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RESEARCH ARTICLE

Age, period and cohort analysis of high cholesterol levels in Iranian adults over a 20-year period

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Abstract

Purpose Hypercholesterolemia is one of the most important modifiable risk factors of non-communicable diseases and data on their values in different societies and their trend of changes should be updated every couple of years. Many studies have focused on assessing the prevalence of high cholesterol. We must emphasise that most of these studies were cross-sectional and did not directly investigate the temporal trends of change for age, period and birth cohort (APC). The aim of this study is to evaluate the effect of age, period and birth cohort on the prevalence of borderline to high cholesterol levels in Iranian adult population.

Methods The data were collected from 110,302 subjects between 25 and 69 years of age over the period of 1990–2011. Data from these subjects were collected by using five national cross-sectional surveys conducted in 1990–91, 1999, 2003, 2007 and 2011. The APC effect on the prevalence of borderline and high cholesterol levels was assessed using the Intrinsic Estimator model.

Results The overall prevalence of borderline cholesterol level among male subjects was found to be lower than that of females (39.8% vs. 46.3%). Similarly, the prevalence of high cholesterol level in men was reported to be 13.1%, which was lower than the 18.0% calculated in women. The prevalence of borderline and high cholesterol levels increased with age in men between the ages of 45–49. Then it stayed quite steady and eventually declined. Then it stayed quite steady and eventually declined. The prevalence in women also increased with age, with its maximum rise after the ages of menopause and a slight decline at the ages of 65–69. As for the birth cohorts, the prevalence of borderline and high cholesterol levels followed a declining trend by going from earlier birth cohorts to the later ones.

Conclusion The present study provides evidence that age, period and birth cohort affect the prevalence of borderline and high cholesterol levels. Thus, these factors should be considered when developing and implementing care plans for people with hypercholesterolemia.

Keywords Lipid profile · Cholesterol · Epidemiology · Hyperlipidemia

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Background

Fifty-eight percent of the total deaths reported in 2008 were attributed to non-communicable diseases, the most important of which included diabetes, cardiovascular diseases, cancers and chronic respiratory disorders [1]. According to the World Health Organization (WHO), the non-communicable disease accounts for a great share of the disease burden (43%). This figure is projected to rise to 60% by 2020. Globally, non-communicable diseases accounted for 73% of all deaths.

Seventy-nine percent of these deaths and 85% of their disease burden will occur in low- and middle-income countries [2]. Iran is one of the 23 countries categorized as low- and middle-income, with a great burden imposed by chronic diseases [1].

According to available statistics, ischemic heart disease is the most important cause of mortality all around the world, ranked as the first and third cause for global burden of diseases in developed and developing countries, respectively [3, 4]. Hypercholesterolemia is one of the main risk factors for ischemic heart disease and atherosclerosis. The role of cholesterol in development of ischemic heart disease, myocardial infarction and atherosclerosis has been established in different studies [5]. The cause of nearly one third of ischemic heart diseases has been reported to correlate with high cholesterol levels and it has been estimated that hypercholesterolemia leads to 4.5% of the total deaths worldwide [6]. On the other hand, high cholesterol level is considered as the third global risk factor for mortality and the fourth cause of disease burden [4]. The prevalence of borderline and high cholesterol levels (cholestrol≥200 mg/dl) in Iran is 41.6% [7]. High total cholesterol caused 190,140 disability-adjusted life years (DALYs) for Iranian populations. Also, hypercholesterolemia is a main risk factors of deaths in Iran [8]. Hosseini et al., reported that Iranian males' cholesterol level had a decreasing trend from 1990 to 2007. However, the level of cholesterol of females was decreasing in ages younger than 45, but it increases afterwards. This study showed that the pattern of cholesterol trend of Iranian population have a considerable difference with those of the other developing and developed countries [9].

Lowering cholesterol level has also been shown to be associated with decreasing prevalence of cardiovascular diseases. One study reported that a 10% decrease in cholesterol levels of men aged 40 years old leads to a 50% decrease in cardiovascular diseases in a five-year period. Hence, hypercholesterolemia is one of the most important modifiable risk factors of non-communicable diseases and data on their values in different societies and their trend of changes should be updated every couple of years.

Various studies have evaluated the trend of changes in cholesterol levels in different populations and according to the ones conducted in the United States, cholesterol levels follow a decreasing trend in both American children and adolescents and adults [6, 10, 11]. Similar trends were also reported in Finland and North Africa [12, 13] but a study conducted in Japan found an increasing trend in their population [14]. Based on the mentioned studies, it seems that cholesterol levels follow different patterns in different populations according to their race and lifestyle, which further highlights the importance of evaluating their trends in different societies.

In order to evaluate a variable's trend of changes in time, epidemiological studies use the three cohorts, age, and period effects. Cohort effect refers to the changes in a specific group of subjects with a common characteristic (which is most commonly their birth year). Age effect evaluates the changes for different age groups and period effect reflects the changes in certain groups (age or cohort) at different time periods. These three effects are entangled and together can show the trend of changes in a variable [15]. To date, many studies have assessed cholesterol levels and their changes all around the world and have shown the variations in the incidence or prevalence of hypercholesterolemia. Various surveys have shown the levels of different physiologic parameters to be affected by the age, period and cohort effects. In some instances, these effects completely change the results. For example, a study showed that the total cholesterol level increases by 21% from the age of 75 to 95. However, when longitudinal analyses are controlled for the period and cohort effects, cholesterol level increases by only 9% and when the analyses are confined to the subjects remaining in the study until the last follow up, this figure reaches 6% [16]. On the other hand, considering the important role of cholesterol in development of cardiovascular diseases, ongoing surveillance of its levels in the population seems necessary.

