Impact of Smoking and Physical Activity on Total Cholesterol Levels, Lipoproteins, and Coronary Heart Disease Risk: Statistical Evidence.

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Abstrac: This study examined the differences in plasma levels of total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TGs) among a sample of individuals free from cardiovascular disease. The aim was to determine the effects of smoking and physical activity, as well as the influence of these factors, on the incidence of ischemic heart disease and stroke. The research included a total of 902 participants, of whom 412 were current smokers and 490 engaged in aerobic exercise. Enzymatic colorimetric methods were used to analyze all studied parameters. The results showed that, for both sexes, smokers had higher levels of plasma total cholesterol, LDL-C, and TGs compared to non-smokers, while HDL-C levels were inversely correlated with smoking. Significant changes were observed in individuals who smoked more than nine cigarettes per day, while those who smoked fewer than ten cigarettes per day showed only minor effects. Regular physical activity was found to improve the plasma lipid profile (total cholesterol, LDL-C, and TGs), with reductions in these parameters depending on the frequency, intensity, and duration of exercise, as measured by the FIT (Frequency, Intensity, Time) scoring of physical activity. Notable reductions were seen only in those who regularly performed aerobic exercise, while HDL-C levels positively correlated with FIT scores and significantly increased only in those with an active lifestyle. Furthermore, no significant differences were found between males and females in any of the parameters tested, regardless of smoking or physical activity.

Key words: Cardiovascular disease; Cholesterol Levels; Physical Activity; Smoking

1.Introduction

Cardiovascular disease (CVD) can be classified alongside cancer and road accidents as a statistical ailment. Living a normal life inherently involves certain risks, which can increase or decrease in direct correlation with various factors. For most populations, it is relatively straightforward to determine the relative morbidity or mortality rates associated with CVD, and it is a valuable epidemiological exercise to correlate this data with other measurable parameters within a population. These correlations are termed "risk factors" and can be categorized in several ways, though a useful approach for coherent discussion is to classify them as primarily genetic, primarily behavioral, or primarily nutritional (John, R., 1997).

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High serum total cholesterol (TC) levels are well-known to correlate positively with an increased risk of coronary heart disease (Stamler, J., 2000; Zhang, X., 2003). However, the relationship between cholesterol and stroke, as well as its subtypes, remains debated. Prospective studies on Americans (Yuan, JM, et al., 2002), Europeans (Lindenstrom, E., 1999), and Japanese-American men (Benfate, R., 2001) suggest a positive association between serum total cholesterol concentration and the risk of ischemic stroke. In contrast, a study conducted in Japan found no link between serum total cholesterol and the risk of ischemic or overall stroke (Nakayama, T., 2001). Other prospective studies involving Japanese men and women (Ueshima, H., 2002), a Chinese cohort (Zhang, XF., 2005), American men (Yuan, JM, et al., 2002), elderly American men (Iribarren, C., 1998), Swedish women (Gatchev, O., 1998), and Scottish men and women (Hart, CL., 2000) showed that serum total cholesterol levels were inversely associated with the risk of intraparenchymal hemorrhage, although not all studies confirmed this finding (Suh, I., 2001).

Cigarette smoking is widely recognized as a major risk factor for ischemic heart disease (IHD) in Western countries (Kannel, WB., 1996; Doll, R., 2002). In Korean populations, low cholesterol levels were found not to provide a protective effect against smoking-related cardiovascular disease (CVD) and atherosclerotic cardiovascular disease (ASCVD) in women (Sun, H., 2006). A previous study reported that smoking had a greater impact on cholesterol levels than diabetes in both sexes (Sharrett, A., 2006). Research on the effects of non-heavy smoking showed negative impacts on HDL-C in healthy young Turkish men, a finding not widely demonstrated in other studies (Cem, B., 2006). Similar results were reported in earlier studies showing a significant association between smoking, low HDL-C, and high serum total cholesterol in Southern European cohorts (Alessandro, M., 2006).

