HYPERCHOLESTEROLEMIA AND ITS RELATED RISK FACTORS AMONG KURDISH POPULATION IN DUHOK, KURDISTAN REGION, IRAQ

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ABSTRACT

Background: Cardiovascular disease is a major health problem in the world and its increasing prevalence is threatening the human health. Hypercholesterolemia is a cardinal risk factor for cardiovascular disease especially coronary artery disease; therefore, its recognition, treatment, and control have become an important clinical and public health issue. This study aimed to estimate the prevalence of hypercholesterolemia and investigate its related risk factors in Kurdish population in Duhok province, Kurdistan Region, Iraq.

Methods: A cross-sectional study was carried out, from January 2021 to December 2022, to investigate serum cholesterol levels in a sample of Kurdish individuals attending out-patient department (OPD) of Medicine at Azadi General Teaching Hospital and Duhok's specialized laboratory center, Duhok, Kurdistan region, Iraq. This study included 616 participants. They were 231 males and 385 females, with age range 20 - 79 years. Participants were enrolled by consecutive sampling procedure. Pregnant women were excluded from the study. Main outcome measures were serum lipids, glucose, glycated haemoglobin and thyroid stimulating hormone.

Results: The overall prevalence of hypercholesterolemia in Kurdish population in Duhok was 39.12% (95% Cl 38.5 - 40.1) with prevalence values of 38.68 % (95% CI 35.17 - 41.33) in men and 39.61% (95% CI 38.40 - 47.38) in women. The prevalence of hypercholesterolemia was higher in urban residents than in rural residents (45.52% vs 30.32%, p=0.001). Moreover, Hypercholesterolemia prevalence was relatively low in individuals younger than 40 years for both men and women, and began to increase at the age of more than 40 year, then decreased at the age of 50 year for men and 60 years for women. Hypertension, alcohol consumption, obesity, hypothyroidism and diabetes were associated with an increased risk of hypercholesterolemia.

Conclusion: hypercholesterolemia prevalence is high among Kurdish population in Duhok governorate. Individuals over 40 years were identified as population at high risk for hypercholesterolemia

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Keywords: Serum cholesterol, hypercholesterolemia, prevalence, Kurdish population

Hypercholesterolemia (HCh) is a major determinant of morbidity and mortality associated with cardiovascular diseases. Hypercholesterolemia is widely recognized as the primary cause of atherosclerosis, as well as it associated with several health consequences, including hypertension, metabolic syndrome, and cardiovascular diseases[1]. In the last decades, the prevalence of hypercholesterolemia has increased worldwide due to rapid economic development and the resultant adverse lifestyle (increased high-fat diets and reduced physical activity)[2].

There are two types of HCh: genetic and

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acquired. The first type is a less common genetic disorder, including homozygotes and hetrozygotes familial hypercholesterolemia (FH); while the second is a condition that affects many populations. Acquired hypercholesterolemia is caused commonly by medical conditions such as hypothyroidism, diabetes mellitus, nephrotic syndrome, and cholestasis. Furthermore, some medications such as cyclosporine and thiazide diuretics, as well as, excessive intake of dietary cholesterol and smoking have been linked with increased risk of HCh[3,4]. However, the commonest cause is polygenic HCh which results from an interaction of unidentified genetic factors compounded by a sedentary lifestyle and an increased intake of saturated and trans-fatty acids[5,6].

Globally, the prevalence of HCh is relatively high. The World Health Organization (WHO) reported a global prevalence of 39% in 2008[7]. Recent estimates have shown that around 28.5 million people from the adult population (aged 20 years or older) have high levels of total serum cholesterol, with the reported prevalence being 11.9%[8]. Data on HCh in the Middle East are controversial. In a study conducted in 14 African and Middle Eastern (AFME) countries, the dyslipidemia level was as high as 70%[9].

However, the prevalence and epidemiological characteristics of HCh in this region have been scarcely studied. To date, most investigations in Iraq have been limited to particular cities or have concentrated on specific ages[10,11]. In this study, we conducted cross-sectional analysis of the Kurdish population of Duhok province to estimate hypercholesterolemia prevalence and investigate its risk factors in the region.

