SENILE CATARACT;
SERUM LIPIDS A MODIFIABLE RISK FACTOR

1. The University of Lahore
2. Assistant Professor CRiMM
   The University of Lahore
3. Associate Professor of
   Ophthalmology
   Lahore Medical and Dental College,
   Lahore
4. Biostatistician IMBB
   The University of Lahore
5. Associate Professor of
   Ophthalmology
   Lahore Medical and Dental College,
   Lahore

Correspondence Address:
Dr. Tayyaba Gul Malik
Associate Professor of
Ophthalmology
Lahore Medical and Dental College,
Lahore

tayyabam@yahoo.com

Ammara Javed[1], Dr. Roquyya Gul[2], Dr. Tayyaba Gul Malik[3], Rabail Alam[4], Dr. Muhammad Khalil[5]

ABSTRACT… Objective: To estimate the serum lipid profile of patients having different types of senile cataract and compare them with that of the controls. **Study Design:** Observational case control study. **Place of study:** Tertiary care centre in the city of Lahore, Pakistan. **Period:** Six months. **Methods:** We selected fifty patients with senile cataract and fifty control individuals from tertiary care hospital of Lahore. History, ophthalmic and systemic examinations were done. Fasting serum samples were taken for estimation of lipid profile from all the subjects. **Results:** In the patient group, female to male ratio was 1.63:1. 78% patients had Nuclear cataract, 16% had cortical and 6% had posterior sub capsular type of senile cataract. Serum Triglycerides, Cholesterol, LDL, HDL and VLDL of patients were compared with controls. The p-value of cholesterol, LDL and HDL was non-significant. The p-value of triglycerides and VLDL was significant. **Conclusions:** Serum Triglycerides and VLDL are modifiable risk factors in the development of senile cataract in Pakistani patients. Serum Triglycerides is the only lipid, which has shown consistent results related to cataract development in different parts of the world. Other lipids show variable results in different countries.

Key words: Cataract, Serum Triglycerides, Serum LDL, Serum cholesterol, Serum HDL, Risk factors for cataract.

Article Citation: Javed A, Gul R, Malik TG, Alam R, Khalil M. Senile cataract; serum lipids a modifiable risk factor for. Professional Med J 2015;22(4):500-506.

INTRODUCTION

There are 1.7 Million blind people in Pakistan and another 170,000 are added to the pool of blindness every year. 80% of blindness is curable since 60% cases are caused by Cataract. Another 16.5 million people have impaired vision, 6.6 million due to cataract, 7 million due to refractive error and 2.9 million due to other causes[1]. According to WHO number of cataract surgeries should be tripled between the year 2000 and 2020 to combat cataract blindness[2].

There are many risk factors for development of cataract. Age is the most common one[3]. Other causes of cataract include trauma, drugs, toxins, radiation, electric shocks, systemic diseases, metabolic disorders and concurrent ocular diseases[4]. Research has been going on in different parts of the world to find out the factors contributing to aging process of lens. Serum Lipids is another risk factor. As lipids are important structural components of cell membranes and have profound effect on membrane fluidity, age-related changes in lipid composition could be a contributing factor for altered protein-lipid interaction leading to cataract formation.

Purpose of this study was to find out which of the lipid components in blood have profound effect in cataract development (in Pakistani patients).

SUBJECTS AND METHODS

Fifty patients with senile cataract from a tertiary care hospital of Pakistan were selected. Clinical history, including ocular as well as systemic history, was taken from each patient. Snellen's visual acuity chart was used to record the visual acuity. Pupillary reaction to light and accommodation was recorded. Slit lamp Biomicroscope was used to identify the type of cataract. Direct and indirect ophthalmoscopes were used to examine the vitreous and retina. Intra ocular pressures were also recorded using Applanation Tonometer. All these clinical diagnostic tests were performed by ophthalmologists.

The inclusion and exclusion criteria for patient selection were as follow:

Inclusion criteria
Male and female patients with senile cataract, age $\geq$ 40 years and non smokers were included in the study.