One notable observation is that exercise generally lowers plasma cholesterol levels. Physical inactivity is considered one of the four major risk factors for coronary artery disease, alongside smoking, unhealthy cholesterol levels, and high blood pressure. Studies suggest that people who modify their diet to control cholesterol are more successful in reducing their risk of heart disease when they also engage in regular aerobic exercise (Fiorito, A., 2005). A study on the effects of physical activity on HDL-C and body mass index (BMI) among Saudi men and women reported significant increases in plasma HDL-C levels and moderate reductions in BMI (Abdul, RA., 2005). Furthermore, common genetic variants associated with HDL-C levels are influenced by physical activity levels, according to a recent study (Ahmed, et al., 2011). The study of Su-Min Jeong, et al(2018) aimed to evaluate whether the change in cholesterol is associated with incidence of CVD among young adults. Antonella and Santo (2020) article discussed the effects of exercise training on lipid metabolism and coronary heart disease.AL Otaibi, Tareq et al(2021) conclusions concentrated on sex cigarette smokers and cute moderate-intensity exercise effects ,as Zhao, Y et al (2024) focused on elevated blood remnant cholesterol and triglycerides related to the risks of cardiometabolic multimorbidity.

We hypothesize that smoking status and cholesterol levels are associated with both early and more advanced forms of atherosclerotic cardiovascular disease (ASCVD), while physical activity may improve the lipid profile and reduce the risk of developing heart disease.

2. Materials and Methods

This study was conducted in the Alqunfudah region and involved adult participants. A total of 902 healthy individuals were included, comprising 412 current smokers and 490 who regularly engaged in aerobic exercise. All participants were healthy, without any treatment for high cholesterol or other lipid-related conditions at the time of the study. The sample included adults with different lifestyles, such as sedentary officers, students, and a few freelancers. A questionnaire was administered to collect sociodemographic information, including age, gender, lifestyle, smoking status, and educational level. Participants were asked about their smoking and exercise habits. The study classified participants as "current smokers" if they had smoked for at least one year, "nonsmokers" if they had never smoked, and "ex-smokers" if they had quit smoking. Current smokers were further categorized by the number of cigarettes smoked daily: 1-9, 10-19, or 20 or more cigarettes per day. The questionnaire also included a detailed assessment of the participants' physical activity, considering frequency (F), intensity (I), and duration (T) of exercise. A scoring system from 1 to 5 was used to rate their level of activity. For exercise frequency, a daily or 6-7 times per week routine received a score of 5, while exercising once a month was scored as 1, with intermediate scores assigned for frequencies in between. The intensity of physical activity was evaluated based on the type of aerobic exercise: "aerobic activity causing heavy breathing and perspiration" was scored as 5, while light aerobic activities (such as normal walking) were scored as 1, with moderate activities receiving scores from 2 to 4. The duration of exercise was scored from 1 to 4, with a maximum score of 4 for exercising more than 30 minutes daily, and a score of 1 for less than 10 minutes per day, with scores of 2-3 for durations between 10 and 30 minutes. The final FIT value was calculated by multiplying the scores for frequency, intensity, and time $(F \times I \times T)$. Participants with scores of 0-7 were classified as sedentary (control group), while those scoring 8-32 were designated as engaging in light activity, 36-75 as moderate, and 80-100 as heavy physical activity. Cholesterol and triglycerides were measured using a calibrator for automated systems (c.f.a.s). For HDL-C, c.f.a.s lipids were used. For plasma total cholesterol and triglycerides, two levels of controls were tested at least once daily: Precinorm U for low control and Precipath U for high control. For HDL-C, Precinorm L and Precipath L were used as the low and high-level controls, respectively.

2.1. Collection of blood samples and isolation of plasma

Venous blood samples were collected from participants in a sitting position using Venoject vacuum containers, between 8:00 and 9:00 AM, following a 12-14 hour overnight fasting period. The samples were drawn into tubes containing heparin, with a final concentration of up to 75 U/ml. The blood was immediately centrifuged at 4,000 rpm for 10-15 minutes using a Labofuge centrifuge (model 400, Germany). The resulting plasma was analyzed fresh (without freezing) for lipoproteins, while cholesterol and triglycerides were measured in plasma samples that had been frozen at -20°C within two hours of collection.

2.2 Methods

For all tests required (total Cholesterol, HDL-C, LDL-C and triglycerides) enzymatic methods, and a Hitachi 912 autoanalyser (Hitachi, Tokyo, Japan) instrument with ready to use Boehringer Mannhiem kits were used. The instrument is calibrated and controlled

pre-running the samples. LDL-C was calculated according to the Friedewald formula (LDL-C = total cholesterol – HDL- C – Triglycerides / 5).

2.3 Statistical Analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS). Data for numerical values were expressed as mean \pm standard deviation (SD). Differences between groups, whether based on exercise or smoking status, were considered statistically significant when the differences were equal to or greater than one standard deviation (SD).

