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Correlation of Cataract with Serum Lipids, Glucose and Antioxidant Activities

A Case-control Study

B Heydari[1], T Kazemi[2], A Zarban[3], S Ghahramani[4]

ABSTRACT

Objective: *The aim of this study is to evaluate the relationship between cataract development and serum lipids, glucose as well as antioxidants in a case-control study.*

Methods: *Ninety patients with cataract and 90 age- and sex-matched healthy controls were investigated. Lipid profiles including triglyceride (Tg), total serum cholesterol (Chol) and cholesterol content in high-density lipoproteins (HDL chol) and low-density lipoproteins (LDL chol) as well as fasting glucose (FBS) were measured for all subjects. Plasma oxidative stress as thiobarbituric acid-reactive substances (TBARS) and the status of antioxidants were studied as ferric reducing/antioxidant power (FRAP) and thiol substance assay.*

Results: *A higher prevalence of abnormal FBS (8.9 vs 1.1%), Tg (26.7 vs 8.9%) and Chol (54.4 vs 30%) was found in cataract patients than the control group (*$p < 0.05$*). Plasma Tg (*$p = 0.02$*), Chol (*$p = 0.001$*) and LDL chol (*$p = 0.04$*) were significantly higher in the cataract group than in the control group. Likewise TBARS (*$p = 0.05$*) as the level of oxidative stress was significantly higher in the case group, and FRAP (*$p = 0.03$*) and thiol (*$p = 0.02$*) assays as the antioxidant activity was significantly lower among cataract patients.*

Conclusion: *This study has shown that hypercholesterolaemia, hypertriglyceridaemia, high LDL chol and high FBS are associated with cataract. Also lower plasma antioxidant levels and higher levels of oxidative stress were seen in cataract patients than healthy controls. These findings indicate a need for health promotional activities aimed at controlling these preventable factors among high risk populations.*

Keywords: Cataract, glucose, lipids, oxidative stress

Correlación de la Catarata con los Lípidos Séricos, la Glucosa, y las Actividades Antioxidante

Un Estudio de Caso-control

B Heydari[1], T Kazemi[2], A Zarban[3], S Ghahramani[4]

RESUMEN

Objetivo: *El objetivo de este estudio es evaluar la relación entre el desarrollo de la catarata y los lípidos séricos, la glucosa, así como los antioxidantes, en un estudio de caso-control.*

Métodos: *Se investigaron noventa pacientes y noventa controles sanos, pareados por edad y sexo. Los perfiles lípidos, incluyendo los triglicéridos (Tg), el colesterol sérico total (Chol) y el contenido de colesterol en lipoproteínas de alta densidad (HDL chol) y lipoproteínas de baja densidad (LDL chol) fueron medidos en todos los sujetos, así como la glucosa en ayunas (FBS). Se estudió el estrés oxidativo en plasma como sustancias reactivas al ácido tiobarbitúrico (TBARS) y el estado de los antioxidantes comopoder reductor férrico/antioxidante (FRAP) y ensayo de tiol.*

Resultados: *Se encontró una prevalencia mayor de FBS anormal (8.9 vs. 1.1%), Tg (26.7* vs *8.9%) y Chol (54.4 vs 30%) en los pacientes con catarata, en comparación con el grupo control (*$p < 0.05$*). El Tg en plasma (*$p = 0.02$*), Chol (*$p = 0.001$*) y LDL chol (*$p = 0.04$*) fueron significativamente más altos en el grupo con catarata que en el grupo control. Igualmente TBARS (*$p = 0.05$*) como nivel de estrés*

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*oxidativo fue significativamente más alto en el grupo de caso, y FRAP (*p = *0.03) y el ensayo de tiol (*p = *0.02) como actividad antioxidante fue significativamente más baja entre los pacientes con catarata.* ***Conclusión:*** *Este estudio mostró que la hipercolesterolemia, la hipertrigliceridemia, el colesterol LDL alto, y el FBS alto se hallan asociados con la catarata. También se observaron niveles más bajos de antioxidante plasmático y niveles más altos de estrés oxidativo en los pacientes con cataratas frente a los controles saludables. Estos hallazgos indican una necesidad de actividades de promoción de la salud a fin de controlar estos factores prevenibles entre la población de alto riesgo.*