Although in our previous survey, we assessed the trend of changes in the mean cholesterol levels of Iranian adults over a period of 17 years [9], no studies have evaluated the age, period and cohort effects on the prevalence of borderline cholesterol level and hypercholesterolemia in the Iranian population. In this regard, the present study aimed to assess the trend of changes in the prevalence of these two entities among Iranian children and adolescents, taking into account the effects of age, period and cohort.

Materials and methods

Study design and setting

The data collected in five Iranian national surveys conducted in 1990–91, 1999, 2003, 2007 and 2011 were analyzed in this study to assess the effect of age, period, and birth cohort on the prevalence of borderline and high cholesterol levels in adults aged 25 to 69 years. A brief description of each selected survey is presented in the following. A full description of the data collection methods in the first four surveys conducted in 1991–2008 has been reported elsewhere [9]. The study

received approval from the local ethics committee, and informed consent was obtained from all study subjects.

Data

National health surveys 1990–91 and 1999

The first and second national health surveys recorded serum cholesterol levels of 13,416 and 19,532 subjects aged 25–69, during June 1990 until March 1992, and April 1999 to February of 2000, respectively. The data collections in these two surveys were conducted by the undersecretary of research, Ministry of Health and Medical Education, by the help of Blood Transfusion Organization and the universities of medical sciences. Random cluster sampling was used to identify a nationally representative sample of people aged 2–69 years, with a sampling fraction of 1/1000.

National surveillance of risk factors for non-communicable diseases, 2003 and 2007

The first two rounds of National Surveillance of Risk Factors of Non-Communicable Diseases carried out in 2003 and 2007, recorded serum cholesterol levels of 52,299 and 19,638 individuals aged 25–69 years, respectively. Forty medical schools from all over the country collaborated for implementation of these two surveys according to the step by step instructions of WHO [2].

National surveillance of risk factors of non-communicable diseases 2011

The Sixth National Surveillance of Risk Factors of Non-Communicable Disease (SuRFNCD) conducted in 2011 used a multistage sampling framework considering counties as primary sampling units, cities or villages as the secondary sampling units (SSU), households as sampling listing unit and 6 to 70 year-old inhabitants as the sampling elementary units. A maximum of two individuals (one <55 and the other ≥55 years old) were allocated in each household using a KISH randomization method. Eventually, serum cholesterol levels were found to have been reported for 5417 subjects aged 25–69 years old in this survey, which were used in the analyses of the present study.

Biochemical analysis

Samples of venous blood were drawn (10 ml) from each subject after an overnight fast. Blood was then transferred to plastic test tube for centrifugation. The samples were then transferred under cold chain to the accredited reference laboratory at the Ministry of Health in Tehran for further analysis.

Serum cholesterol level was measured via enzymatic method using Pars Azmoon kit. Ten percent of all measurements were performed at a WHO certified reference lab in Tehran for quality control. Total cholesterol level measured to be between 200 to 239 mg/dl was considered as borderline, while concentrations above 240 mg/dl were categorized as high cholesterol levels.

Statistical analysis

Our study aimed to identify the effects of age, period, and birth cohort on the prevalence of borderline to high cholesterol. Age-period-cohort models were applied using an intrinsic estimator (IE) method developed by Yang [17, 18]. To account for the gender difference analysis were carried out for males and females separately. The "apc_ie" command statement was used in the STATA software version 11.0 (Stata Corp., College Station, TX, USA) to perform the analyses.

Results

A total of 110,302 subjects aged 25 to 69 years old were included from the five national surveys as the total sample population. Distribution according to gender and the number of subjects in each survey presented in Table 1. The survey conducted in 2003 provides the highest proportion of samples (47.4%.). On the other hand, the survey conducted in 2011 comprise the smallest proportion of the overall sample (4.9%).

The prevalence of borderline and high serum cholesterol levels by age and gender are presented in Table 2 for each of the five surveys. By subtracting age from study period a total of 13 five-year birth cohorts were generated for the analysis. Subjects born in 1921–1925 comprised our first birth cohort while the last birth cohort included subjects born in 1981–1985. Only subjects of five birth cohorts (from 1941 and 1965) were followed throughout the entire 20-year period. Table 3 presents the prevalence of borderline and high serum cholesterol levels according to birth cohort and gender. Tables 4 and 5 demonstrate the coefficients of estimation calculated for age, period and cohort effects on prevalence of borderline and high serum cholesterol levels for men and women separately.

The overall prevalence of borderline cholesterol level among male subjects was found to be lower than that of females (39.8% vs. 46.3%). Similarly, the prevalence of high cholesterol level in men was reported to be 13.1%, which was lower than the 18.0% calculated in women.