3. Results

The study included a total of 902 healthy adults: 412 participants were assessed for smoking habits, and 490 participants were assessed for aerobic exercise. Current smokers were divided into four groups (with each group further divided into two subgroups based on gender) according to the number of cigarettes smoked per day: Level 1 = non-smokers, Level 2 = 1-9 cigarettes, Level 3 = 10-19 cigarettes, and Level 4 = 20 or more cigarettes. The 490 participants engaged in exercise were also categorized into four groups according to their FIT (Frequency, Intensity, Time) scores: sedentary, light, moderate, and heavy activity, with scores ranging from 1 to 5 based on the level of activity. Each of these exercise groups was further subdivided by sex. The results were presented as mean values for total cholesterol, HDL-C, LDL-C, and triglycerides for both males and females in each subgroup for the two factors.

3.1 Effect of Smoking on Plasma Total Cholesterol and Lipoproteins

The plasma lipid levels across different smoking categories are shown in Table 1. Among the lipid parameters, HDL-C was the only one that significantly differed between groups, showing a negative stepwise correlation with increasing levels of smoking [R=-0.978][R=-0.978]. The adjusted HDL-C values were:

- Level 1 (non-smokers): Males = $46 \pm 4.1 \text{ mg/dL}$, Females = $48 \pm 4.0 \text{ mg/dL}$
- Level 2 (1-9 cigarettes/day): Males = 44 ± 3.6 mg/dL, Females = 44 ± 4.4 mg/dL
- Level 3 (10-19 cigarettes/day): Males = 36 ± 6.6 mg/dL, Females = 37 ± 6.3 mg/dL
- Level 4 (\geq 20 cigarettes/day): Males = 34 \pm 5.9 mg/dL, Females = 34 \pm 6.0 mg/dL

The number of individuals with low HDL-C levels (<40 mg/dL) increased with the number of cigarettes smoked per day, including among non-smokers:

- Level 1 (non-smokers) = 10.9%,
- Level 2 (1-9 cigarettes/day) = 11.6%,
- Level 3 (10-19 cigarettes/day) = 20.2%,
- Level 4 (\geq 20 cigarettes/day) = 23.1%.

The increase was particularly significant in Levels 3 and 4 compared to non-smokers (Level 1).

The mean LDL-C values for both sexes at Level 1 (non-smokers) were at the borderline and showed a positive stepwise correlation with smoking levels [R=0.995][R=0.995][R=0.995] (Table 1). The values were:

- Level 1: Males = 128 mg/dL, Females = 129 mg/dL
- Level 2: Males = 129 mg/dL, Females = 130 mg/dL
- Level 3: Males = 133 mg/dL, Females = 136 mg/dL
- Level 4: Males = 137 mg/dL, Females = 140 mg/dL

There was a perfect positive stepwise correlation between total cholesterol and smoking levels [R=1.00][R=1.00][R=1.00] and a strong positive correlation for triglycerides [R=0.998][R=0.998][R=0.998]. These correlations were especially evident at Levels 3 and 4, where the increases in both total cholesterol and triglycerides were significant.

Table(1):Plasma lipids and lipoproteins in different levels of smoking groups.

(Values are Means)

Level		Mean (mg/dl)					
		N	HDL-C	LDL-C	T.C	TGs	
Level 1	Mate	67	46±4.1	128±5.1	201±12.2	14016.6	
	Female	52	48±4.0	129±5.8	203±11.7	14216.9	
Level 2	Mate	50	44±3.6	129±6.6	206± 7.9	14616.3	
	Female	36	44±4.4	130±.7.0	206± 8.2	148±6.6	
Level 3	Male	57	36±6.6	133±6.7	212± 8.8	158±7.7	
	Female	42	37±6.3	136±7.2	214±8.1	160±7.7	
Level 4	Male	59	34±5,9	137±7.0	220±12.1	170±7.2	
	Female	49	3416.0	140±7.9	222+12.0	178±7.3	

C: Low Density Lipoprotein Cholesterol, T.C: Total Cholesterol, TGs: Triglycerides.