Palabras claves: Catarata, glucosa, lípidos, estrés oxidativo

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INTRODUCTION

Cataract is a major cause of blindness and low vision worldwide. It is estimated that 44.1% of blind cases and 51.6% of patients with low vision have cataract (1). The opacity of the crystalline lens of the eye results in visual defects in cataract. The development of cataract is a complex, multifactorial process and several factors such as genes, gender, diabetes, geographic location, UV light exposure, level of education, occupational status and nutritional factors in the daily diet have been found to be associated with cataract formation. Age is the most important risk factor and about 85 per cent of involved patients have age-related cataract (2). This type of cataract is called "senile cataract". It is the main cause of blindness in patients over 45 years (3). It is estimated that a ten-year delay in the onset of cataracts could decrease the number of cataract surgeries by 45 per cent, thus considerably diminishing care cost (4).

Other unchangeable risk factors are female gender, corticosteroid use and systemic diseases (such as diabetes). Although, there is no way to prevent corticosteroid-induced cataract and other mentioned factors, some risk factors for cataract are modifiable and the disease can be prevented by the elimination of these factors. Cigarette smoking and ocular UV-B light exposure are confirmed as the two major modifiable risk factors for cataract (5).

The surgical extraction of the cataract is performed when the disease leads to functional disorders. Patients with cataracts in low resource areas and developing countries have a decreased chance for surgery due to economic reasons. This results in an increased risk of blindness in such populations.

In 1999, the World Health Organization (WHO) and the International Agency for the Prevention of Blindness (IAPB) launched a joint initiative known as 'VISION 2020: The Right to Sight' which aims to reduce preventable blindness by the year 2020 (6). Detection and elimination of blindness-causing diseases and related risk factors help achieve this objective and cataract as the main reason of blindness is at the top of these issues. Recent studies investigated the role of several preventable factors in development of cataract such as blood biochemicals or antioxidative capacity (7). Although cataract is a multifactorial disease, oxidative stress has been identified as an initiating factor for the development of maturity onset cataract (8).

There are two main reasons to study relationships between risk for cataract and preventable factors. Firstly, surgical treatment is not available or safe for cataract in all layers of the population, particularly in low resource settings, and secondly, there will be significant financial savings and improvements in quality of life if health rather than old age is extended, especially given the rapidly growing elderly segment of the population. The aim of this study was to evaluate the relationship between cataract development and serum lipids and glucose as well as antioxidants in a case-control study.

SUBJECTS AND METHODS

The study was carried out at Vali-e-Asr Hospital, affiliated to Birjand University of Medical Sciences, Southern Khorasan in the east of Iran. This prospective study was approved by the Institutional Ethical Review Committee.

The cases consisted of consecutive cataract patients who attended the ophthalmology clinic of the hospital or underwent cataract surgical procedure between March 2005 and February 2006. The controls were age- and sex- matched companions of the patient or non-cataract patients who attended the hospital during the same period. During selection of both groups, it was made sure that they were free from any chronic disease or metabolic disorder. Also individuals with steroid use or who smoked cigarettes were not included. The diagnosis of cataract was based on biomicroscopy evaluation. The procedure was explained to patients in detail and all of them signed an informed consent statement to participate in the study. Brachial vein blood samples were obtained from the patients in all groups after an overnight fast, to measure the values of fasting blood glucose (FBS), triglyceride (Tg), total serum cholesterol (Chol), and cholesterol content in high-density lipoproteins (HDL chol) and low-density lipoproteins (LDL chol). After all the blood samples were taken, fasting glucose and lipid profile were measured by routine enzymatic methods (Parsazmoon kits; Tehran, Iran) using an autoanalyzer (Tokyo Boeki Prestige 24i, Japan).

The antioxidant status of plasma was also assessed with three different methods. The ferric reducing/antioxidant

power (FRAP) assay was used to measure the total antioxidant activity of plasma. This method was previously described by Benzie and Strain (9). Ferric reducing/antioxidant power was measured as the total antioxidant capacity of plasma for the studied subjects. It uses antioxidants as reductants in a colorimetric method. In this assay, at low pH, a ferric-tripyridyltriazine (FeIII-TPTZ) complex is reduced to the ferrous form, which is blue coloured and monitored by measuring the change in absorbance at 593 nm. The change in absorbance is directly proportional to the reducing power of the electron-donating antioxidants present in plasma. The absorbance change is translated into a FRAP value (in µmol/L) by relating the change of absorbance at 593 nm of test sample to that of a standard solution of known FRAP value (9). To examine the plasma protein oxidation, we measured free protein thiol levels using 5, 5'-dithiobis (2-nitrobenzoic acid) [DTNB] according to a previous method (10). Thiol-group containing antioxidants may be simply assayed by reaction with DTNB which affords yellow coloured 5-thio-2-nitro-benzoic acid with absorption at 412 nm (10).

