12). One-third of ischemic heart disease cases worldwide are secondary to hypercholesterolemia, and the disease is responsible for an estimated 2.6 million (4.5%) deaths worldwide (13). Evidence suggests that elevated triglyceride (TG) levels are associated with ischemic stroke (14). Hypertriglyceridemia and low HDL cholesterol levels are common in individuals with obesity and type 2 diabetes mellitus (T2DM), which in turn increases the risk of cardiovascular disease (11, 15, 16). Hedayatnia et al (2020) found in their study that blood triglyceride levels are significantly associated with myocardial infarction in men (17). Thus, all changes in the lipoprotein profile are associated with the risk of cardiovascular disease (18). Because the prevalence of dyslipidemia varies in different regions due to cultural, social, environmental, economic, and ethnic differences (19, 20), the major associated factors also vary in different societies.

Studies have identified some factors associated with dyslipidemia, such as lifestyle, genetic factors, environmental factors, dietary factors, and obesity, but more research is needed to identify associated risk factors and develop methods to manage dyslipidemia in different populations (8, 21-23). It is noteworthy that WHO has set the control of cardiovascular disease and diabetes (together with respiratory disease and cancer) and their underlying risk factors as the first major target to reduce 25% of deaths from noncommunicable diseases by 2025 (13). Therefore, further studies in different communities to determine the factors associated with dyslipidemia can help reduce complications and promote cardiovascular health and identify appropriate preventive measures. In Iran, the risk of cardiovascular disease is significantly high and the management of blood lipid levels is often suboptimal, despite the increasing attention of the health care team and individuals. Also, the prevalence of dyslipidemia in Iran has increased in the last decade due to cultural-economic diversity and lifestyle changes. On the other hand, most of the studies in the country have been conducted on patients with small sample size; therefore, further studies on the prevalence of dyslipidemia and its potential risk factors are needed to reduce the burden of cardiovascular diseases. Therefore, the aim of this study was to determine the prevalence of dyslipidemia and identify associated risk factors in the population of Fasa Persian cohort.

Materials and Methods

Study design and population

We conducted this cross-sectional study to determine the prevalence of dyslipidemia and its

associated factors in adolescents by analyzing data from a population-based cohort study in 2021. The Fasa-Persian Cohort is one of 22 cohorts conducted in Iran with the aim of investigating factors influencing the incidence of cardiovascular disease in the age group 35-70 years. Several experts have formulated recommendations for lipid screening, including the "lipid profile" to assess cholesterol and triglyceride levels. These guidelines vary with respect to the recommended age for initiation of screening and the frequency of screening for dyslipidemia. In general, it is recommended that routine lipid screening begin in men at age 35 years (in the absence of other cardiovascular risk factors) or at age 25 years (if the patient has other cardiovascular risk factors). Similarly, it is suggested that routine lipid screening in women should begin at age 45 years (in the absence of other cardiovascular risk factors) or at age 30 to 35 years (if the patient has other cardiovascular risk factors) (3). The Fasa Persian cohort in Sheshdeh and Qara Bolagh region started in 2015 with an initial sample size of 10, 129 subjects and baseline information including a comprehensive questionnaire of demographic variables, socioeconomic status, medical information (history of communicable and noncommunicable diseases, physical examinations, blood pressure and pulse, oral and dental condition, nutritional status via food frequency questionnaire (FFQ 125)), history of smoking/opium use, anthropometric measurements; Electrocardiography (ECG), body composition, biological samples (blood, urine and nails), these were completed for 10, 129 participants in 2016. This information was collected in the form of face-to-face interviews by interviewers trained by the central team of the Persian cohort (24, 25).

Inclusion and exclusion criteria

All subjects in the age group of 35-70 years in Sheshdeh and Qara-Balagh region who gave informed consent to participate in the cohort study. Subjects who could not answer the questions, mental patients, and physically disabled subjects were excluded from the study.