MATERIALS AND METHODS:

Study design, population and sample collection:

The data for this study were derived from a cross-sectional survey centred on lipid disorders (hypercholesterolemia and hypertriglyceridemia) and related risk factors (the Duhok Lipid Disorders Study, DLDS). The LDS was conducted in Duhok city from January 2021 to December 2022, aiming to investigate the prevalence and genetic factors for lipid disorders, the first part was on hypertriglyceridemia[12]. We obtained a representative sample of individuals with age range of 20 and above who attended out-patient department (OPD) of Medicine at Azadi General Teaching Hospital and Duhok's specialized laboratory center, Duhok, Kurdistan region, Iraq; as attendant of patients. We registered a total of 616 participants for the study over the course of seven months, of these, 231 males and 385females.

Participants were enrolled by consecutive sampling procedure and instructed to attend the Duhok specialized laboratory center in the morning after an overnight fasting for 12-14 hours. Subjects completed a pre-test questionnaire including anthropometric data and residency. Participants living in countryside were classified as rural residents, whereas those living in larger urban settings (Duhok city) were classified as urban residents. Pregnant women were excluded from the study.

Blood samples were collected between 9:00-11:30 a.m., about 10 mls of blood were withdrawn by venipuncture from the anticubital vein and collected in a gel tubes. A sample of 2 ml of blood were collected immediately into DMD-DISPO tube containing K3-EDTA as anti-coagulant for measuring HbA1c percent, the sera were separated by centrifugation using a HITACHI centrifuge (model O5P-21) at 5000 rpm for 10 minutes and used for measuring serum lipids, glucose and TSH. All the biochemical measurements were done by standard laboratory procedure using clinical chemistry

analyzer Cobas 6000 Roche (open, automated, discrete and random access).

Definition of variables:

Hypercholesterolemia was defined as serum cholesterol level ≥ 240 mg/dl[13,14]. Hypertension was defined as systolic blood pressure (SBP) ≥ 140mmHg and /or diastolic blood pressure (DBP) ≥ 90 mmHg, a self-reported history of hypertension or use of antihypertensive medications[15]. Diabetes mellitus (DM) was defined according to American Diabetes Association (ADA), either as a self-reported history of DM, or by fasting serum glucose level of > 126 mg/dL, Random serum glucose > 200 mg/dL or HbA1c level of > 6.5%.[16] Body mass index was calculated as weight (in Kilograms) divided by the square of height (in meters; kg/m2). According to the WHO criteria, BMI was categorized into underweight (<18.5 kg/m2), normal weight 18.5-24.9kg/m2), overweight (25.0-29.9 kg/m2) and obese (>30 kg/m2)[17]. Based on the guidelines for dyslipidemia prevention and treatment in adults (NCEP ATP) , normal TC level was defined as < 200 mg/dl, mild-moderate HCh as serum TC 200 - 239 mg/dl, and severe HCh as serum TC ≥ 240 mg/dl; normal TG < 150 mg/dl, borderline high TG 150 – 199 mg/dl, high TG 200 – 499 mg/dl; and very high TG ≥ 500 mg/dl; optimal LDL-C < 100 mg/dl, near optimal 100 -129 mg/dl, borderline high LDL-C 130 – 159 mg/dl, high LDL-C 160 – 189 mg/dl, and very high LDL-C ≥ 190 mg/dl; low HDL-C < 40 mg/dl, high HDL-C > 60 mg/dl[13,18]. Thyroid status was defined according to the level of TSH as normal (TSH: 0.27 – 4.2 mIU/L), hypothyroidism (TSH: > 4.2 mIU/L) or hyperthyroidism (TSH < 0.27)[19].

Ethical approval:

The study was approved by the scientific committee of College of Medicine, University of Duhok and by the research ethics committee of Directorate General of Health (Reference number 13072021-7-15, in 13, Jul, 2021) After we interviewed the participants, we explained the purpose of the study to each subject and received verbal consent.

Statistical analysis:

Descriptive statistics were calculated for all demographic characteristics and laboratory results. Category variables were presented as percentage. Additionally, continuous variables were assessed for normality using the student t-test to compare category variables between male and female participants. Chi-square test (X2) test was used to compare groups. Data were processed using Statistical Package for Social Science (SPSS 25, IBM: USA). All tests were two-sided, and differences were considered statistically significant at the level of $p \leq 0.05$.