Lipid peroxidation was measured by TBARS (thiobarbituric acid reactive substances) production. Serum levels of TBARS were determined with the spectrophotometric method as previously described (11). Briefly, with malondialdehyde (MDA) as the standard, the coloured layer reaction in this method was measured at 532 nm. The TBARS concentrations (measured as MDA) were calculated as µmol/L [11].

Mean ± standard deviation was calculated for all parameters in the study groups. Differences between the biochemical profile and antioxidant status for the two groups were compared using one-way analysis of variance (ANOVA) and *t*-test, using SPSS version 15 for Windows (Chicago, IL). Chi-square test was performed for assessment of abnormal biochemical test values in each group. Statistical significance was inferred at $p \leq 0.05$.

RESULTS

Overall, 90 case-control pairs were included in the study. The two groups were matched for age and gender. Thus, male to female proportion was 1:1 in each group and mean age was 60.2 ± 8.0 years in cataract patients *vs* 58.3 ± 8.7 in the control group ($p > 0.05$).

The mean values of laboratory tests and the result of the *t*-test, presented in Table 1, showed considerable comparability between the patients and control subjects. The cases were significantly more likely to have the higher plasma level of Tg (154.2 ± 95.3 *vs* 126.9 ± 53.8, $p = 0.02$), Chol (206.0 ± 45.2 *vs* 182.2 ± 34.3, $p = 0.001$) and LDL chol (138.8 ± 37.3 *vs* 128.7 ± 28.9, $p = 0.04$). However, there were no differences between the two groups regarding the mean HDL chol (41.1 ± 9.9 *vs* 38.8 ± 10.1, $p = 0.12$) and FBS (96.5 ± 36.3 *vs* 93.4 ± 13.1, $p = 0.45$).

Table 1: Fasting blood glucose and plasma lipids in the study groups

	Case (mean ± SD)	Control (mean ± SD)	*p*-value
Tg mg/dL	154.2 ± 95.3	126.9 ± 53.8	0.02
Chol mg/dL	206.0 ± 45.2	182.2 ± 34.3	0.001
LDL chol mg/dL	138.8 ± 37.3	128.7 ± 28.9	0.04
HDL chol mg/dL	41.1 ± 9.9	38.8 ± 10.1	0.12
FBS mg/dL	96.5 ± 36.3	93.4 ± 13.1	0.45

Chol: total serum cholesterol; FBS: fasting blood glucose; HDL chol: cholesterol content in high-density lipoproteins; LDL chol: cholesterol content in low-density lipoproteins; SD: standard deviation; Tg: triglyceride.

The frequency of abnormal values for serum lipids and glucose in each group was compared (Table 2). The percentage of abnormal values of Tg (26.7% *vs* 8.9%, $p = 0.02$), Chol (54.4% *vs* 30%, $p = 0.001$), and FBS (8.9% *vs* 1.1%, $p = 0.03$) was significantly higher in cataract patients. Antioxidant capacity and oxidative stress of serum was measured and mean value of the tests were compared between the two groups (Table 3). The average levels of oxidative stress (TBARS) in plasma (micromoles of MDA per litre) exhibited high levels of plasma TBARS in cataract patients ($p < 0.05$). Total antioxidant capacity was measured by FRAP and thiol assays and the test values for cataract patients exhibited a value significantly lower than the control group ($p < 0.05$).

Table 2: The prevalence of dyslipidaemia and abnormal fasting glucose in the study groups

	Case No (%)	Control No (%)	*p*-value	OR (95% CI)
Tg ≥ 150 mg/dL	24 (26.7%)	8 (8.9%)	0.002	3.7 (1.6, 8.8)
Chol ≥ 200 mg/dL	49 (54.4%)	27 (30%)	0.001	2.8 (1.5, 5.2)
LDL chol ≥ 130 mg/dL	49 (54.4%)	44 (48.9%)	0.46	1.2 (0.7, 2.2)
HDL chol < 40 mg/dL	40 (44.4%)	49 (54.4%)	0.18	0.67 (0.37,1.2)
FBS ≥ 126 mg/dL	8 (8.9%)	1 (1.1%)	0.03	8.7 (1.1, 9.07)

Chol: total serum cholesterol; CI: confidence interval; FBS: fasting blood glucose; HDL chol: cholesterol content in high-density lipoproteins; LDL chol: cholesterol content in low-density lipoproteins; OR: odds ratio; Tg: triglyceride.