Definition of Dyslipidemia

For each person enrolled in the study, 15-25 mL of fasting blood was collected according to established standards. Primary tests including blood lipids, biochemical indices, CBC, etc. were performed and the results were recorded for each individual. To define dyslipidemia, the parameters of the blood samples collected at baseline were used. These parameters included total cholesterol ≥240 mg/dL, LDL cholesterol > 160 mg/dL or HDL cholesterol < 40 mg/dL, or triglycerides > 200 mg/dL, the presence of at least one of which was considered dyslipidemia (11).

Statistical Analysis

Frequencies and percentages were used to report variables classified by age group and sex. Independent samples t-test was used to compare blood parameters in age and sex subgroups. Univariate and multivariate logistic regression models were also used to assess the relationship between covariates and dyslipidemia. In this way, variables with a significance level of less than 0.2 in the univariate analysis were included in the multivariate model to control for confounding. An adjusted odds ratio (AOR) with a 95% confidence interval (95%CI) was used to report associations. In all analyses, a significance level of less than 0.05 was considered significant. The Statistical Package for the Social Sciences (SPSS) software (version 26.0) was used for data analysis.

Results

In this study 10129 subjects including 4572 (45.1) men and 5557 (54.9) women aged 35 to 70 years participated. The mean of total cholesterol was 185.08± 39.16 mg/dL, LDL cholesterol was 107.83± 32.59 mg/dL, HDL cholesterol was 51.01± 15.89 mg/dL and TG was 131.8± 82.41 mg/dL. The mean concentration of

total cholesterol, LDL, HDL was higher in women than in men (P<0.001), but the mean concentration of TG was higher in men than in women (P<0.001) (Table 1). The highest mean TG concentration was found in men in the age group 44-35 years and in women in the age group 55-64 years. The highest concentrations of total cholesterol were found in men and women in the age groups >65 and 55-64 years, respectively. Table 1 shows the demographic characteristics of the subjects.

Table 1. Mean and standard deviation of lipid profile according to sex and age groups

Sex/ Age	Total	Triglycerides	Total cholesterol	LDL cholesterol	HDL cholesterol
Male	N (%)	Mean± SD	Mean± SD	Mean± SD	Mean± SD
35-44	1846 (40.4)	142.21± 6.93	176.71± 36.62	102.53± 30.67	45.79± 13.45
45-54	1378 (30.1)	139.98± 4.16	181.27± 38.07	105.95± 31.42	47.49± 14.48
55-65	1096 (24)	126.97± 3.62	178.41± 39.23	105.24± 32.51	47.89± 14.56
>65	252 (5.5)	110.37± 8.73	182.21± 39.36	106.11± 32.02	53.02± 17.47
Total	4572 (100)	136.14±91.37	178.74± 37.89	104.41± 31.45	47.20± 14.37
Female					
35-44	2180 (39.2)	117.01±71.89	182.09± 35.80	105.42± 30.25	53.53± 16.58
45-54	1777 (32)	132.48± 4.34	193.63± 39.59	112.88± 33.49	54.29±1 5.98
55-64	1240 (22.3)	140.04± 8.57	198.66± 40.93	116.16± 35.12	54.58± 16.34
≥65	360 (6.5)	134.68± 9.17	194.83± 44.85	112.25± 38.15	55.65± 17.33
Total	5557 (100)	128.23±74.07	190.30± 39.42	110.64±33.25	54.15± 16.39
P-Value Men Vs. Women		<0.001	<0.001	<0.001	<0.001

The prevalence of dyslipidemia in all study participants was 33.6% (95%CI: 32.7-34.6), which was significantly higher in men than in women (P<0.001). The prevalence of high cholesterol, high LDL, low HDL, and high TG was 8.2% (95%CI: 7.6-8.7), 5.8% (95%CI: 5.3- 6.3), 20.1% (95%CI: 19.4- 20.8), and 13.31% (95%CI: 12.6- 13.9), respectively. The prevalence of low HDL and high TG was higher in men than in women, and the prevalence of high total cholesterol and high LDL was significantly higher in women than in men (P<0.001). The prevalence of dyslipidemia by sex and age group is shown in Table 2. The mean fasting blood glucose (FBS) was 95.29±33.57 mg/dL in subjects with dyslipidemia and 91.3±26.92 mg/dL in healthy subjects (p<0.001).