RESULTS:

Demographic characteristics and clinical laboratory results

Table 1 presents the demographic characteristics and clinical laboratory results of the participants. The study included 616 participants, consisting of 231(37.5%) men and 385(62.5%) women, with a median age of 47 years. Approximately 58% of the participants were urban residents. Furthermore, 19.3% were cigarette smokers, 5.8% were alcoholic and 93.5% were overweight and obese. The prevalence of hypertension and DM was 40.3% and 31.8% respectively. All selected demographic characteristics and clinical laboratory results were compared between males and females. It was found that, in women, there was a higher proportion of urban residents, hypertension and individuals with DM. The proportion of smoking and drinking was lower in women compared with men (P=0.001). Moreover, women had higher levels of FSG, HbA1c and TSH in comparison with men ($p < 0.001$).

Table 1: Demographic and laboratory characteristics of studied subjects

Variables	Overall (n=616)	Males (n=231) Mean±SD	Females (n=385) Mean±SD	*p*-value
Age(years)	47.63±10.63	46.32±10.25	48.42±10.79	0.018
Median(IQR)	47(20,67)	46(20,86)	47(20,67)	
Residence, n (%) Urban Rural	358(58.1) 258(41.9)	99(43.2) 132(56.8)	259(67.2) 126(32.8)	< 0.010
Smoking, n (%) Yes No	119(19.3%) 497(80.7%)	114(49.35) 117(50.65)	5(1.30) 380(98.70)	0.001
Alcohol, n (%) Yes No	36(5.8) 580(94.2)	35(15.15) 196(84.85)	1(0.26) 384(99.74)	0.001
BMI, n (%) Normal Overweight Obese	40(6.5) 362(58.8) 214(34.7)	16(6.93) 105(45.45) 110(47.62)	24(6.24) 257(66.75) 104(27.01)	0.001
Hypertension, n (%) Yes No	248(40.3%) 368(59.7%)	86(37.23) 145(62.77)	162(42.08) 223(57.92)	0.230
DM, n (%) Yes No	196(31.8) 420(68.2)	57(24.68) 174(75.32)	139(36.10) 246(63.90)	0.031
TC (mg/dl)	230.40±36.6	227.78±35.37	231.98±36.70	0.169
TG (mg/dl)	203.31±105.41	213.47±116.31	194.43±98.21	0.030
HDL-C (mg/dl)	47.56±10.30	43.6±8.67	49.86±10.48	< 0.0001
LDL-C (mg/dL)	148.01±31.76	147.83±33.01	148.12±31.01	0.912
Glucose (mg/dl)	123.66±57.21	118.00±47.21	133.45±61.79	<0.001
HbA1C (%)	6.48±1.81	6.18±1.49	6.66±1.96	<0.001
TSH (mIU/L)	3.72±7.50	2.77±6.38	4.28±8.05	<0.001

Unless specified, data are presented as mean ±standard deviation.

Independent Student's t-test was used to compare the means of variables.

$P \leq 0.05$ was considered significant.

n=number, SD=standard deviation, BMI=body mass index, WC=waist circumference, SBP=systolic blood pressure, DBP=diastolic blood pressure, DM = diabetes mellitus, TC = total cholesterol, TG= triglyceride, HDL-C= high-density lipoprotein cholesterol, LDL-C= low-density lipoprotein cholesterol, HbA1c=hemoglobinA1c, TSH=thyroid stimulating hormone.

Serum cholesterol levels and hypercholesterolemia prevalence:

Table 2 shows the serum cholesterol level and HCh in 616 individuals from Duhok governorate. The mean serum cholesterol was 230.40±36.6, in men it was 227.78±35.37 mg/dl and 231.98±36.70 mg/dl in women (p=0.160). The prevalence of HCh was 39.12% (95% Cl 38.5 to 40.1). In men, it was 38.68% (95%Cl 35.17-41.33), with no significant difference compared with 39.61 %(95% Cl 38.40-47.38) in women (p=.0.57). In participants below the age of 40 years (n= 95), 33.64% had HCh while in those above

the age of 40 years (n= 421), 43.84% had HCh. Higher serum cholesterol levels and HCh were observed in participants from urban areas than in those from rural areas (p<0.001). Additionally, individuals who were aged >40 years, engaged in drinking and had hypertension had higher serum cholesterol levels and higher prevalence of HCh (p<0.05). Moreover, participants who were obese exhibited higher prevalence of HCh (p<0.001).