	HDL-C	LDI	L-C T.C	T.C	
	TGs				
R	-0.978	0.995	1.	00	
	0.998				
P	0.022	0.005	0.0001	0.002	

Source : Analysis Results

Table 2 presents the lipid profiles for different groups of physical activity among males and females. Similar to the smoking groups, HDL-C was the only lipid parameter that varied significantly among the physical activity groups, showing a positive stepwise correlation with increasing levels of physical activity [R=0.995][R = 0.995][R=0.995]. The HDL-C values were:

• Sedentary: Males = 46 ± 5.1 mg/dL, Females = 47 ± 5.6 mg/dL

- Light: Males = $47 \pm 5.9 \text{ mg/dL}$, Females = $49 \pm 6.5 \text{ mg/dL}$
- Moderate: Males = 54 ± 8.9 mg/dL, Females = 57 ± 7.3 mg/dL
- Heavy: Males = 62 ± 9.0 mg/dL, Females = 63 ± 8.1 mg/dL

These values indicate a significant effect on HDL-C in the moderate physical activity group and an even stronger effect in the heavy activity group, where HDL-C levels were the highest. Overall, the HDL-C levels increased in correlation with the FIT score for physical activity.

The mean LDL-C levels were highest in the sedentary group compared to the other physical activity groups (Table 2) and decreased progressively with higher FIT scores [R=-0.998][R=-0.998][R=-0.998]. The lowest LDL-C values were found in the heavy physical activity group. The values were:

- Sedentary: Males = 134 ± 6.0 mg/dL, Females = 135 ± 6.7 mg/dL
- Light: Males = 128 ± 5.1 mg/dL, Females = 130 ± 6.1 mg/dL
- Moderate: Males = $117 \pm 5.9 \text{ mg/dL}$, Females = $120 \pm 5.8 \text{ mg/dL}$
- Heavy: Males = 103 ± 6.6 mg/dL, Females = 107 ± 8.0 mg/dL

Physical activity also had a clear effect on total cholesterol and triglyceride levels in both males and females. A slight decrease was observed in the light activity group, with more substantial reductions in both the moderate and heavy activity groups. Total cholesterol and triglycerides decreased progressively from the sedentary to heavy activity groups, with the lowest mean values observed in the heavy activity group.

Mean total cholesterol levels were:

- Sedentary: Males = $204 \pm 6.9 \text{ mg/dL}$, Females = $207 \pm 7.2 \text{ mg/dL}$
- Light: Males = $200 \pm 8.0 \text{ mg/dL}$, Females = $204 \pm 8.3 \text{ mg/dL}$
- Moderate: Males = 187 ± 7.5 mg/dL, Females = 188 ± 7.9 mg/dL
- Heavy: Males = 170 ± 7.2 mg/dL, Females = 176 ± 7.3 mg/dL

Mean triglyceride concentrations showed a similar trend to total cholesterol, with the following values:

- Sedentary: Males = 140 ± 9.8 mg/dL, Females = 142 ± 9.1 mg/dL
- Light: Males = 137 ± 8.7 mg/dL, Females = 139 ± 8.4 mg/dL
- Moderate: Males = 120 ± 6.7 mg/dL, Females = 121 ± 6.0 mg/dL
- Heavy: Males = 107 ± 6.7 mg/dL, Females = 111 ± 7.4 mg/dL

Overall, the results demonstrate a clear positive impact of increasing levels of physical activity on lipid profiles, particularly for HDL-C, LDL-C, total cholesterol, and triglycerides.

Table (2): Plasma lipids and lipoproteins in different levels of physical activity groups.

Physical activity group		N	Mean (mg/dl)			
			HDL-C	LDL-C	T.C	TGs
	Man	69	46±5.1	134±6.0	204±6.9	140±9.8
Sedentary	Woman	91	47±6.1	135±6.7	207±7.2	142±9.1
Light	Man	88	47±5.9	128±5.1	200±8.0	137±8.7
Light	Woman	121	49±6.2	130±6.1	204±8.3	139±8.4
Moderate	Man	41	54±8.9	117±5.9	187±7.5	120±6.7
Moderate	Woman	28	57± 7.3	120±5.8	188±7.9	121±6.0
Heavy	Man	30	62±9.0	103±6.6	170±7.2	107±6.7
Heavy	Woman	22	63±8.1	107±8.0	176±7.3	111±7.4

Correlation coefficient between FIT and each of the four parameters.