Exclusion criteria
Patients with cataract other than senile cataract or history of steroid intake and ocular trauma were excluded. Diabetic and hypertensive patients or patients having systemic or other ocular diseases of anterior and posterior segment were also not included in the study.

There were fifty control subjects (healthy individuals) with $\geq$ 40 years of age. They were not suffering from senile cataract or any other type of cataract and systemic diseases.

Materials
The materials used in the current study were 5cc BD syringes, alcohol swabs, 5ml vaccutainers for the collection of blood sample, centrifuge (Model Sigma 3k 30) machine for the separation of serum, eppendorffs for storing the serum, a storage box. Fasting blood samples were collected from fifty patients of senile cataract visiting the outdoor and 50 fasting blood samples from control group. Aseptic precautions were taken to draw blood from the subjects. The serum was separated from all blood samples and proceeded for lipid profile analysis. Patient proforma and consent forms were filled before sampling.
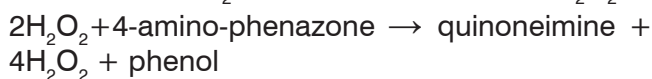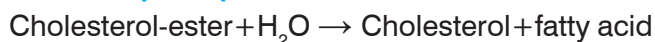
Estimation of lipid profile included cholesterol, triglyceride, high density lipoprotein (HDL), low density lipoprotein (LDL), and very low density lipoprotein (VLDL). HUMAN lipid liquicolor method included enzymatic calorimeter test for all lipid profile with lipid clearing factor (LCF).

Estimation of Cholesterol level by Cholesterol liquicolor (CHOD-PAP-method)
Estimation of Cholesterol was done using CHOD-PAP-method (Kit Company Human, Catalog # 10017). Cholesterol was determined after enzymatic hydrolysis and oxidation. The indicator quinoneimine was formed from hydrogen peroxide and 4-aminophenazone in the presence of phenol and peroxidase.

Reaction principle
$$Cholesterol\text{-}ester + H_2O \rightarrow Cholesterol + fatty\ acid$$
$$Cholesterol + O_2 \rightarrow Cholestene\text{-}3\text{-}one + H_2O_2$$
$$2H_2O_2 + 4\text{-}amino\text{-}phenazone \rightarrow quinoneimine + 4H_2O_2 + phenol$$

The assay conditions for the estimation of cholesterol were wavelength: 500 nm, optical path: 1 cm and temperature: 20-25 degree C. Only one reagent blank per series was required.

Cholesterol concentration (C) was calculated with the following formula:
$$C = 200\ X\ \frac{\Delta A\ sample\ [mg/dl]}{\Delta Standard}$$

or

$$C = 2.28\ X\ \frac{\Delta Sample\ [mmol/l]}{\Delta Standard}$$

Cholesterol concentration over 260 mg/dl or 6.7 mmol/l was considered high.

Estimation of Triglycerides by Triglycerides liquicolor (GPO-PAP Method)
Estimation of Triglycerides was done using GPO-PAP-method (Kit Company Human, Catalog # 10720). The triglycerides were determined after enzymatic hydrolysis with lipases. Indicator was quinoneimine formed from hydrogen peroxide, 4-amino-antipyrine and 4-chlorophenol under the catalytic influence of peroxidase.

Reaction principle
$$Triglycerides \rightarrow glycerol + fatty\ acids$$
$$Glycerol + ATP \rightarrow glycerol\text{-}3\text{-}phospate + ATP$$
$$Glyerol\text{-}3\text{-}phosphate + O_2 \rightarrow dihydroxyacetone\ phosphate + H_2O_2$$
$$H_2O_2 + 4\text{-}aminoantipyrine \rightarrow quinoneimine + HCL + H_2O_2 + 4\text{-}Chlorophenol$$

The assay conditions were similar to the cholesterol estimation.

