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Lipid profile in individuals under 50 years of age with corneal arcus

Habib Ojaghi[1*], **Ali Lasemi Imani**[2], **Firouz Amani**[2]

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Authors' Affiliation:
[1]Department of Surgery, School of Medicine and Allied Medical Sciences, Imam Reza Hospital, Ardabil University of Medical Sciences, Ardabil, Iran
[2]School of Medicine and Allied Medical Sciences, Ardabil University of Medical Sciences, Ardabil, Iran

[*]**Corresponding Author**
Department of Surgery, School of Medicine and Allied Medical Sciences, Imam Reza Hospital, Ardabil University of Medical Sciences, Ardabil, Iran
Email: habibojaghi@yahoo.com

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ABSTRACT

Introduction: The corneal arcus is a condition in which a yellowish white ring is formed in the stromal tissue of the peripheral cornea and is separated from the limbus by a clear corneal margin. In some studies, the presence of corneal arcus under the age of 50 has been associated with hyperlipidemia, which could increase the risk of cardiovascular complications in forementioned patients. *Materials and Methods:* This cross-sectional study was performed on patients less than 50 years of age referred to the ophthalmology clinic of Imam Reza Hospital in Ardabil who underwent corneal arcus examination during July 2021 to November 2021. Patients were enrolled in the study by census method. The collected data were entered into SPSS version 22 software and then analyzed. *Results:* A total of 59 cases were included in the study. 36 (61%) of cases were male and 74.6% were overweight or obese. 50.8% of subjects had triglycerides equal to or above 150 mg/dl. Additionally, 15.3% of cases with normal hyperlipidemia were using serum lipid-lowering drugs. There was no significant relationship between age and blood lipid levels ($p > 0.05$). The prevalence of corneal arcus was higher at older ages and in people with a higher Body Mass Index (BMI), but this association was not statistically significant. *Conclusion:* The prevalence of corneal arcus increased with age. The prevalence of overweight, obesity and abnormal lipid profiles were remarkably but non-significantly high in our patients under 50 years of age with corneal arcus.

Keywords: Corneal arcus, Lipid profile.

1. INTRODUCTION

The corneal arcus is a condition in which a yellowish-white ring forms in the stromal tissue around the cornea and is separated from the limbus by clear margins (0.3 to 1.00 mm in diameter) (Helvaci et al., 2012). Typically, the first sign of a corneal arcus starts at the lower pole and then involve the upper pole (Ang et al., 2011). Materials accumulated in the corneal arcus are mainly composed of low-density lipoproteins, phospholipids and triglycerides. The diameter of these particles is between 40 and 200 nm, which are similar to the size of particles accumulated in atherosclerotic lesions (Ayhan et al., 2016).

The prevalence of corneal arcus has been shown to increase with age. Studies have shown that this condition could be occurred in more than 80% of

people over the age of 60; therefore, researchers have also called the corneal arcus senilis (Helvaci et al., 2012; Ang et al., 2011). However, this pathological condition is sometimes seen in people under the age of 40, in which case it is called juvenile corneal arcus. The corneal arcus is the most common peripheral opacity of the cornea. Although it is not associated with specific ocular or visual complications, it is pathologically caused by extracellular deposition of fat particles in corneal stromal tissue (Crispin, 1989). Lipid infiltration from the limbus arteries without degenerative changes seems to be a more important underlying cause than aging alone (Ang et al., 2011). The structural changes of collagen fibrils in the peripheral parts of the cornea and the increased permeability of the limbal vessels in the formation of the corneal arcus are similar to the mechanism of atherosclerosis formation. Various studies have shown that corneal arcus is rarely the only clinical sign (Lock et al., 2018) and can often be a sign of high blood pressure (Ang et al., 2011), high body mass index (Chua et al., 2004), diabetes mellitus and smoking (Ang et al., 2011). Studies have also shown an association of the corneal arcus with conditions such as cardiovascular disease and stroke (Jonas et al., 2011). Previous studies have shown an association of high serum lipid levels and familial hyperlipoproteinemia (especially types II and III) with early types of corneal arcus (Helvaci et al., 2012). In some studies, the early onset corneal arcus has been suggested as the first sign of familial hyper lipoproteinemia (Macchiaiolo et al., 2014). However, the relationship between the juvenile corneal arcus and the abovementioned issues has been less studied. Therefore, the aim of present study was to evaluate serum lipid levels in patients less than 50 years of age with corneal arcus.