Table 2. The prevalence of high total cholesterol, high LDL, low HDL and high triglyceride concentrations according to sex and age (%)

Sex/ Age	Total	High triglycerides	High total cholesterol	High LDL cholesterol	Low HDL cholesterol	dyslipidemia
Male	N	N (%)	N (%)	N (%)	N (%)	N (%)
35-44	1846	333 (18)	105 (5.7)	75 (4.1)	609 (33)	820 (44.4)
45-54	1378	233 (16.9)	84 (6.1)	61 (4.4)	411 (29.8)	572 (41.5)
55-64	1096	110 (10)	57 (5.2)	51 (4.7)	307 (28)	401 (36.6)
≥65	252	14 (5.6)	17 (6.7)	11 (4.4)	50 (19.8)	74 (29.4)
Total of men	4572	690 (15.1)	263 (5.8)	198 (4.3)	1377 (15.1)	1867 (40.8)
Female						
35-44	2180	196 (9)	129 (5.9)	281 (12.9)	83 (3.8)	513 (23.5)
45-54	1777	235 (13.2)	199 (11.2)	186 (10.5)	135 (7.6)	496 (27.9)
55-64	1240	182 (14.7)	188 (15.2)	149 (12)	137 (11)	416 (33.5)
≥65	360	45 (12.5)	48 (13.3)	42 (11.7)	38 (10.6)	115 (31.9)
Total of women	5557	658 (11.8)	564(10.1)	393 (7.1)	658 (11.8)	1540 (27.7)
P-Value Men Vs. women		<0.001	<0.001	<0.001	<0.001	<0.001

The comparison of the prevalence of dyslipidemia in the strata of different variables is shown in Table 3. As can be seen, the prevalence of dyslipidemia is higher in married subjects and lower in divorced subjects. It is most common in subjects with higher BMI. Dyslipidemia is also more common in alcoholics, opium users and smokers.

Table 3. Compare the prevalence of dyslipidemia based sex, marital status, age groups, BMI, smoking, opium use and alcohol consumption

Variable		Total	dyslipidemia N (%)		P-Value
Sex	Male	4572	1867	40.8	<0.001
	Female	5557	1540	27.7	
Marital status	Single	373	111	29.8	0.046
	Married	9009	3062	34.0	
	Widow	645	210	32.6	
	Diverse	102	24	23.5	
Age groups (year)	35-44	4026	1333	33.1	0.211
	45-54	3155	1068	33.9	
	55-64	2336	817	35.0	
	≥65	612	189	30.9	

BMI	<18.49	583	111	19.0	<0.001
	18.5- 24.99	4123	1194	29.0	
	25- 29.99	3625	1406	38.8	
	≥30	1775	686	38.6	
Active smoking	Yes	2734	1112	40.7	<0.001
	No	7395	2295	31.0	
Passive smoking	Yes	1883	736	39.1	<0.001
	No	8246	2671	32.4	
Opium use	Yes	2353	968	41.1	<0.001
	No	7776	2439	31.4	
Alcohol Consumption	Yes	211	100	47.4	<0.001
	No	9918	3307	33.3	

The results of the logistic regression are presented in Table 4. The variables sex, opium use, active smoking, FBS and BMI influence dyslipidemia. Men were 1.68 times more likely to have dyslipidemia than women. Opium and cigarette smokers were 1.15 and 1.36 times more likely to have dyslipidemia than non-smokers, respectively. Also, the higher the BMI, the greater the likelihood of dyslipidemia compared to the reference group (below 18.5), and subjects with a BMI above 30 have the highest rate of obesity.