The age, period and cohort-based variations

Age effects

The coefficient of borderline cholesterol prevalence showed an exponentially increasing trend among women, up to the

Table 1 Sample sizes according to study year and sex

Study year	Men (%)	Women (%)	Total (%)	Percentage from total
1990	5927 (44.8)	7489 (55.8)	13,416 (100)	12.16
1999	8432 (43.2)	11,100 (56.2)	19,532 (100)	17.71
2003	25,125 (48.0)	27,174 (52.0)	52,299 (100)	47.42
2007	9371 (47.7)	10,267 (52.3	19,638 (100)	17.80
2011	2024 (37.4)	3393 (62.6)	5417 (100)	4.91
Total	50,879 (46.1)	59,423 (53.9)	110,302 (100)	100.0

age of 50–54 years and afterward an increasing trend with a constant slope (Fig. 1b). The male data showed an increasing trend up to the age of 55–59 years with the slope gradually decreasing, then it declined until the age of 60–64 and eventually rose again to reach its maximum at the age of 65–69 years (Fig. 1a).

As for the high cholesterol prevalence, the coefficients in men followed an increasing trend to reach its maximum at the age of 45–49, then gradually declined until the age of 60–64 and again drastically increased up to the age of 65–69 (Fig. 2a). Coefficients calculated for high cholesterol data in women followed a rather sigmoid trend with a slight increase up to the age of 40–44, the slope rising for the coefficient figure to reach its maximum at the age of 55–59 and then a gradual decline until the age of 65–69 years (Fig. 2b).

Period effects

As depicted in Figs. 1c, d, the coefficients calculated for the variations in the prevalence of borderline cholesterol levels followed a similar pattern in both genders. The coefficients did not show a significant change between periods of 1990, 1995 and 2000, peaked at the 2005 period and again decreased to reach its minimum at the 2010 period. Similar trends were also observed for the coefficients of the high cholesterol prevalence (Figs. 2c, d).

Birth cohort effects

The coefficients of birth cohort effects for borderline cholesterol prevalence in men showed considerable fluctuations, drastically increasing from the 1921–25 cohort to reach its maximum at the 1926–30 cohort. After that, the figures followed an overall decreasing trend (Fig. 1e). As for women, data showed an increase from the 1921–25 cohort to 1926–30

Table 2 Prevalence (%) of borderline and high cholesterol by age, sex, and study

Age	1990 (n = 13,416)		1999 (n = 19,532)		2003 (n = 52,299)		2009 (n = 19,638)		2011 (n = 5417)		Total (n = 110,302)	
	Borderline	High	Borderline	High	Borderline	High	Borderline	High	Borderline	High	Borderline	High
Men												
25–29	29.4	9.3	26.0	7.0	30.0	8.1	21.4	5.6	16.7	2.8	27.0	7.4
30–34	32.5	10.4	32.9	11.1	36.0	10.7	27.2	7.2	25.2	3.8	33.0	10.0
35–39	38.4	15.0	33.8	11.6	42.3	14.0	32.4	10.1	27.3	6.4	37.9	12.8
40–44	41.5	15.9	38.7	14.6	47.8	16.2	35.9	12.3	28.7	6.4	42.9	14.9
45–49	42.8	17.4	40.9	15.2	49.8	16.8	40	12.5	27.5	9.2	45.7	15.6
50–54	39.5	16	42.2	15.5	49.7	18.3	36.4	11.3	34.6	4.3	44.6	15.8
55–59	39.9	14.4	41.1	15.5	51.9	17.6	37.2	11.2	35	8.0	45.6	15.1
60–64	41.1	13.2	37.5	14.2	49.6	16.1	39.1	11.4	31.2	7.7	45	14.4
65–69	40.0	15.1	39.7	11.4	42.9	28.6			30.8	7.7	38.4	12.1
Total	37.1	13.4	35.2	12.1	45.1	14.9	33.9	10.3	28.8	6.2	39.8	13.1
Women												
25–29	31.3	10.4	30.0	9.1	31.4	8.4	23.0	7.0	18.1	4.3	29.1	8.5
30–34	34.9	11.5	33.4	11.3	36.5	10.8	30.4	8.3	20.9	4.6	33.8	10.4
35–39	35.8	11.7	36.0	11.9	43.4	13.7	35	9.1	24.3	7.7	38.6	12.0
40–44	38.2	13.4	41.0	13.9	48.7	15.9	38.2	12.3	31.1	7.5	43.3	14.2
45–49	40.7	14.7	42.7	18.3	56.6	21.3	48.1	17.6	38.8	14.7	50.8	19.3
50–54	49.3	21.5	51.5	23.9	67.2	32.0	54.4	21.7	52.6	15.8	60	26.9
55–59	54.1	24.3	52.2	26.5	69.4	34.8	57.4	23	48.2	18.8	62.8	29.7
60–64	55.4	24.7	56.8	25.3	71.8	35.9	57.8	26.1	48.5	15.5	64.2	30.3
65–69	53.8	25.7	55.2	26.9	80.0	40.0			48.9	17.7	53.2	24.2
Total	39.8	15.0	39.7	15.3	53.2	21.6	43.1	15.6	36.6	11.8	46.3	18.0