2. MATERIALS AND METHODS

This cross-sectional study was performed on patients with corneal arcus under 50 years of age who referred to the ophthalmology clinic of Imam Reza Hospital in Ardabil, Iran, during July 2021 to November 2021. All patients who were diagnosed with corneal arcus during an ophthalmologic examination with a slit lamp were included in the study. A total of 59 patients were included in the study using census method. Patients were included in the study by considering inclusion and exclusion criteria. Inclusion criteria included: Age less than 50 years, presence of corneal arcus based on slit lamp examination and having informed consent. Exclusion criteria included: Unwillingness to participate in the study, presence of primary corneal disease and history of corneal surgery. Data such as age, sex, blood pressure, body mass index, history of smoking and alcohol use, history of serum lipids lowering drugs using, xanthelasma, history of cardiovascular disease and cerebrovascular events were collected in a checklist. Laboratory tests such as cholesterol, triglyceride (TG), fasting blood sugar (FBS), LDL (Low Density Lipoprotein), HDL (High Density Lipoprotein) and HbA1C (Glycosylated Hemoglobin Type A1C) measurements were performed for all patients. Test results entered in checklist. According to Harrison's book of internal medicine, normal values for each of the indicators of cholesterol (less than 200), triglycerides (less than 150), LDL (less than 130), HDL (between 40 and 60), FBS (less than 100), two hours postprandial blood sugar (2hppBS) (less than 140) and HbA1C (4.5 to 6%) was considered.

The range of normal body mass index was 18-24.9, followed by overweight (25-29.9) and obesity (>30) (Jameson et al., 2020). Based on criteria presented at the American Academy of Ophthalmology, the classification of corneal arcus severity was as follows (Weisenthal et al., 2019): Mild: Details of the iris are easily seen. Medium: Details of the iris are difficult to see. Severe: Details of the iris are not visible.

Data analysis

Data are presented in the form of tables, graphs and statistical indicators using descriptive statistical methods. Relationships between variables were analyzed using statistical tests such as Chi-square. The collected data were entered into SPSS version 22 software. A p-value less than 0.05 were considered to be statistically significant.

Ethical considerations

The declarations of *Helsinkis tenets* and ethics research committees of the University of Medical Sciences of Ardebil were followed in all the study steps and written informed satisfaction was received from patients in our research. The study was approved by the Research Council of the School of Medicine IR.ARUMS.REC.1399.095.

3. RESULTS

A total of 59 patients were included in the study, of which 23 were female (39%) and 36 were male (61%). Most of the subjects were between 40-49 years old (67.8%). In addition, 49.2% of cases were overweight. The mean BMI of normal individuals was 22.7 ± 1.6, the mean BMI for overweight and obese individuals was 28.2 ± 1.8 and 34.4 ± 5.8, respectively (Table 1). The mean cholesterol of the subjects was 199.81 ± 30.45 that most of the subjects (54.2%) had normal cholesterol. The mean LDL and HDL in the subjects were

114.56 ±24.55 and 46.3±9.6, respectively. The mean triglyceride of the subjects was 175.9±125 and 29 (49.2%) of the subjects had normal triglycerides. Most of the subjects had normal FBS and 2hppBS (86.4%) (Table 2). Furthermore, 48 (86.4%) had no history of smoking. Additionally, 57 (96.6%) of the subjects denied alcohol consumption (Table 1).

Table 1 Demographic characteristic of patients

Parameters	N (%)
Age(year)	
20-29	4 (6.8%)
30-39	15 (25.4%)
40-49	40 (67.8%)
Sex	
Male	36 (61%)
Female	23 (39%)
BMI(Kg/m^2)	
Normal (18-24.9)	15 (25.4%)
Overweight (25-29.9)	29 (49.2%)
Obesity (≥30)	15 (25.4%)
Positive history of smoking	11 (18.6%)
Positive history Of alcohol Consumption	2 (3.4%)

N, number; BMI, Body Mass Index

Table 2 Blood chemistry characteristics of patients

Parameters	N (%)
Cholesterol (mg/dl)	
Borderline high (200-239)	21 (35.5%)
High (≥240)	6 (10.3%)
LDL≥130	13 (22%)
Abnormal HDL (mg/dl)	
<40	14 (23.7%)
≥60	6 (10.2 %)
Abnormal Triglyceride (mg/dl)	
≥150	33 (50.8%)
Positive history of HBL	8(13.6%)
Positive history of serum lipid lowering drugs	9 (15.3%)
Abnormal blood sugar	
FBS ≥100 mg/dl	8 (13.6%)
2hpp BS ≥ 140 mg/dl	8 (13.6%)
HbA$_1$C > 5.6%	5 (8.5 %)

N, number; LDL, Low Density Lipoprotein; HDL, High Density Lipoprotein; HBL, Hyper Beta Lipoproteinemia; FBS, Fasting Blood Sugar; HbA$_1$C, Glycosylated Hemoglobin Type A1C

The amount of serum lipids increases with age due to the low physical activity and low metabolism. Thus, cholesterol and triglyceride levels are higher in people over 40 years of age than in other groups. However, the association of age with serum lipid levels was not statistically significant (P> 0.05) (Table 3).