Table 4. Logistic regression analysis of the relationship between different factors on dyslipidemia

Influencing Factors		β	OR	95% CI		P- Value
				Lower	Upper	
Gender	Male vs. female	0.626	1.87	1.68	2.091	<0.001
Alcohol consumption	Yes Vs. No	0.223	1.25	.94	1.67	.125
Opium use	Yes Vs. No	0.139	1.15	1.01	1.31	.031
Active Smoking	Yes Vs. No	0.307	1.36	1.15	1.61	<0.001
Passive Smoking	Yes Vs. No	-0.162	0.85	0.72	1.01	.060
Age	35-44 (Ref)	-	-	-	-	-
	45-54	0.039	1.04	.94	1.15	.427
	55-64	0.104	1.11	.99	1.24	.062
	≥65		.97	.81	1.18	.796
BMI	<18.49 (Ref)		-	-	--	
	18.5- 24.99	0.774	2.17	1.74	2.72	<0.001
	25- 29.99	1.376	3.96	3.16	4.97	<0.001
	≥30	1.499	4.48	3.53	5.69	<0.001
FBS		0.005	1.005	1.003	1.006	<0.001

Discussion

Dyslipidemia is considered to be highly significant and requires special attention due to the risk of atherosclerosis cardiovascular disease. This study focused on the prevalence of dyslipidemia and related factors in the Fasa Persian Cohort in Iran. In this study, the prevalence of dyslipidemia in the general population was 33.6% with prevalence of total hypercholesterolemia 8.2%, high LDL 5.8%, low HDL 20.1%, and hypertriglyceridemia 13.31%. Dyslipidemia was also more common in men than in women. According to a meta-analysis study in 2014, the prevalence of dyslipidemia is higher in men than in women in almost all studies in Iran, but in the southern coastal areas, Arak and Rasht in Iran, dyslipidemia is more common in women (26). The reason for this difference may be due to different lifestyle and dietary culture or physical activity. These factors may lead to different prevalence of dyslipidemia in different parts of the world (27). The global burden of dyslipidemia has increased over the past thirty years (28). Therefore, it is necessary to take measures to control dyslipidemia to reduce the burden of cardiovascular disease. This study showed that the prevalence of dyslipidemia in men is associated with high triglyceride levels. According to the results, triglyceride levels are higher in men than in women, especially in men aged 35-44 years. Of course, women also have high triglyceride levels by the age of 55. Consistent with this study, Karpov in Russia showed that men's triglyceride levels are 16.4% higher than women's. Based on this, it can be said that the prevalence of hypertriglyceridemia increases with age regardless of gender (29). In addition, this study showed low HDL levels in men, which is consistent with studies in various countries such as Japan, China, and Korea (30-32). Low HDL levels combined with high triglycerides or cholesterol may lead to lipid peroxidation and systemic inflammation (33, 34).

Several studies have reported an inverse relationship between TG and HDL (35, 36). Higher HDL levels in women may reduce mortality from cardiovascular disease (31). Elevated triglyceride levels are involved in the development and progression of atherosclerosis and may lead to myocardial infarction, stroke, and peripheral vascular disease (37). Significant increases in triglyceride levels can also lead to fatty liver disease and pancreatitis (38). A healthy lifestyle including proper diet, regular exercise, smoking cessation, and weight loss are some of the suggested strategies to reduce triglyceride levels (39). This study showed that the prevalence of dyslipidemia was higher in women than in men in terms of total cholesterol and LDL, which is consistent with various studies (32, 40). Pirillo reported in his study that in 2018 in different parts of the world, including Asia, Africa, Oceania, Europe, America, and Australia, the level of total cholesterol was higher in women than in men, and only in Central Europe was the level of total cholesterol equal in women and men (28). High LDL levels are the eighth leading risk of death in 2019, and more than one-third of deaths from ischemic heart disease and stroke are associated with high LDL levels in both developed and developing countries (41). This study identified several risk factors for dyslipidemia, including gender differences, body mass index, smoking, and opiate use. According to the results of this study, men are 1.68 times more likely to have dyslipidemia than women, which is similar to the results of some other studies. Results In a study conducted by Li Y et al. (2018) in China, men had a higher prevalence of dyslipidemia than women (30). In Wang's study, the prevalence of dyslipidemia in women was significantly higher in the entire study population, which is inconsistent with the results of our study (42). The reason for this difference may be that in Iran, the main consumers of health education and lipid management centers are women, and

men are less welcome to the programs of these centers.