Table 2: Serum cholesterol level and prevalence of hypercholesterolemia in various groups.

Variables	Serum cholesterol (mg/dl) mean±SD	*p*-value	Hypercholesterolemia % (95 %CI)	*p*-value
Total (n= 616)	230.40±36.6		39.12 (38.5 to 40.1)	
Age				0.005
<40 (n= 95)	219.32±42.63	0.001	33.64(21.65-38.81)	
≥40 (n= 421)	233.34±34.29		43.84(43.08-49.36)	
Gender				
Male	227.78±36.37	0.16	38.68(35.17-41.33)	0.57
Female	231.98±36.70		39.61(38.40-47.38)	
Residence				
Urban	239.51±38.0	<0.001	45.52(38.12-47.43)	<0.001
Rural	218.73±34.0		30.32(25.75-35.32)	
Smoking				
Yes	230.84±37.88	0.54	40.39(38.50-42.97)	0.23
No	228.57±30.89		38.89(37.29-46.10)	
Alcohol Drinking				
Yes	247.05±22.87	0.005	71.20(65.26-73.20)	<0.05
No	229.37±37.06		37.75(28.25-38.71)	
Obese				
Yes	230.90±35.83	0.001	59.63(49.83-66.72)	< 0.001
No	226.88±39.02		27.35(24.0-42.28)	
Hypertension				
Yes	236.91±32.03	0.0001	45.49.53(40.34-54.68)	< 0.05
No	226.02±38.82		29.53(27.98-34.61)	
Diabetes mellitus				
Yes	229.34±38.29	0.62	44.47(41.73-48.70)	0.049
No	230.90±35.83		36.48(33.81-35.45)	
Hypothyroidism				
Yes	234.29±39.78	0.28	45.96(39.14-47.89)	0.073
no	229.77±36.07		34.55(32.86-39.89)	

Data are presented as mean±SD and percentages, as indicated.

Independent Student's t-test was used to compare the means of variables and Chi-square test was used to compare percentages.

P ≤ 0.05 was considered significant.

n=number, SD=standard deviation

Age and gender distribution of the prevalence of hypercholesterolemia:

In both men and women, the prevalence of HCh was relatively low in individuals younger than 40years, and began to increase at the age of >40, then decreased at the age of 50 for men and 60 for women (Figure 1). In respect to severe HCh (TC ≥

240 mg/dl),241 of the studied individuals had severe HCh; the age groups 40-49 years and 50-59 years had higher prevalence of HCh (31.9 and 31.1%, respectively) than other age groups as shown in figure 4.2.