Table 3 Relationship between serum lipids and age

Parameters (mg/dl)	Age			P – Value
	20 – 29 n = 4	30 – 39 n = 15	40 – 49 n = 40	
Cholesterol	195.7±22.1	196.3±31.50	200.6±30.6	0.76
LDL	113.5±20.1	113.1±26.1	114.7±2.4	0.93
HDL	39.50±6.1	46.7±10.6	46.5±9.4	0.81
Triglyceride	167.7±36.2	137.2±57.3	189.4±144.5	0.23

LDL, Low Density Lipoprotein; HDL, High Density Lipoprotein

Although no significant relationship was observed between the intensity of corneal arcus and hyperlipidemia (P> 0.05), but cholesterol and LDL levels were non significantly higher in cases with higher arcus intensity (Table 4)

Table 4 Relationship between corneal arcus grading and serum lipids

Parameters (mg/dl)	Corneal arcus grading			P - Value
	Mild n = 20	Moderate n = 24	Severe n = 15	
Cholesterol	193.8±36.4	199.1±23.6	208.8±31.3	0.36
LDL	105.8±29.1	117.5±20.8	121.321.3	0.13
HDL	44.4±11.3	46.3±8	48.8±9.5	0.41
Triglyceride	205.4±19.8	156.2±62.8	168±55.1	0.42

LDL, Low Density Lipoprotein; HDL, High Density Lipoprotein

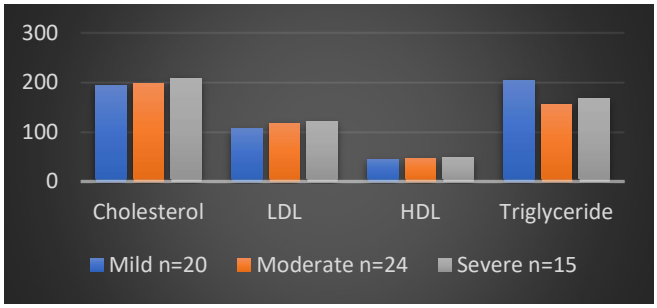

Figure 1 The relations between serum lipids and corneal arcus grading

According to Chi-square test, no significant relationship was found between gender and corneal arcus intensity (P = 0.73). There was no significant relationship between corneal arcus intensity and age and BMI (P> 0.05).

4. DISCUSSION

Corneal arcus is a very common, bilateral and benign degeneration of the peripheral part of the cornea and can occur at any age; but it is much more common in the elderly as part of the aging process. Pathologically, fat droplets occupy the entire thickness of the cornea; but they are denser in the superficial and deep layers and are relatively scattered in the stroma layer. There are no symptoms in these people. Its presence under the age of 50 is usually associated with hypercholesterolemia and it is necessary to evaluate the level of serum lipids in these people (Hashemi et al., 2014). Regarding the lack of sufficient studies on the level of blood lipids in patients under 50 years of age with corneal arcus, the present study was performed.

In the present study, there was no significant relationship between age and serum lipid levels (P> 0.05). No significant relationship was observed between corneal arcus intensity with serum lipid, BMI and age (P> 0.05). There was no significant relationship between gender and corneal arcus intensity (P = 0.73). Regarding the low prevalence of corneal arcus and its rarity under 50 years of age, specific studies on the relationship of lipid profile, other laboratory and anthropometric indicators with corneal arcus formation are very low worldwide.

In the present study, the prevalence of corneal arcus was higher in men than women. In a study by Weisenthal et al., (2019) the prevalence of corneal arcus was significantly higher in men than women under the age of 50. In the study of Raj et al., (2015) the outbreak of corneal arcus was found to be higher in men than women in all age groups. Other previous studies showed that the

corneal arcus was superior in men in all age groups and races than women (Crispin, 2002) which were consistent with the present study.

Almost all studies have shown that bilateral corneal arcus at a young age is always associated with impaired fat metabolism such as LCAT deficiency, fish eye disease and tangier. However, the main cause of this deposition in old age, rather than being related to disorders of fat metabolism is related to increased permeability of limbal arteries. Following this increase in permeability, lipids, especially LDL, pass through this vascular structure and deposit in the peripheral parts of the cornea (Munjal and Kaufman, 2020). In our research, the spread of corneal arcus grows with age. In most of the studies, the prevalence of corneal arcus increased with age, which our findings were consistent with these studies.