Table 3 Prevalence (%) of borderline and high cholesterol by birth cohort, age, and study year

Cohort	1990 (n = 13,416)		1999 (n = 19,532)		2003 (n = 52,299)		2009 (n = 19,638)		2011 (n = 5417)	
	Borderline	High	Borderline	High	Borderline	High	Borderline	High	Borderline	High
Men										
1921–25	40.0	15.1								
1926–30	41.1	13.2								
1931–35	39.9	14.4	39.7	11.4						
1936–40	39.5	16.0	37.5	14.2	42.9	28.6				
1941–45	42.8	17.4	41.1	15.5	49.6	16.1	39.1	11.4	30.8	7.7
1946–50	41.5	15.9	42.2	15.5	51.9	17.6	37.2	11.2	31.2	7.7
1951–55	38.4	15	40.9	15.2	49.7	18.3	36.4	11.3	35.0	8.0
1956–60	32.5	10.4	38.7	14.6	49.8	16.8	40	12.5	34.6	4.3
1961–65	29.4	9.3	33.8	11.6	47.8	16.2	35.9	12.3	27.5	9.2
1966–70			32.9	11.1	42.3	14	32.4	10.1	28.7	6.4
1971–75			26.0	7.0	36.0	10.7	27.2	7.2	27.3	6.4
1976–80					30.0	8.1	21.4	5.6	25.2	3.8
1981–85									16.7	2.8
Total	37.1	13.4	35.2	12.1	45.1	14.9	33.9	10.3	28.8	6.2
Women										
1921–25	53.8	25.7								
1926–30	55.4	24.7								
1931–35	54.1	24.3	55.2	26.9						
1936–40	49.3	21.5	56.8	25.3	80.0	40.0				
1941–45	40.7	14.7	52.2	26.5	71.8	35.9	57.8	26.1	48.9	17.7
1946–50	38.2	13.4	51.5	23.9	69.4	34.8	57.4	23	48.5	15.5
1951–55	35.8	11.7	42.7	18.3	67.2	32	54.4	21.7	48.2	18.8
1956–60	34.9	11.5	41.0	13.9	56.6	21.3	48.1	17.6	52.6	15.8
1961–65	31.3	10.4	36.0	11.9	48.7	15.9	38.2	12.3	38.8	14.7
1966–70			33.4	11.3	43.4	13.7	35	9.1	31.1	7.5
1971–75			30.0	9.1	36.5	10.8	30.4	8.3	24.3	7.7
1976–80					31.4	8.4	23	7.0	20.9	4.6
1981–85									18.1	4.3
Total	39.8	15.0	39.7	15.3	53.2	21.6	43.1	15.6	36.6	11.8

cohort and then had no significant changes until the 1956–60 cohort. Then it declined to reach its minimum level at the 1976–80 cohort, and then slightly increased in the 1981–85 cohort (Fig. 1f).

Similarly, the coefficients calculated for the birth cohort effects on high cholesterol prevalence showed some fluctuations among men (Fig. 2e), while in women data followed a more homogenous decreasing pattern to reach its minimum at the 1976–80 cohort and a slight increase in the 1981–85 cohort (Fig. 2f).

Discussion

To the best of our knowledge, this is the first study evaluating the variations in the prevalence of borderline to high cholesterol levels in Iranian adults over a period of 20 years. According to our findings, the prevalence of borderline and high cholesterol levels increase with age in men until the ages of 45–49. Then it stays quite steady and eventually declines. The prevalence in women also increases with age, with its maximum rise after the ages of menopause and a slight decline at the ages of 65–69. The relationship between cholesterol levels and aging has been established by numerous studies [19–22] and our findings are compatible with previous studies in this regard. Moreover, the specific changes in the prevalence of borderline and high cholesterol levels by age in women are also congruent with the findings of previous studies showing a significant increase in cholesterol levels after menopause [23–25].

The final decline observed in both genders could be due to the fact that when people are younger, they have a lower

Table 4 Intrinsic Estimates for the rate of borderline and high cholesterol of Iranian men