Triglycerides concentration (C) was calculated with the following formula:

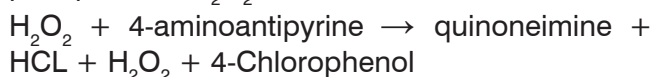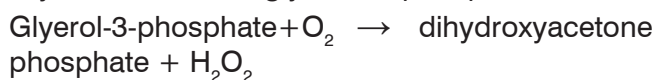$$C = 200 \times \frac{\Delta \text{ A Sample [mg/dl]}}{\Delta \text{ A Standard}}$$

or

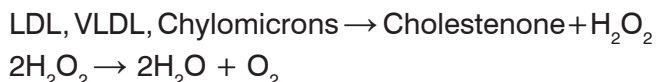$$C = 2.28 \times \frac{\Delta \text{ A Sample [mmol/l]}}{\Delta \text{ A Standard}}$$

Triglyceride concentrations over 200 mg/dl or 2.28 mmol/l was considered high.

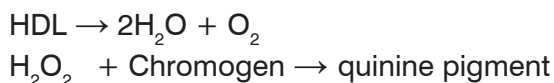## Estimation of HDL concentration by HDL liquicolor Method

Estimation of HDL was done using HDL-PAP-method (Kit Company Human, Catalog # 10018`). The assay combined 2 specific steps. In first step chylomicron, VLDL, LDL and Cholesterol were specifically eliminated and destroyed by enzymatic reaction. In second step remaining cholesterol from HDL fraction was determined by well established specific enzymatic reaction in presence of specific surfactants for HDL.

Reaction principle:
1st step:
LDL, VLDL, Chylomicrons $\rightarrow$ Cholestenone $+ H_2O_2$

$2H_2O_2 \rightarrow 2H_2O + O_2$

2nd Step:
HDL $\rightarrow 2H_2O + O_2$

H_2O_2 + Chromogen $\rightarrow$ quinine pigment

Contents of vial were reconstituted with exactly 4ml of sterilized distilled water. Vial was closed and swirled carefully to dissolve all lysophilisate, avoiding foaming. It was allowed to stand for 30 minutes before use. The assay conditions for the estimation of HDL were wavelength: 578 nm, optical path: 1 cm and temperature 20-25 degree C. Only one blank per series was sufficient.

HDL Concentration (C) was calculated by the given formula:

$$C = 150 \times \frac{\Delta A \text{ sample (mg/dl)}}{A \text{ Standard   (mg/dl)}}$$

Estimation of VLDL (very low density lipoprotein)
VLDL was estimated by simple calculation. Calculations included Triglycerides which was determined by the HUMAN kit method.

$$VLDL = \frac{\text{Triglycerides mg/dl}}{5}$$

Estimation of LDL (Low density lipoprotein)
LDL was also estimated by simple calculation. Calculations included HDL and VLDL which were determined by the HUMAN kit method.

$$LDL = HDL \text{ mg/dl} + VLDL \text{ mg/dl}$$

STATISTICAL ANALYSIS
The statistical analysis was done by using SPSS version 16.0 to investigate the role of lipid parameters in the development of age-related cataract. Moreover, the percentage of different types of senile cataract groups was analyzed.

RESULTS
In the present study, there were 31 females and 19 male patients (F: M = 1.63:1). The types of senile cataract were Nuclear, Cortical and Posterior sub capsular. Patients who had more than one type of lens changes were categorized according to the more prominent type of lens change.

In the control group, there were 32 females and 18 males (F: M = 1.77:1).

Lipid profile analysis in senile cataract patients and control individuals
Lipid profile analysis in senile cataract patients showed high value of cholesterol, triglyceride, LDL and VLDL in 7, 29, 1 and 19 patients respectively. While 9 patients showed low HDL value. Out of total 50 controls, 47 showed normal levels of serum Cholesterol and 3 showed abnormal levels. 31 individuals showed normal levels of TG while 19 showed abnormal levels. HDL levels were normal in 43 and abnormal in 7 individuals. VLDL levels were normal in 11 individuals and abnormal in 39. While LDL was normal in all control individuals.

The mean of cholesterol in control group and senile cataract patients was 171.4±3.8 (Median 182) and 169.3±4.3 (Median 166) respectively.

The *p*-value of cholesterol was non-significant (NS) as shown in Table II.