		Sout	rce: Analysis	Results	
	P	0.004	0.002	0.004	0.008
108	R	0.995	-0.998	-0.996	-0.992
TGs		HDL-C	LD	L-C	T.C

In comparison, the study shows that physical activity improves cholesterol levels by lowering total cholesterol, LDL-C, and triglycerides, while raising HDL-C. In contrast, cigarette smoking has the opposite effect, leading to an increase in total cholesterol, LDL-C, and triglycerides, and a decrease in HDL-C.

4. Discussion

This study involved a total of 902 healthy subjects, with 412 participants assessed for smoking and 490 for aerobic exercise. All subjects were in good health and were not undergoing any treatment for cholesterol or lipid disorders at the time of the study. Most of the participants were employed professionals, some were students, and a few were freelancers. The questionnaire collected data on age, gender, lifestyle, behaviors, and educational level. The results demonstrated varying effects of smoking and aerobic exercise on the plasma lipid profile and lipoproteins in all the participants.

The characteristics of non-smokers and current smokers are presented in Table 1. Among the 412 participants, 119 (28.9%) were non-smokers, and 293 (71.1%) were current smokers. Of the current smokers, 64.6% had smoked for over 10 years, while the remaining smoked for over 7 years. Among current smokers, 29.3% smoked 1-9 cigarettes per day, 33.8% smoked 10-19 cigarettes per day, and 36.9% smoked 20 or more cigarettes per day. In general, current smokers had significantly higher plasma concentrations of total cholesterol, LDL-C, and triglycerides compared to non-smokers, while HDL-C levels were higher in non-smokers. In level 2 smokers (both genders), HDL-C levels were, on average, 3 mg/dl lower than those of non-smokers (level 1) and continued to decrease with the number of cigarettes smoked daily. HDL-C levels were significantly lower in levels 3 and 4, averaging 9.5 mg/dl and 13 mg/dl less,

respectively. This trend has been observed in previous studies, such as Yuan (2002), which found a significant association between cigarette smoking, low HDL-C, and high total cholesterol, contributing to coronary heart disease.

The mean plasma total cholesterol levels for both genders increased with the number of cigarettes smoked daily by current smokers. The differences between each level and non-smokers were 5, 11, and 19 mg/dl for males, and 3, 11, and 19 mg/dl for females, respectively. A slight increase was observed at level 2, with a significant increase in levels 3 and 4. Similar trends were observed for both LDL-C and triglycerides, which showed considerable and significant increases at levels 3 and 4. In Saudi Arabia, many people have a strong preference for animal products, and the amount and type of fat in their diet are believed to influence plasma lipid profiles. Consumption of saturated fats increases plasma triglycerides, total cholesterol, and LDL cholesterol levels. It is well-known that animal products are the primary source of dietary cholesterol, which was reflected in this study, as even the mean values of total cholesterol, LDL-C, and triglycerides for non-smokers were borderline for both Saudi men and women.

Table 2 shows that among the 490 Saudi adults assessed for aerobic exercise, 160 (32.7%) were sedentary, while 330 (67.3%) engaged in some form of aerobic activity. Of those with an active lifestyle, 209 (63.3%) engaged in light, 69 (20.9%) in moderate, and 52 (15.8%) in heavy physical activity. Overall, the study found that exercise reduced plasma total cholesterol, LDL-C, and triglycerides while increasing HDL-C. These findings are consistent with other studies, such as Fiorito (2005), which indicated that individuals who modified their diet and maintained regular physical activity successfully reduced their heart disease risk by improving their lipid profiles.

In both sexes, the sedentary group exhibited the highest plasma levels of total cholesterol, LDL-C, and triglycerides, while HDL-C levels were the lowest compared to other physical activity groups. Plasma total cholesterol in the sedentary group was, on average, 4 mg/dl higher for males and 3 mg/dl higher for females compared to the light physical activity group, and levels continued to decrease with increasing FIT scores. This decrease was significant in both the moderate and heavy groups. For example, in the moderate and heavy physical activity groups, total cholesterol levels were 17 and 34 mg/dl lower for males and 19 and 31 mg/dl lower for females, respectively, compared to the sedentary group. LDL-C levels followed a similar pattern, with differences of 6, 11, and 14 mg/dl for males and 5, 10, and 13 mg/dl for females between each successive group. Plasma triglycerides also decreased with increased physical activity, significantly so in the moderate and heavy groups (33 mg/dl for males and 31 mg/dl for females in the heavy group, and 20 mg/dl for males and 19 mg/dl for females in the moderate group) compared to the sedentary group, while only slight reductions were observed in the light group (3 mg/dl for both males and females).