Effect	Borderline cholesterol				High cholesterol			
	Coefficient	95% CI		*P*	Coefficient	95% CI		*P*
Age effect								
25–29	−0.0921	−0.1127	−0.0716	<0.001	−0.05	−0.0625	−0.0374	<0.001
30–34	−0.0443	−0.063	−0.0256	<0.001	−0.0221	−0.0335	−0.0107	<0.001
35–39	−0.0197	−0.0389	−0.0005	0.045	−0.0061	−0.0178	0.0057	0.309
40–44	0.0061	−0.0135	0.0257	0.542	0.0119	−0.0001	0.0239	0.052
45–49	0.0171	−0.0025	0.0368	0.087	0.0228	0.0108	0.0348	<0.001
50–54	0.0245	0.0048	0.0441	0.015	0.0131	0.0011	0.0251	0.033
55–59	0.0341	0.0148	0.0535	0.001	0.0089	−0.0029	0.0207	0.138
60–64	0.0157	−0.0032	0.0345	0.103	−0.0008	−0.0124	0.0107	0.886
65–69	0.0586	0.0387	0.0785	<0.001	0.0223	0.0101	0.0344	<0.001
Period effect								
1990	0.0019	−0.0111	0.0149	0.77	0.0099	0.002	0.0179	0.014
1995	−0.0092	−0.0226	0.0041	0.176	0.0031	−0.0051	0.0113	0.458
2000	−0.0059	−0.0193	0.0075	0.39	0.0014	−0.0067	0.0096	0.729
2005	0.0951	0.082	0.1082	<0.001	0.0291	0.0211	0.0371	<0.001
2010	−0.082	−0.0958	−0.0681	<0.001	−0.0436	−0.052	−0.0352	<0.001
Cohort effect								
1921–25	−0.0247	−0.0638	0.0145	0.217	−0.0089	−0.0328	0.015	0.466
1926–30	0.047	0.018	0.0759	0.001	0.0177	0	0.0354	0.049
1931–35	0.0159	−0.0091	0.0408	0.212	0.0023	−0.013	0.0176	0.768
1936–40	0.0289	0.0063	0.0516	0.012	0.0206	0.0067	0.0344	0.004
1941–45	0.0079	−0.0128	0.0285	0.456	0.0061	−0.0065	0.0188	0.341
1946–50	0.0144	−0.0073	0.0361	0.193	−0.0026	−0.0159	0.0106	0.699
1951–55	0.0132	−0.0087	0.0351	0.237	−0.003	−0.0164	0.0104	0.663
1956–60	0.0052	−0.0161	0.0264	0.632	−0.0139	−0.0269	−0.0009	0.036
1961–65	−0.0129	−0.0327	0.0069	0.201	−0.0061	−0.0182	0.0061	0.327
1966–70	−0.0091	−0.0304	0.0122	0.402	−0.0036	−0.0166	0.0094	0.591
1971–75	−0.0255	−0.0488	−0.0021	0.032	−0.0203	−0.0346	−0.006	0.005
1976–80	−0.0314	−0.0587	−0.004	0.025	−0.011	−0.0277	0.0057	0.198
1981–85	−0.0289	−0.0752	0.0174	0.221	0.0226	−0.0058	0.0509	0.119
Constant	0.3707	0.3625	0.3789	<0.001	0.1296	0.1246	0.1347	<0.001

tendency to pursue their health issues and are reluctant to start medical treatments for lab findings that have not yet caused them any signs and symptoms. As the subjects with high cholesterol levels get older, they are started on cholesterol lowering medications and this is reflected as the drop in the prevalence of borderline and high cholesterol levels in the last age groups evaluated in this study.

We also observed the prevalence of borderline and high cholesterol levels to be following a declining trend by going from earlier birth cohorts to the later ones. This observation might be due to the significant improvements in health care in Iran [26]. As time goes by, further evidence is becoming available on the effects of nutritional habits, physical activity and lifestyle on the serum cholesterol levels. Correspondingly, the guidelines are constantly being updated as to how and when to tackle the issue of high serum cholesterol concentrations.

Moreover, nationwide educational programs are being implemented to guide mothers about the importance of their children's health [27]. With the increasing knowledge about health care in the Iranian population, it seems that the overall health status of people is improving [28] which could be the underlying cause of the lower borderline and high cholesterol prevalence in the later birth cohorts as compared to the earlier cohorts.

Regardless of the overall declining trend, as depicted in Figs. 1e, f, 2e, f, the prevalence of both borderline and high cholesterol levels increased in the last birth cohort of 1981–1985. These observations could be attributed to the dietary changes in the Iranian population during the 1980s. As reported in previous studies, during this period consumption of dairy products, fruits and vegetables significantly decreased, whereas a considerable increase was observed in the consumption of various types of oil and sugar, leading to a rise in the prevalence of obesity among Iranians [29].

The findings of the present study provide valuable data to policy makers. Based on this study, various strategies are required to control serum cholesterol levels for different ages, and these preventive measures should be designed for men and women separately. It seems the changes in lifestyle and increasing community awareness have decreased the incidence of borderline and high cholesterol in recent birth cohorts. The relative increase in borderline and high cholesterol in 2005 is an issue that should be taken into consideration. Policy makers should look for the reasons for this increase, in order to implement preventive measures against it in the future.

Table 5 Intrinsic Estimates for the rate of borderline and high cholesterol of Iranian women