Types of senile cataract	No. of patients	Percentage
Nuclear	39	78%
Cortical	8	16%
Posterior Sub Capsular	3	6%

Table-1. Percentage of different types of senile cataract.

The mean of triglycerides in control group and senile cataract patients was 127.02± 5.7 (Median 117.5) and 162.2±7.2 (Median 162.5) respectively. Whereas *p*-value of triglycerides was found significant (*).

In control group and senile cataract patients mean HDL was 48.8 ±1.2 (Median 50.5) and 46.6±1.9 (Median 45) respectively. While *p*-value of HDL was non-significant (NS).

The mean of LDL in control group and senile cataract patient's was 74 ±1.8 (Median 73.5) and 79.7±2.9 (Median 76) respectively and the *p*-value of LDL was observed to be non significant as shown in Table II.

The mean of VLDL in control group and senile cataract patients was 32.3± 1.2 (Median 23.5) and 33.1±1.5 (Median 33) respectively. The *p*-value of VLDL was significant (*) as shown in Table II.

Analysis of Lipid profile in different types of Senile Cataract

The summary of the lipid profile analysis in different types of senile cataract is shown in Table III. To find out whether a specific type of dyslipidemia is responsible for nuclear, cortical or posterior sub capsular opacities, we compared the values of serum lipids among different types of cataract. Although number of patients in each type of cataract was not sufficient to draw a definite conclusion but a rough comparison can be an initiative for further studies. Serum cholesterol was high in 15% patients of nuclear cataract (total 39) and 12.5% of cortical cataract

Lipid Parameter	Groups	Mean	Median	Std. error of mean	Minimum	Maximum	*p*-value
Cholesterol (150-200mg/dl)	Control	171.4	182	3.8	106	209	0.461[NS]
	Patients	169.3	166	4.3	105	246	
Triglycerides (>35mg/dl)	Control	127.02	117.5	5.7	68	196	<0.0001*
	Patients	162.2	162.5	7.2	83	274	
HDL >35mg/dl)	Control	48.84	50.5	1.2	31	65	0.1[NS]
	Patients	46.6	45	1.9	25	84	
LDL (<130 mg/dl)	Control	74	73.5	1.8	44	103	0.08[NS]
	Patients	79.7	76	2.9	47	137	
VLDL (up to 35 mg/dl)	Control	32.308	23.5	1.2	7	39	<0.0001*
	Patients	33.1	33	1.5	17	55	

Table-II. Statistical analysis of lipid parameters in senile cataract patients and control group. NS (non significant) and asterisk (*) shows significant *p*-value.

Type of Senile Cataract	Lipid profile									
	Cholesterol		Triglycerides		HDL		LDL		VLDL	
	Normal	High	Normal	High	Normal	Low	Normal	High	Normal	High
Nuclear	33	6	19	20	32	7	38	1	27	12
Cortical	7	1	1	7	8	0	8	0	1	7
Posterior Sub Capsular	3	0	1	2	1	2	3	0	3	0

Table-III. Analysis of Cholesterol, Triglycerides, HDL, LDL and VLDL among different types of Senile cataracts

(total 8 patients) while it was normal in all patients (3) who had posterior sub capsular cataract. Serum triglycerides were raised in 51.28% of nuclear cataract patients, 87.5% of cortical cataract and 66.67% of posterior sub capsular cataract patients. Low HDL levels were seen in 17.95% patients with nuclear cataract, 66.67 % of posterior sub capsular cataract and none had low HDL in patients with cortical lens opacities. LDL was high in only 2.56% of nuclear cataract patients while normal in all patients with cortical and posterior sub capsular opacities. VLDL was high in 30.77% of nuclear cataract and 12.5% of cortical cataract patients. It was normal in all patients with posterior sub capsular opacities.

DISCUSSION
Senile Cataract is one of the major public health problems, which if not detected and treated in time, can lead to permanent vision threatening complications. So far, much work is done and still going on to identify non-modifiable and modifiable risk factors. This study seeks to identify serum lipids as biochemical risk factor for senile cataract in a small group of Pakistani patients. This can help to modify the aging process of lenses and affect the prognosis and management of age related cataracts.

