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# RESEARCH ARTICLE

## BEGINNING OF CATARACT AND ACCUMULATION OF COPPER, LEAD AND CADMIUM IN SMOKERS OF REWA, M.P.

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**ABSTRACT**

Cataract is the major cause of visual impairment and blindness (about 42%) in the world. which is the main cause of avoidable blindness. 90% of cases belong to low and middle income countries including India. Two third of blindness in the world is reported in women. As the old people are increasing due to increased life expectancy number of blind and visually impaired are increasing due to cataract, resulting in social burden all over the world. Cigarette smokers are more at risk for developing cataract at an earlier age than non smokers.



## INTRODUCTION

Cataract is defined as opacity within the clear lens inside the eye that reduces the amount of incoming light and results in deterioration of vision. Natural lens is a crystalline substance and a precise structure of water and protein to create a clear passage for light. Cataract is often described as being similar to looking through a waterfall or waxed paper (Robert *et al.,* 2010). Approximately 10.8 million people worldwide had cataract-induced vision loss in 2010 (Bourne *et al.,* 1990). The physiopathology of cataract is not fully understood (Bobrow *et al.,* 2015). It is believed that oxidative stress may initiate cataract formation through modification of lens epithelium: the excessive generation of reactive molecules can cause oxidative damage to functional DNA, proteins and lipids in lens cells, overwhelm the antioxidant defense system (such as superoxide dismutase, catalase, lipid peroxidases), impair DNA repair mechanisms, enhance apoptosis of lens epithelial cells, and induces protein and lipid aggregation in lens (Spector, 1995). Previous studies reported that concentrations of serum anti-oxidative enzymes and products of oxidative stress were relevant to the risk of cataract, although the association might vary across different subtypes (Beebe *et al.,* 2010). Other risk factors for cataract include gender (Chang *et al.,* 2011) (women are at greater risk), diabetes and infrared (Lydahl, 1984) and UV-B radiation (Brian *et al.,* 2001). Cigarette is composed of tobacco, paper, additives and filter. Approximately 600-1400 additives are used in cigarette manufacturing (Ebisike *et al.,* 2004). Toxic metals are found in cigarettes which cannot be metabolized in humans and have bio-accumulative ability.

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Metal contents in tobacco depend on soil of agriculture land (Chiba and Masironi, 1992), and its nearby source of contamination (Pappas *et al.,* 2007). It also depends on how tobacco is being processed (Verma *et al.,* 2010). The concentrations of toxic metals, cadmium, lead and copper found in different brands of the world were 1.76-3.20 µg/gm (Mean: 2.71 µg/gm), lead 1.05-3.10 µg/gm (Mean: 2.07 µg/gm) and copper 5.18-17.6 µg/g respectively (Mean: 9.70 µg/gm) (Pourkhabbaz and Pourkhabbaz, 2012). Two types of cells are found in humans and vertebrate lenses. A single layer of cuboidal epithelial cells are present anteriorly which is the only site of lenticular cell division. The lens fiber cells lie posteriorly (Bhat, 2001), which lack mitochondria (Huang *et al.,* 2008). Nutrients and metabolites reach these fiber cells via gap junctions (Goodenough *et al.,* 1980). The lens has no blood vessels and is multi cellular. Aqueous humor is a clear fluid and function like blood for the a vascular structures i.e. lens and cornea (Goldmann, 1950). With the help of active transport anions, cations & other molecules reach aqueous humor against concentration gradient across blood aqueous barrier (Yamaguchi *et al.,* 2006). Protein transporters help in this process present in cell membrane (Paul *et al.,* 2010). A complex network of gap junctions mostly of connexin46 and connex in 50 is essential for normal survival of lens. Any change in these channels may lead to decrease or modified communications (Beyer, 1993). Concentration of protein in human eye lens is 400 mg/ml, the major part of it are crystalline which are water soluble (Xia *et al.,* 1996). Small heat shock proteins are important chaperones found in human lens especially alpha –B crystalline and alpha-A crystallines. Chaperones help in folding of long chains of amino acids and thus prevent aggregation of protein (Peschek *et al.,* 2009), Both crystalline are important for lens transparency (Cherian