Effect	Borderline high cholesterol				High cholesterol			
	Coefficient	95% CI		p	Coefficient	95% CI		p
Age effect								
25–29	−0.0976	−0.1154	−0.0799	<0.001	−0.064	−0.0779	−0.0501	<0.001
30–34	−0.0935	−0.1096	−0.0774	<0.001	−0.0534	−0.0661	−0.0408	<0.001
35–39	−0.0876	−0.1042	−0.071	<0.001	−0.0504	−0.0635	−0.0374	<0.001
40–44	−0.0625	−0.0794	−0.0455	<0.001	−0.0449	−0.0581	−0.0316	<0.001
45–49	−0.0212	−0.0382	−0.0042	0.014	−0.0097	−0.023	0.0037	0.155
50–54	0.0648	0.0479	0.0818	<0.001	0.0429	0.0296	0.0563	<0.001
55–59	0.0816	0.0649	0.0983	<0.001	0.0661	0.053	0.0792	<0.001
60–64	0.1036	0.0873	0.1199	<0.001	0.0608	0.0481	0.0736	<0.001
65–69	0.1124	0.0952	0.1296	<0.001	0.0525	0.0391	0.066	<0.001
Period effect								
1990	−0.0316	−0.0428	−0.0204	<0.001	−0.0124	−0.0213	−0.0036	0.006
1995	−0.02	−0.0316	−0.0084	0.001	−0.0035	−0.0126	0.0055	0.443
2000	−0.0104	−0.022	0.0012	0.078	0.0096	0.0005	0.0186	0.039
2005	0.1169	0.1056	0.1282	<0.001	0.0551	0.0462	0.064	<0.001
2010	−0.0549	−0.0668	−0.043	<0.001	−0.0487	−0.058	−0.0393	<0.001
Cohort effect								
1921–25	0.0026	−0.0312	0.0364	0.88	0.028	0.0015	0.0545	0.039
1926–30	0.0443	0.0193	0.0693	0.001	0.0265	0.0069	0.0462	0.008
1931–35	0.031	0.0094	0.0525	0.005	0.0173	0.0004	0.0342	0.044
1936–40	0.0361	0.0166	0.0557	<0.001	−0.0012	−0.0165	0.0142	0.879
1941–45	0.0182	0.0004	0.0361	0.045	0.0126	−0.0014	0.0266	0.077
1946–50	0.0337	0.015	0.0524	<0.001	0.0125	−0.0022	0.0272	0.094
1951–55	0.0404	0.0215	0.0593	<0.001	0.0193	0.0045	0.0341	0.011
1956–60	0.0521	0.0338	0.0705	<0.001	0.0031	−0.0113	0.0175	0.671
1961–65	0.0161	−0.001	0.0333	0.065	0.0014	−0.012	0.0148	0.838
1966–70	−0.0066	−0.025	0.0118	0.481	−0.0144	−0.0288	0.0001	0.051
1971–75	−0.0564	−0.0765	−0.0362	<0.001	−0.0316	−0.0474	−0.0158	<0.001
1976–80	−0.1093	−0.133	−0.0857	<0.001	−0.0537	−0.0723	−0.0352	<0.001
1981–85	−0.1024	−0.1424	−0.0623	<0.001	−0.02	−0.0514	0.0114	0.212
Constant	0.4353	0.4282	0.4424	<0.001	0.1743	0.1687	0.1799	<0.001

There have been similar studies conducted in different populations on the prevalence of high cholesterol levels, but neither have simultaneously evaluated the effects of age, period and cohort. For instance, Carroll et al. (2012) assessed the changes in the prevalence of high cholesterol levels in American adults aged 20 and over, evaluating data gathered from 6 national surveys conducted during 1999 to 2010. According to their findings, the prevalence of high cholesterol levels gradually decreased from 18.3% in the 1999–2000 period to 13.4% in the 2009–2010 period. Similar to our findings, they reported that the prevalence to be higher among women throughout the evaluated period; declining from 19.1% to 14.3% and 17.2% to 12.2% in women and men, respectively. The differences between the two genders were found to be greater among subjects aged 60 and over [30].

In another study conducted in Switzerland, Morabia et al. evaluated 12,271 individuals (6164 men and 6107 women in Geneva) aged 35 to 74 over a period of 11 years from 1993 to 2003. According to their findings, the prevalence of hypercholesterolemia, defined as a total plasma cholesterol level ≥ 250 mg/dl, followed an increasing pattern in both genders; from 21% to 30% in men and from 18% to 26% in women [31]. In a similar study, Estoppey et al. reported the changes in the prevalence of hypercholesterolemia in Swiss adults (49,261 subjects), over a period of 1997–2007, according to the subjects' self-declaration. These researchers also, found an increasing trend in the prevalence of hypercholesterolemia from 11.9% in 1997 to 14.7% in 2002 and 17.4% in 2007 [32]. As can be seen, the results of the two surveys were incongruent with ours regarding the trend of changes and the