In this particular study, when we compared serum Cholesterol, LDL and HDL of senile cataract patients with normal age matched controls, it was found insignificant. On the other hand, serum Triglycerides, and VLDL of cataract patients were significantly higher than normal controls. This can be compared with the results found in Iran where, increased serum levels of Triglycerides (p= 0.02) were seen in senile cataract patients. While, serum cholesterol (p= 0.001) and LDL

(p=0.04) was also high in Iranian study, which were normal in our patients. However, there was no difference between serum HDL of cataract patients and normal subjects (p=0.12)[5]. Contrary to that, Meyer et al found low serum HDL in cataract patients[6]. Similarly, animal studies have also shown decreased serum HDL as a risk factor for cataract development[7].

Another Asian study by Rajiv Raman and colleagues revealed high serum Triglycerides as a risk factor for cataract development[8]. There are other studies, which show association of high serum triglycerides and low HDL with the development of senile cataract[6,9,10,]. Interestingly, Donnelly et al noted that high serum Triglycerides predispose specially women to early senile cataract[11].

It is a known fact that cataract formation is directly related to the oxidative stress and HDL has antioxidant properties. So, Low HDL leads to oxidative damage which promote the formation of lens opacities[12]. As Cataract is a multi-factorial disease, few studies including this particular study, have shown no relation of serum HDL and senile cataract[13, 14].

Cholesterol content in the lens membrane is highest than any known membrane in the body. So, if cholesterol metabolism is disturbed, it can lead to lens opacification[15]. A study done in Florida showed that both men and women with cataracts had lower cholesterol concentrations than normal subjects[16]. In contrast to this, our study showed normal serum cholesterols in cataract patients. When we compared the values of serum lipids among different types of cataract, it was evident from our study that serum triglycerides were high

in all types of cataract patients and highest in cortical cataract patients (87.5%). Hiller et al found that posterior sub capsular opacities in man were associated with high Triglycerides[9]. Similarly, Framingham study showed association between serum Triglycerides and posterior sub capsular cataract[17]. There are other studies, which have shown a positive relation of high Triglycerides with posterior sub capsular cataract[18]. Our study was more consistant with the results of Paunskinis et al. He found high serum Triglycerides proportionally related with any cataract sub type. The only difference was that his study showed this relation in women, while this particular study has shown no gender difference. Contrary to that, Rajiv Raman showed high Triglycerides as a risk factor for nuclear cataract[19]. When HDL levels were compared among different cataract types, we found low HDL more related with posterior sub capsular cataract than the other two types. It was similar to Framingham offspring heart study[9]. Similar results were described by Hiller et al regarding relation of HDL and posterior sub capsular cataract[9]. Contrary to this, another study found that low HDL was associated with cortical cataract[20]. Beaver Dam Eye Study showed low HDL associated with cortical cataracts as well[20].

Further studies with more patients need to be done to reveal the relation of different cataract sub types with different lipids.

CONCLUSIONS

Among the modifiable risk factors, high serum Triglycerides and VLDL play a role in the development of senile cataract in Pakistani patients. Serum Triglycerides is the only lipid, which has shown consistent results related to cataract development in different parts of the world. Other lipids show variable results in different countries. Further studies are needed to find out the relation of type of senile cataract with different types of serum lipids.

Copyright© 21st Jan, 2015.

REFERENCES

1. Jadoon Z, Bourne R, Dineen B, et al. **The Pakistan National Blindness and Visual Impairment Survey research design, eye examination methodology and results of pilot study**. Ophthalmic Epidemiology 2007; 333:12321–333.

2. Thomas JL, Gregory LS, Louis BC. **Lens and cataract**. In: American Academy of Ophthalmology Basic and Clinical Science Course. Vol. 11. 2007-2008. page.71.

3. Courtney P. **The National Cataract Surgery Survey: I. Method and descriptive features.** Eye Lond 1992; 5: 487–92.

4. Ralph C, Eagle JR. **Eye pathology: an atlas and text**. 2nd edition. Philadelphia,USA: Llippincott Williams and Wilkins; 2011. Page 108.