This study demonstrated a strong positive correlation between HDL-C levels and physical activity. The lowest plasma HDL-C levels were recorded in the sedentary group, with levels increasing progressively with higher physical activity (FIT scoring). This increase was statistically significant in the heavy and moderately active groups but marginally significant in the light group. Adjusted HDL-C levels were, on average, 1.5 mg/dl higher in the light group, 8-10 mg/dl higher in the moderate group, and 16 mg/dl higher in the heavy group compared to the sedentary group. These findings indicate that gender does not significantly affect plasma lipid and lipoprotein levels for any of the

parameters examined. Consistent with this, several epidemiological studies have confirmed that regular physical activity is associated with increased HDL-C levels, which reduces the risk of coronary heart disease (CHD) as higher HDL-C levels are linked to lower heart disease risk. Aerobic activity can also help manage weight, diabetes, and high blood pressure while increasing heart and breathing rates. One study (Fiorito et al., 2005) examined 1,442 subjects (627 males, 815 females) aged over 20 years, selecting individuals based on sex, age, smoking status, and cardiovascular diseases to analyze the relationship between energy expenditure in physical activity (EEPA/day) and HDL-C levels in each group. The results suggested a statistically significant relationship between HDL-C and EEPA in all non-smokers, especially among non-smokers without CVD, with no significant difference related to age, strongly supporting the findings of the present study.

Given the preference for animal products, the limited number of Saudi people following regular aerobic exercise programs, and the prevalence of unhealthy lifestyles, middleaged adults in Saudi Arabia are particularly susceptible to health issues if proper precautions are not taken.

Conclusion:

This study examined the effects of smoking and physical activity on lipid profiles and the influence of these factors on the risk of coronary heart disease (CHD) and stroke. The findings demonstrated that regular aerobic exercise improved lipid profiles, increased HDL-C, and reduced total cholesterol, LDL-C, and triglycerides. Conversely, smoking had the opposite effect on plasma cholesterol levels. Moderate and heavy smokers showed significantly elevated total cholesterol, LDL-C, and triglycerides, along with reduced HDL-C, increasing their risk of serious cardiovascular problems and heart disease in the future.

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References

- [1]. Abdul R. A., and Syed R. M., (2005). Effects and a dose response relationship of physical activity on high density lipoprotein cholesterol and body mass index. Saudi Med J; 26(7):1107-1111.
- [2]. Ahmed T, Chasman DI, Buring JE, et al. (2011). Physical activity modifies the effects of LPL, LIPC, and CETP polymorphisms on HDL-C levels and the risk of myocardial infarction in women of European ancestry. Circ cardiovasc Genet; 4:74-80.