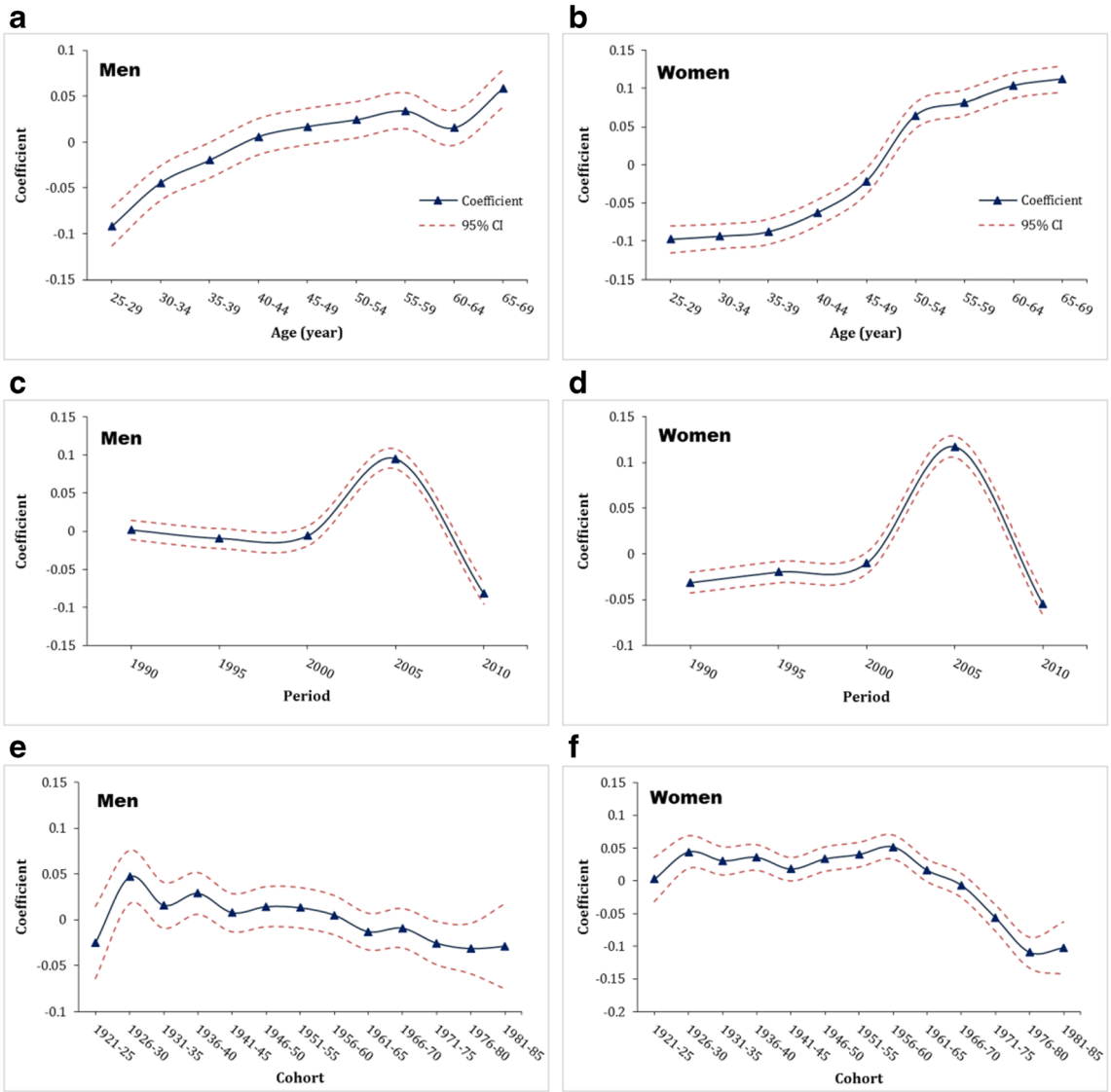

Fig. 1 Age (**a** and **b**), period (**c** and **d**), and birth cohort (**e** and **f**) effects on borderline cholesterol prevalence

difference between male and female subjects. The prevalence of hypercholesterolemia was also considerably higher than the Iranian population, even with the higher cut-off level the first study used for defining high cholesterol levels.

Arnett et al. evaluated the trend of changes in the prevalence of hypercholesterolemia over a period of twenty years, from 1980 to 1982 to 2000–2002 (data of 20,757 males and females), using data gathered through five national surveys in Minnesota. They found the mean prevalence of borderline cholesterol levels to be 54.9% in men and 46.5% in women, in the period of 2000–2002. In the same period, the prevalence of hypercholesterolemia was reported to be 23.9% in men and 17.3% in women. According to their findings, none of these age-adjusted values were significantly different from that of the 1995–1997 period. Nevertheless, the changes in the prevalence of borderline cholesterol levels showed a linear downward trend for both genders while the prevalence of hypercholesterolemia showed no significant variations in the studied period [33].

As can be seen, there are significant discrepancies between the results of surveys conducted in different populations, which highlights the role of environmental and life-style related factors in the prevalence of hypercholesterolemia and stresses the importance of implementing such surveys for different populations, separately. As mentioned, none of these studies have simultaneously included the effects of age, period and cohort in their analyses. It should be emphasized that these three effects are correlated with each other from a mathematical point of view and they are also entangled in a conceptual sense, so they should not be evaluated individually. This is the rationale behind adjusting for the other two factors, when evaluating one of them, as