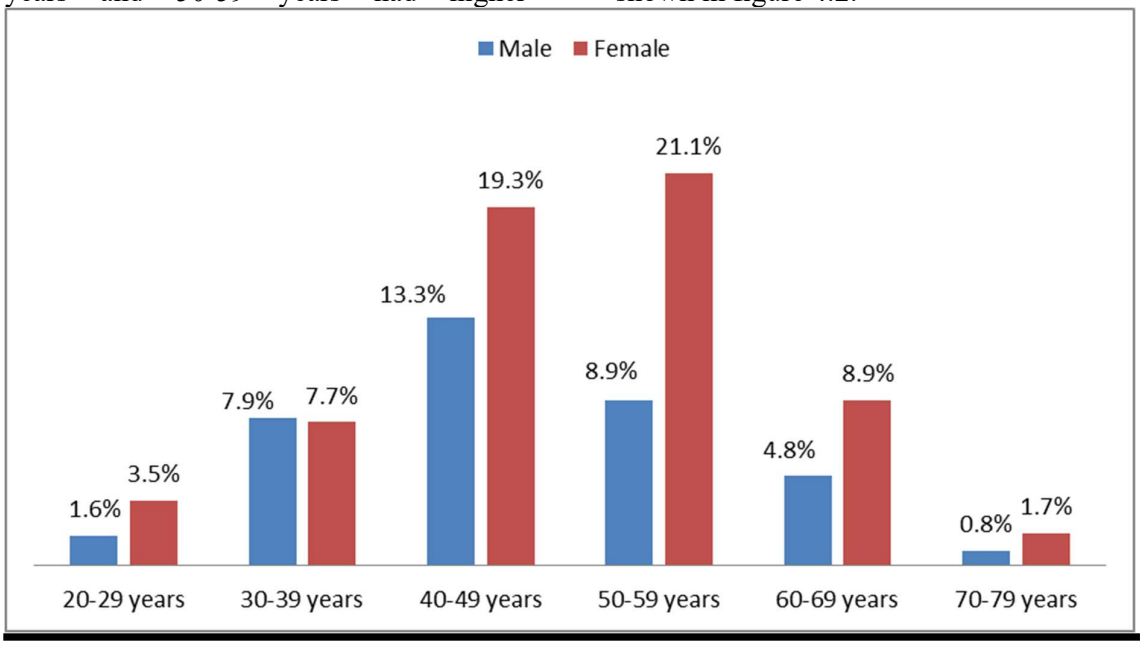

Figure 1: Age and gender distribution of the prevalence of hypercholesterolemia in 616 individuals.

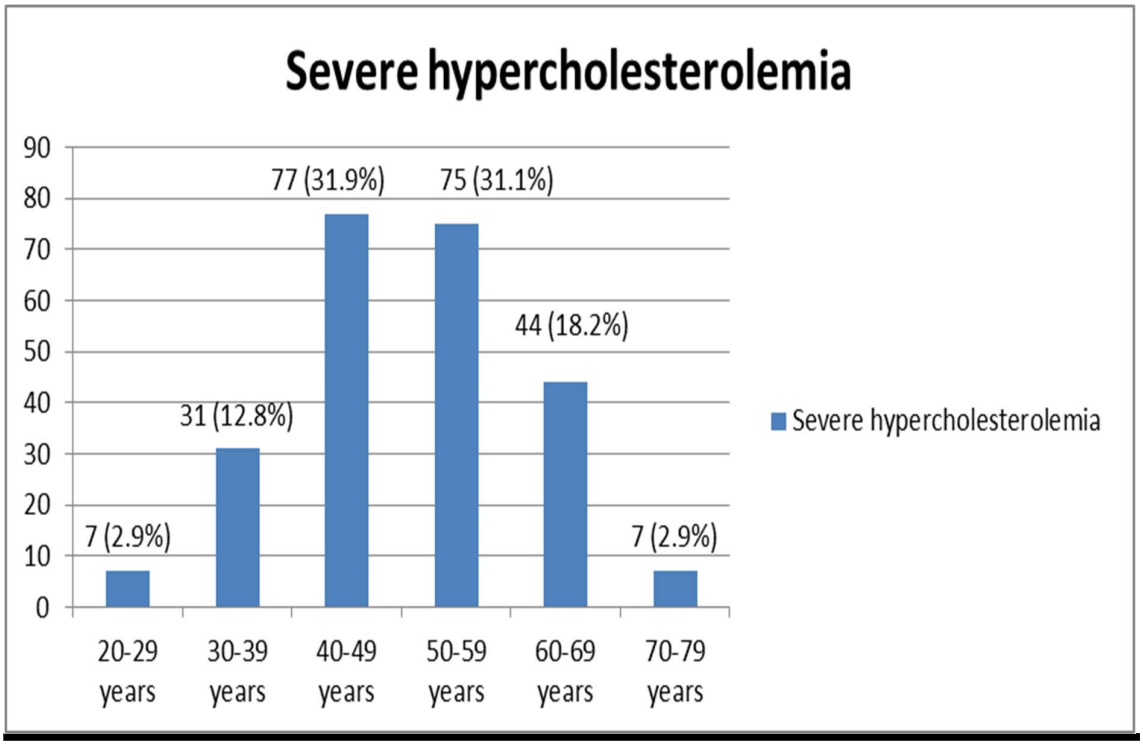

Figure 2: Prevalence of severe hypercholesterolemia (TC ≥ 240 mg/dl) in different age groups (n= 241).