- [3].Alessandro M, Mariapoala L, Strecko N, and Aulikki N.,(2006). The relationship of serum cholesterol and smoking habits with risk of typical and atypical coronary heart disease death in the European cohorts. International J. of Cardiology.106: 157-163.
- [4].ALOTAIBI, TAREQ et al(2021). Acute Running and Coronary Heart Disease Risk Markers in Male Cigarette Smokers and Nonsmokers: A Randomized Crossover Trial. Medicine & Science in Sports & Exercise 53(5):p 1021-1032, May 2021. | DOI: 10.1249/MSS.0000000000002560.
- [5]. Antonella Muscella, Erika Stefàno, and Santo Marsigliante (2020). The effects of exercise training on lipid metabolism and coronary heart disease. American Physiological Society, HEART AND CIRCULATORY PHYSIOLOGY. Volume 319 Issue 1 July 2020 Pages H76-H88 https://doi.org/10.1152/ajpheart.00708.2019. PubMed32442027.
- [6]. Benfate R, Yano K, Hwang LJ, et al. (1994). Elevated serum cholesterol is a risk factors for both coronary heart disease and thromboembolic stroke in Hawaiian Japanese men . Stroke .25:814-20.
- [7]. Cem, B., Cerkan, T., Hurkan, K., Alia, I., Ayhan, O., and Ersoy, I., (2006). Effects of non-heavy smoking on HDL-C in healthy Turkish young men. Acta .61 (4): 411-415.
- [8]. Doll R, Peto R., (2002). Mortality in relation to smoking: 22 years observation of male British doctors, Br Med .2:1525-36.
- [9]. Fiorito, A., Bove, M., Linarello, S., Gaddi, A., Smith, W. (2005). Influence of physical activity on high density lipoprotein cholesterol (HDL-C) plasma levels in Massa Lombarda project cohort Supplement I.15:24-25.
- [10]. Gatchev O, Rastam L, Lindberg G, et al. (1993). Subarachnoid hemorrhage, cerebral hemorrhage, And serum cholesterol concentration in men and women. Ann Epidemiol .3:403-9.
- [11]. Hart CL, Hole DJ, Smith GD., (2000). The relation between cholesterol and haemorrhagic or ischemic stroke in the Renfrew/Paisley study. J Epdemiol Community Health .54:874-5.
- [12]. Iribarren C, Jacobs DR, Sadler M, Claxton AJ, Sidney S., (1993). Low total serum cholesterol and intracerebral hemorrhagic stroke: is the association confined to elderly men? The Kaiser Permanente Medical Care Program . Stroke. 27: 1993-8.
- [13]. *John R.*, (1997). Cholesterol content of foods. University of Adelaide, Australia. ed. 3:1-2.
- [14]. Kannel WB, McGee DL, Castelli WP., (1993). Latest perspective on cigarette smoking and cardiovascular disease: the Framingham study. J Cardiac Rehab .4:467-77.
- [15]. Lindenstorm E, Boysen G, Nyboe J., (1994). Influence of total cholesterol, high density lipoprotein cholesterol and triglycerides on risk of cerebrovascular disease: the Copenhagen City Heart Study. Br Med J. 309:11-5.
- [16]. Nakayama T, Date C, Yokoyama T, et al. (1997). A15.5-year follow-up study of stroke in Japanese Provincial City: the shibata Study. Stroke. 28:45-52. [17]. Sanchis-Gomar F, Perez-Quilis C, Leischik R, Lucia A (2016). Epidemiology of coronary heart disease and acute coronary syndrome. Ann Transl Med. 2016;4:256.
- [18]. Stamler J, Daviglus ML, Garside DB, et al. (2002). Relationship of baseline serum cholesterol levels in 3 large cohorts of younger men to long-term

- coronary , cardiovascular, and all-cause mortality and to longevity. JAMA . 284: 311-8.
- [19]. Suh I, Jee SH, Kim HC, et al. (2001). Low serum cholesterol and haemorrhagic stroke in men: Korea Medical Insurance Corporation Study. Lancet . 357: 922-5.
- [20]. Sharrett A, et al. (2006). Smoking, diabetes, and blood cholesterol differ in their association with subclinical atherosclerosis. Atherosclerosis. 186:441-447.
- [21]. Su-Min Jeong, et al. (2018). Effect of Change in Total Cholesterol Levels on Cardiovascular Disease Among Young Adults. Journal of the American Heart Association. Volume 7, Number 12. https://doi.org/10.1161/JAHA.118.008819
- [22].Sun H, Jangyong P, Inho J, Jakyoung L, Soojin, Y, Yangsu J.,(2006). Smoking and atherosclerotic cardiovascular disease in women with lower levels of serum cholesterol. Atherosclerosis. 23:3-23.
- [23]. The Pooling Project Research Group. Relationship of blood pressure, (1999). Serum cholesterol, smoking habits relative weight and ECG abnormalities to incidence of major coronary events: final report of the pooling project. J Chronic Dis. 31:201-306.
- [24]. *Ueshima H, Iida M, Shimamoto T, et al.*(2002). Multivariate analysis of risk factors for stroke Eight-year follow-up study of farming villages in Akita, Japan. Prev Med. 722-40.
- [25]. Yuan JM, ross RK, Wang XL, et al. (1996). Morbidity and mortality in relation to cigarette smoking in Shanghai, China. JAMA. 275: 1646-50.
- [26]. Zhang X, Patel A, Horibe H, et al. (2003). Asia Pacific Cohort Studies Collaboration. Cholesterol, coronary heart disease and stroke in the Asia Pacific region. Int J Epidemiol. 32: 563-72.
- [27]. Zhang XF, Attia J, Este C, Yu XH, Wu XG., (2005). A risk score predicted coronary heart disease and stroke in a Chinese cohort. J Clin Epidemiol. 58:951-8.
- [28]. Zhao, Y., Zhuang, Z., Li, Y. et a(2024)l. Elevated blood remnant cholesterol and triglycerides are causally related to the risks of cardiometabolic multimorbidity. Nat Commun 15, 2451 (2024). https://doi.org/10.1038/s41467-024-46686-x.