Table 3: Oxidative stress and antioxidant status in the study groups

	Case (mean ± SD)	Control (mean ± SD)	*p*-value
FRAP µmol/L	473.8 ± 121.6	516.2 ± 138.7	0.03
Thiol µmol/L	285.4 ± 60.5	306.0 ± 58.4	0.02
TBARS µmol/L	2.57 ± 0.89	2.31 ± 0.85	0.05

FRAP: ferric reducing/antioxidant power
TBARS: thiobarbituric acid reactive substances

DISCUSSION

The results of this study showed significant increase in Chol, Tg and LDL chol in cataract patients than the control group. Several recent studies have examined the relationship between selected serum lipids and lipoproteins and the occurrence of lens opacities (12, 13). Meyer *et al* (12) indicated the strong association between low levels of HDL chol cholesterol and high LDL:HDL ratios on one hand and the development of cataract on the other. Also, Hiller *et al* (13) found that a high level of Tg was associated with an increased risk of posterior subcapsular cataract (PSC) in men, and this result was significant after age and multivariable adjustment were made. They indicated that men with low HDL chol levels were also at increased risk of PSC, although this result was at a borderline level of significance. An animal study (14) showed that hyperlipidaemia and low HDL chol levels may be risk factors for the onset of diabetic cataracts. Also, they demonstrated that diabetic cataracts may be accelerated by hyperlipidaemia and low HDL chol in rats.

In the present study, the mean FBS was not significantly different between the two groups, but the prevalence of abnormal FBS was significantly higher in cases than in controls. In a population-based longitudinal study by Tan *et al* (15), patients with baseline impaired fasting glucose (IFG), or with either IFG or diabetes, had an increased risk of developing cortical cataract. They stated that increasing serum glucose was related to a higher risk of incident cortical cataract. Diabetes was also a predictor for the development of nuclear cataract, and newly diagnosed diabetes predicted the development of PSC. This result is similar to that of an Iranian study on 155 age- and sex- matched pairs in which PSC patients had significantly higher glucose levels than with other types of cataract (16). These findings highlight the harmful effect of glucose on lens which has been previously indicated in research showing the relationship of diabetes and cataract (17, 18). The hyperglycaemic conditions in the presence of oxidative stress have a more adverse effect on the lens. This finding has been established by some animal studies (19, 20). In our study, the results showed that the plasma total antioxidant power of the cataract patients was significantly decreased, and it can result from excessive free radical production and antioxidant depletion in the body. Several studies have been performed in the field of the protective effect of antioxidants on changes in lens opacity. Similarly, this study found an association between cataract and high levels of oxidative stress among cases in the present study than the control group. On the other hand, our cataract patients had lower levels of antioxidants which were measured by two laboratory assay (FRAP and thiol assessment). These findings are in accordance with a study by Hashim and Zarina (21) in which paraoxonase 1 activity (as an antioxidant) decreased in their cataract patients and this contributed to the higher risk of cataract formation. Also they found that plasma MDA and *ox* LDL levels (as a marker of oxidative stress) were higher in patients suffering from cataract.

Several studies have demonstrated the effect of oxidative stress on cataract formation especially in older patients (22, 23). Based on this data, the role of antioxidants on the prevention of cataract formation has been studied within the last two decades (7). Thus, some efforts have been dedicated to evaluating the role of dietary antioxidants on prevention of cataract (24). Therefore, it is recommended to use substances containing antioxidants which may be beneficial for cataract prevention as well as several other disorders that may have arisen due to oxidative stress. Numerous studies have documented the beneficial effects of antioxidants on delaying the onset of lens changes in senile cataract. A study in India found an association between use of green tea and the delay in the formation of lens opacity and cataract (24).

Based on the present study, cataract patients had a likelihood of dyslipidaemia, high level of blood glucose and high plasma level of antioxidants which could result in cataract development. It is therefore necessary to plan control programmes and screenings for these factors in high risk populations and also to control and reduce the development of disease among patients diagnosed early.

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