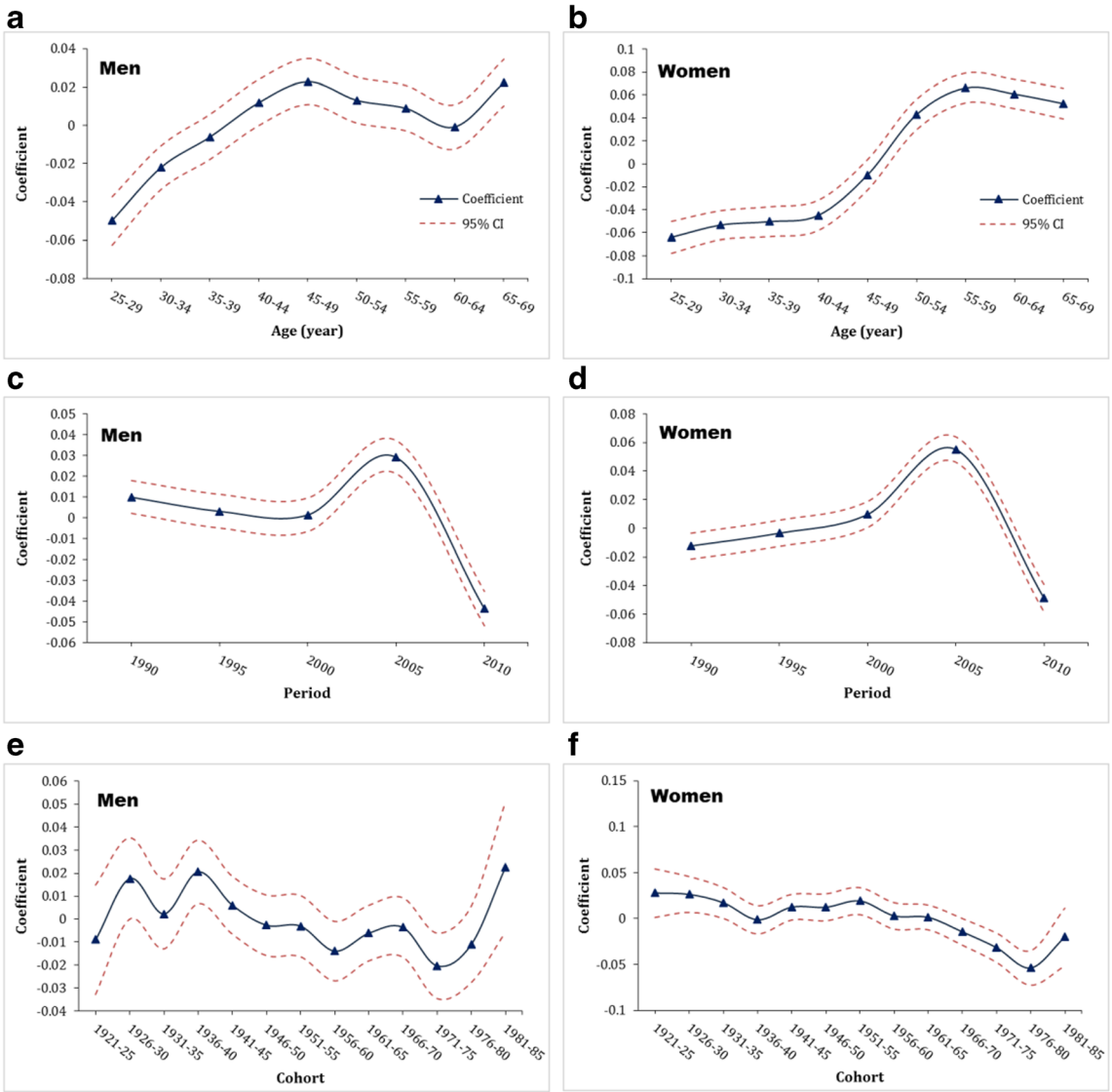

Fig. 2 Age (**a** and **b**), period (**c** and **d**), and birth cohort (**e** and **f**) effects on high cholesterol prevalence

performed in the present study. Another strength of this study was the use of a similar standard method, and the same biochemical kits in all the 5 national surveys, for measuring the serum cholesterol levels, which can reduce the measurement bias in our findings to a great extent.

However, the advancement of technology in the manufacture of medical equipment during the study period (1990 to 2011) can increase the accuracy of measuring serum cholesterol levels, and this may indicate a slight error in the evaluation of total cholesterol in the first periods. This limitation is not just for the present study and is a minor issue for all longitudinal research. In addition, the risk factors of hypercholesterolemia, such as lifestyle and nutritional habits, have changed over the studied period in Iran. These changes affect the level of cholesterol although they have not been investigated in this study. Nevertheless, the assessment of period effect indirectly includes the effect of lifestyle changes on serum cholesterol levels.

Conclusion

The present study showed that the prevalence of borderline and high cholesterol levels increase with age in men until the ages of 45–49. Then it stays quite steady and eventually declines. The prevalence in women also increases with age, with its maximum rise after the ages of menopause and a slight decline at the ages of 65–69. As for the birth cohorts, the prevalence of borderline and high cholesterol levels followed a declining trend by going from earlier birth cohorts to the later ones. Overall, the present study provided evidence that showed age, period and birth cohort affect the prevalence of

high cholesterol levels and these factors should be taken into account when hypercholesterolemia is being dealt with.

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Data acquisition: FA; AR; KE; JK; MB.
Analysis: MH, MY.
Interpretation of data for the work: MH; MY; KM; MY.
Drafting the work: MY; MB; MH.
Revising draft critically for important intellectual content: All authors.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Ethics approval and inform consent The study designs were approved by Tehran University of Medical Sciences Ethics Committee. In this study an informed consent was given from participants.

Role of the sponsor The Tehran University of Medical Sciences had no role in the design and conduct of the study; collection, management, and analysis of the data.

Abbreviations *APC,* Age, period and cohort; *IE,* Intrinsic estimator; *SSU,* Secondary sampling units; *SuRFNCD,* Sixth National Surveillance of Risk Factors of Non-Communicable Disease; *WHO ,* World Health Organization

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