Comparison of serum cholesterol levels with FSG, HbA1c and serum lipid levels:

As shown in table 3, individuals with severe HCh demonstrated higher levels of FBS, HbA1c, HDL-C and TG level in

comparison with participants in the normocholesterolemia group ($p < 0.05$). Moreover, individuals with severe HCh exhibited higher values of BMI and blood pressure compared to normocholesterolemia group ($P < 0.01$). To further clarify the correlation of serum cholesterol level with FBS, HbA1c and serum lipid levels Pearson's correlation coefficient was applied. Meanwhile, SCh exhibited an almost linear relationship with TG and HbA1c (Table 4).

Table 3: association of biochemical and anthropometric parameters with cholesterol level in studied subjects stratified by serum total cholesterol level

Variables	Total (n=616)	Normocholesterolemia (< 200 mg/dl) (n=100)	Mild-moderate-HCh (200 - 239) (n=275)	Severe HCh (≥ 240 mg/dl) (n=241)	p-value
TC (mg/dl)	230.40±36.61	166.09±21.98	227.61±10.36	260.28±21.9	< 0.001
Glucose(mg/dl)	123.66±57.21	107.48±48.0	122.78±51.63	133.30±65.84	< 0.05
HbA1C (%)	6.48±1.81	6.20±1.73	6.37±1.71	6.72±1.94	< 0.05
HDL-C(mg/dl)	47.82±10.66	46.12±9.40	46.87±9.25	49.61±12.31	< 0.05
LDL-C (mg/dl)	148.01±31.76	90.81±17.55	150.0±11.86	169.41±21.68	0.001
TG (mg/dl)	200.57±108.74	149.46±72.07	185.07±85.06	239.46±130.43	< 0.05
TSH (mIU/L)	3.72±7.50	3.29±4.39	3.40±6.85	4.26±9.06	0.352
BMI (kg/m)	28.99±3.37	26.91±3.80	29.60±3.13	29.16±3.12	< 0.01
SBP(mm/Hg)	129.60±16.35	121.0±14.73	131.85±15.97	130.60±16.32	< 0.01
DBP (mm/Hg)	82.42±9.63	77.90±9.87	83.74±9.32	82.80±9.35	< 0.01

Data are presented as mean±SD
$P \leq 0.05$ was considered significant.
Independent Student's t-test was used to compare the means of variables.

Table 4: Pearson's correlation coefficients (r) of cholesterol with other serum lipids, FSG and HbA1c in the normocholesterolemia and hypercholesterolemia groups.

Variables	Normocholesterolemia group		Hypercholesterolemia group	
	r	p	r	P
FSG	0.061	0.531	0.124	0.005
HbA1c	0.040	0.640	0.128	0.004
HDL-C	0.082	0.382	0.129	0.003
LDL-C	0.701	0.001	0.766	< 0.001
TG	0.311	0.001	0.332	0.001*

$P \leq 0.05$ is significant (*), r = correlation coefficient, FSG=Fasting serum glucose, HbA1c=hemoglobinA1c, HDL-C= high-density lipoprotein cholesterol, LDL-C= low-density lipoprotein cholesterol, TG=triglyceride.

DISCUSSION

Using the most recent and regionally representative sample of population from Duhok Governorate, this study found that HCh was highly prevalent with a prevalence rate of 39.12%. It is noticeable that this prevalence of HCh was surprisingly higher than in most regions of Iraq; for example, it exceeded the rate of 32.7% in a southern Iraqi population [20], but it was nearly similar to that reported in the population of a northern province of Iraq where the HCh prevalence was 44.6%[21]. Moreover, the prevalence of HCh was even higher than in some Arabic countries, as in Saudia Arab kingdom (8.5%)[22], Iran (34.5%)[23], and close to Turkish (37.5 %)[24]. The high prevalence of HCh among Kurdish population in Duhok Governorate might be attributed to the distinct geographical characteristics and lifestyles of Duhok. Duhok is one of the good living standard areas in Iraq. Inhabitants of this region tend to include fast foods and more sweet in their daily diets. In addition, lack of exercise and sedentary life style is widespread, particularly among the older population. Previous research has shown that above dietary patterns (fast food) are rich in fat, while consistent long-term consumption of such food with alcohol consumption can contribute to the development of HCh [25]. However, the commonest cause is polygenic HCh which results from an interaction of unidentified genetic factors compounded by a sedentary lifestyle and an increased intake of saturated and trans-fatty acids[26].