In a study by Raj et al., (2015) serum triglyceride levels were reported to be higher than normal in 58.3% of patients with juvenile corneal arcus. In the present study, more than half of the patients had abnormal triglyceride levels, which was consistent with the aforementioned study. However, no correlation was found between triglyceride levels and the intensity of arcus. In a study by Azimi et al., (2009) no association of triglyceride levels with corneal arcus formation was found in patients older than 30 years which was inconsistent with our study. It should be noted that in the present study, regarding the absence of the control group, it cannot be concluded that there is no relationship between triglyceride level and arcus formation.

Accelerated corneal arcus formation is generally associated with hyperlipoproteinemia, especially LDL proliferation. This association became clear when Forsius, (1954) first showed that circulatory lipid disorders were considerably related to the corneal arcus formation at a young age and such a correlation is not always established in the elderly. Parwaresch et al., (1976) found that familial hyperlipoproteinemia of types IIa and IIb are the most common underlying diseases found in patients with corneal arcus under the age of 50 years. In cases where the corneal arcus developed at a very young age, the prevalence of familial type IIa hypercholesterolemia was higher (Parwaresch et al., 1976). In a study by Winder et al., (1998) familial hypercholesterolemia with heterozygous inheritance was identified as one of the effective factors in corneal arcus development.

The study by Segal et al., (1986) showed that both the formation of Xanthelasma and corneal arcus in young men were strongly associated with elevated serum cholesterol levels, especially LDL. In the present study, 22% and 45.8% of patients with corneal arcus had higher than normal LDL and cholesterol levels respectively, however, no significant correlation was found between LDL and cholesterol levels with corneal arcus intensity. Of course, the percentage of people with abnormal blood lipid levels was also higher, including people who had a history of taking lipid-lowering drugs and had normal blood lipids at the time of the study. In a study by Lertchavanakul et al., (2002) HDL levels were significantly lower in men aged 30-49 years with corneal arcus; however, no difference in HDL was observed in other age groups of patients, either at younger and older ages or in women. In the present study, more than one-third of the patients had abnormal HDL levels.

In our research, the mean cholesterol, triglyceride, HDL and LDL cholesterol profiles were 199.81, 175.90, 46.34 and 114.56, respectively. In a study by Qhorbani et al., (2015), 27 studies on the general public were evaluated as Meta-analyzes. Cholesterol, triglyceride, HDL and LDL levels were reported as 195.7, 169.8, 45.4 and 120.5, respectively. In a study by Larco et al., (2020) HDL and LDL were reported to be 193, 139, 47 and 120, respectively. Finally, by descriptive comparison of these values with the values obtained from the present study, it can be inferred that blood lipid levels are probably outside the normal range in the population with corneal arcus. This is especially true for higher triglycerides in the present study when compared with previous studies. However, this relationship is not conclusively provable due to the lack of a control group in our study. Furthermore, the lipid profile in patients with corneal arcus is more disturbed than other people, nevertheless, no correlation was found between the level of each of the lipid profile parameters and the intensity of the corneal arcus in our research.

In a study by Azimi et al., (2009) a weak correlation was reported between fasting blood sugar and the intensity of corneal arcus incidence. In the study of Hashemi et al., (2014) there was no association between the presence of corneal arcus and diabetes. In the present study, no relationship of FBS levels and 2hppBS with the intensity of arcus was found, which could be due to insufficient sample size in the present study. In a study by Helvaci et al., (2012) smoking was introduced as a weak risk factor in corneal arch formation. Smoking has been introduced as a dangerous invoice for corneal arcus development, especially at a young age (Chua et al., 2004). The prevalence of smoking among our patients was lower than initially assumed and no association was found between smoking and the intensity of the corneal arcus, which one possible reason could be the concealment of smoking by patients.

In a study by Jonas et al., (2011) alcohol consumption has been suggested as one of the dangerous invoice for corneal arcus formation, even in old age. However, in the present study, the prevalence of alcohol consumption among patients was reported to be only 3.4%; an important possible reason could be the concealment of alcohol consumption by patients due to the customary and social ugliness of this issue in Iran.

5. CONCLUSION

The prevalence of corneal arcus increases with age. Furthermore, the most of our patients had abnormal triglyceride levels. The prevalence of overweight, obesity and abnormal lipid profiles were remarkable in patients under 50-years of age with corneal arcus. Finally, it is also recommended to conduct a similar study but using the control group and a higher number of cases.

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Author Contributions

All authors contributed to the design of the study, as well as data collection and analysis and the writing of the manuscript. All authors read and approved the final manuscript.

Ethical approval

The study was approved by the Medical Ethics Committee of (Ethical approval code: IR.ARUMS.REC.1399.095)

Informed consent

Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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