According to the results of this study, subjects with a body mass index above 30 are more likely to have dyslipidemia. The results of some studies in different parts of the world are consistent with the results of this study (30, 42, 43). Gebreegziabiher reported in his study that dyslipidemia increased significantly with BMI. 79.3% of overweight subjects and 95.2% of obese subjects had dyslipidemia (43). In the study of Li Y et al., dyslipidemia was associated with problems such as obesity, abdominal obesity, and hypertension (30). In Wang's study, the risk of dyslipidemia was mainly associated with obesity in men and hypertension in women (42). Obesity has increased dramatically worldwide in recent decades and is a risk factor for cardiovascular disease, which may be caused by dyslipidemia (44).

This study showed that dyslipidemia was 1.36 times higher in smokers than in nonsmokers. Mouhamed et al (2013) showed in their study that smoking is associated with dyslipidemia and increased triglycerides and decreased HDL (45). Wang et al. (2021) showed that gender, smoking, central obesity, average daily salt intake, average daily oil intake, T2DM, hypertension and physical activity were associated with dyslipidemia (46). The negative effect of smoking is caused by increased insulin resistance and the profile of the disorder is similar to insulin resistance, increased TG and decreased HDL (47). Therefore, since smoking-induced dyslipidemia can be prevented and corrected, the development of educational programs in this regard, especially among young subjects, is essential.

This study showed that the odds of dyslipidemia increased 1.15 times with opium use. The results of some studies are consistent with the results of the present study and the relationship between opium addiction and dyslipidemia (48). Rahimi et al. reported a decrease in HDL levels in opium addicts in their study (49). However, some other studies reported no significant association between opium addiction and dyslipidemia (50, 51). The hypocholesterolemia observed in opium addicts is attributed to the lack of healthy food because addicts spend their money on drugs instead of food (52).Therefore, there is a difference in the effect of opium on lipid indices in humans. Differences in opioid-induced dyslipidemia may be related to oral versus inhaled use and duration of use.

Strengths and Limitations

This was a study based on data from the Persian Fasa cohort in Iran, which examined several risk factors related to dyslipidemia such as gender, body mass index, smoking and opium. This study also has limitations. First, this cohort study included only rural residents and did not include the prevalence of dyslipidemia in urban residents. Second, the participants in this cohort study represent only about 20 percent of the total rural population of Fasa.

Conclusion

The prevalence of dyslipidemia in the community studied was reported to be high. Considering that the high prevalence of dyslipidemia can lead to serious and health-threatening complications, including cardiovascular complications, it is necessary for health system managers to make necessary plans to reduce the prevalence of dyslipidemia and improve the level of health. It is also necessary to make a policy to encourage men to use the services of health centers to maintain their health.

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Conflicts of Interest

The authors declare that they have no competing interests.

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Ethical Considerations

Written informed consent was obtained from each participant to participate in the first phase of the cohort study. Participants were assured of anonymity and confidentiality of their information. The study protocol adhered to the tenets of the Declaration of Helsinki. The study protocol was approved by the National and Regional Ethics Committee of FUMS (code IR.FUMS.REC.1399.169) and the Research Board of Fasa University of Medical Sciences (number code: 99176).

Code of Ethics

IR.FUMS.REC.1399.169

Authors' Contributions

Study Design: AD, SHK, MB, MF, MRB and MS; Data collection: AD; Software: AD; Data analysis: MA and AD, SR; Writing (original draft): SHK, BS, AK and AD; Review and Editing: SHK, MB, AD, BS, And AK; Project administration: AD; All authors revised the manuscript for important intellectual content and approved the final version.

Data Availability Statement

The data that support the findings of this study are not publicly available but can be available from the corresponding author upon reasonable request.

List of Abbreviations

Body mass index (BMI), low density lipoprotein (LDL), High-density lipoproteins (HDL), Triglyceride (TG), food frequency questionnaire (FFQ), electrocardiography (ECG), adjusted Odds Ratio (AOR).

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