Similar to previous studies, our findings revealed no gender disparity in serum cholesterol levels and prevalence of HCh, and these results increased as individuals aged[27,28]. Peak of HCh was observed in men above 40 years of age and women above 50 years of age. We deduced that the high HCh prevalence in younger men was mainly correlated to a sedentary life associated with metabolic changes, while in elderly women it was primarily associated with metabolism and hormonal levels. Furthermore, there was a relatively higher HCh prevalence among urban residents compared with rural residents (45.52% vs 30.32%, $p<0.001$). This discrepancy can be attributed to the differing dietary habits and lifestyles between these two groups, which were in line with previous research findings[29]. In developed urban areas, defined as having a higher living standard and a fast-paced lifestyle, residents were more likely to consume greater amount of cholesterol-rich animal products and high-fat foods while engaging in less physical activities[30,31].

In addition to age and urban–rural differences, our study revealed that being overweight or obese, alcohol consumption, diabetes, hypertension and hypothyroidism were all associated with an increased risk of HCh. Moreover, the association between obesity and HCh has been barely probed. In abnormally obese individuals, fatty acids from visceral fat had a more direct entry into the bloodstream through the portal vein, resulting in elevated cholesterollevels[32].

Analyzing an association of HCh and TSH, we found a significant higher cholesterol levels and HCh prevalence in subjects with Hypothyroidism,. Hypothyroidism has a different impact on blood lipid components; generally, it tends to increase levels of TC, especially apolipoprotein B (ApoB)-containing lipoprotein cholesterol, like LDL-C. A higher degree of ApoB-containing lipoprotein cholesterol is found in patients with TSH >10 mIU/L compared to those with TSH 4.0–10.0 mIU/L. Regardless of the thyroid status, circulating TSH level is always positively correlated with levels of ApoB-containing lipoprotein cholesterol. Hence the higher TSH level is, the greater are the risks of dyslipidemia[33].

Moreover, we reported a significant relationship between diabetes and hypercholesterolemia. Subjects with T2DM, even when in good glycemic

control, there are abnormalities in lipid levels[34]. It is estimated that 30-60% of patients with T2DM have dyslipidemia. Specifically, patients with T2DM often have an increase in serum TG levels, increased VLDL and IDL, and decreased HDL-C levels[35].

The results confirm a relationship between alcohol consumption and hypercholesterolemia, as the levels of serum cholesterol and prevalence of hypercholesterolemia were higher in alcoholic subjects than that in non-alcoholic. These results are in accordance with previous studies[36]. Alcohol consumption is commonly associated with a disturbance of lipid metabolism, fat accumulation in the liver, hepatic steatosis, and hepatic cirrhosis. Alcoholic fatty liver is often associated with hyperlipidemia and alcoholic hepatitis. The mechanisms of the lipid accumulation are increased cholesterol synthesis in the liver and decreased release of serum lipoproteins.[37]. It is well-known that hypertension and dyslipidemia are two major risk factors accounting for cardiovascular disease. Clinically, hypertension and dyslipidemia often coexist, which may be associated with the fact that they share the same pathophysiological mechanisms, such as endothelial cell damage, inflammation, oxidative stress, and atherosclerosis of the arteries. It has been shown that there is a synergistic effect between hypertension and dyslipidemia, indicating that the risk of death and cardiovascular events is significantly higher in patients with both disorders than the combined risk of hypertension and dyslipidemia alone[38, 39].

This research used a population- based study design with a diverse age distribution, random sampling and a reasonably large sample size. However, due to the cross- sectional design, this study is unable to provide insights into the cause and effect relationships.

CONCLUSION:

In summary, this study highlighted the high prevalence of HCh among Kurdish population in Duhok governorate. Young men over 40 years and women over 50 years were identified as being at high risk for HCh. It is crucial to emphasis the importance of promoting healthy diets and implementing early interventions to manage dyslipidemia, obesity and blood glucose levels in these populations. Additionally, advocating for moderation of alcohol consumption could be an effective strategy.

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پوختە

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پێشەکی و ئارمانج: ....

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الخلاصة

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الخلفية والأهداف: .....

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