5. Heydari B, Kazemi T, Zarban A, Ghahramani S. **Correlation of cataract with serum lipids, glucose and antioxidant activities a case-control study**. West Indian Med J 2012; 61(3)

6. Meyer D, Parkin D, Maritz FJ, Liebenberg PH. **Abnormal serum lipoprotein levels as a risk factor for the development of human lenticular opacities**. Cardiovasc JS Afr 2003; 14: 60-4.

7. Tsutsumi K, Inoue Y, Yoshida C. **Acceleration of development of diabetic cataract by hyperlipidemia and low high-density lipoprotein in rats**. Biol Pharm Bull 1999;22: 37-41.

8. Raman R, Pal SS, Adams J, Rani PK, Vaitheeswaran K, Sharma T. **Prevalence and Risk Factors for Cataract in Diabetes: Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study, Report No. 17.Invest**. Ophthalmol. Vis. Sci 2010; vol. 51(12): 6253-6261.

9. Hiller R, Sperduto RD, Reed GF, D'Agostino RB, Wilson PW. **Serum lipids and age-related lens opacities: a longitudinal investigation: the Framingham Studies**. Ophthalmology. 2003;110:578–583.

10. Paunksnis A, Bojarskiene F, Cimbalas A, Cerniauskiene LR, Luksiene DI,Tamosiunas A. **Relation between cataract and metabolic syndrome and its components**. Eur J Ophthalmol. 2007;17:605–614.

11. Donnelly CA, Seth J, Clayton RM, Phillips CI, Cuthbert J, Prescott RJ. **Some blood plasma constituents correlate with human cataract**. Br J Ophthalmol.1995;79(11):1036–1041.

12. Klimov AN, Gurevich VS, Nikiforova AA, et al. **Antioxidative activity of high density lipoproteins in vivo**. Atherosclerosis. 1993;100:13– 18

13. Marks RG, Hale WE, Perkins LL, May FE. Stewart RB. **Cataracts in Dunedin Program participants: an evaluation of risk factors**. J Cataract Refract

Surg.1988; 14:58–63.

14. Miglior S, Bergamini F, Migliavacca L, Marighi P, Orzalesi N (1989);. **Metabolic and social risk factors in a cataractous population: a case –control study**. Dev Ophthalmol.1989; 17:158–164.

15. Cenedella RJ. **Cholesterol and cataracts**. Surv Ophthalmol. 1996;40(4):320-37.

16. Marks RG, Hale WE, Perkins LL, May FE, Stewart RB. **Cataracts in Dunedin Program participants: an evaluation of risk factors**. J Cataract Refract Surg. 1988 ;14(1):58-63.

17. Husain R, Tong L, Fong A, et al. **Prevalence of cataract in rural Indonesia**. Ophthalmology 2005;112(7):1255–1262.

18. Jahn C.E, Janke M, Winowski H,Von Bergmann K, Leiss O, Hockwin O. **Identification of Metabolic Risk Factors for Posterior Subcapsular Cataract** 1986; 18(2):112-6

19. Raman R, Pal SS, Adams J, Rani PK, Vaitheeswaran K, Sharma T. **Prevalence and Risk Factors for Cataract in Diabetes: Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study**, Report No. 17.Invest. Ophthalmol. Vis. Sci 2010; vol. 51(12): 6253-6261.

20. Sabanayagam C, Wang JJ, Mitchell P, Tan AG, E. Shyong ai E, Aung T, Seang-Mei Saw SM, Tien Yin Wong TY. **Metabolic Syndrome Components and Age-Related Cataract: The Singapore Malay Eye Study**. Invest. Ophthalmol. Vis. Sci. 2011; 52(5): 2397-2404.

"Time and tide wait for no man."

Geoffrey Chancer

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Ammara Javed	Data acquiring	
2	Dr. Roquyya Gul	Study design	
3	Dr. Tayyaba Gul Malik	Manuscript writing	
4	Rabail Alam	Stastics	
5	Dr. Muhammad Khalil	Manuscript writing	