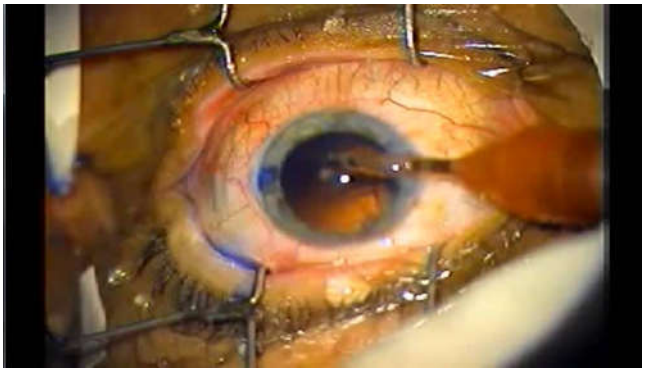
and Abraham, 1995) and survival of lens (Nakamoto and Vígh, 2007). The C-terminal extension of Alpha B crystalline is responsible for recognizing & selecting of unfolded protein substrate. Removal of C-terminal extension in Alpha B crystalline reduces the chaperone activity. In alpha-A crystalline C terminal hinge loop is flexible & takes part in zinc binding (Rafat and Manuel, 1999). In most of the ocular diseases including cataract, oxidative stress and metabolites of polyunsaturated fatty acids play a major role (Njie-Mbye *et al.,* 2013). Oxidative stress leads to lipid peroxidation, protein denaturation, damage to DNA and mitochondria (Wickens, 2001). Antioxidants help in removing free radicals and try to maintain cell function (Saleh *et al.,* 2010). Toxicity of metals is mainly due to generation of reactive oxygen & nitrogen species (oxidative stress). These metals may combine with enzymes & proteins having thiol groups. Several antioxidant enzymes contain sulfhydryl groups at their active site. Metals inactive these site due to binding with sulfhydryl group. Heavy metals compete with other metals for same binding sites (Dräger and Balkema, 1987). Even heavy metals can replace already bound metals and thus their concentrations increases in eye (Jamall and Roque, 1989), Once heavy metals bound it becomes difficult to displace them (Sarna *et al.,* 1980). Increased rate of telomere shortening in human lens cells due to oxidative stress and per oxidative damage to lens cell membranes results in lipid peroxidation, which are the triggering mechanism of cataractogenesis (Babizhayev *et al.,* 2011). Cadmium is known to cause its deleterious effects by deactivating DNA repair activity (McMurray and Tainer, 2003). Cigarette smoking results in 50% increase in oxidative DNA damage in smokers as seen by increase in excretion of DNA repair product 8-Hydroxydeoxyguanosine in urine (Loft *et al.,* 1992).

**Signs and symptoms:** Signs and symptoms vary depending on the type of cataract, though considerable overlap occurs. People with nuclear sclerotic or brunescent cataracts often notice a reduction of vision. Those with posterior subcapsular cataracts usually complain of glare as their major symptom (Posterior Supcapsular Cataract, 2013). The severity of cataract formation, assuming no other eye disease is present, is judged primarily by a visual acuity test. The appropriateness of surgery depends on a patient's particular functional and visual needs and other risk factors, all of which may vary widely (*Emmett*).

***Prevention:*** Risk factors such as UV-B exposure and smoking can be addressed. Although no means of preventing cataracts has been scientifically proven, wearing sunglasses that counteract ultraviolet light may slow their development (Javitt et la., 1996). While adequate intake of antioxidants (such as vitamins A, C, and E) has been thought to protect against the risk of cataracts, clinical trials have shown no benefit from supplements, though evidence is mixed, but weakly positive, for a potential protective effect of the nutrients lutein and zeaxanthin (Barker, 2010). Statin use is somewhat associated with a lower risk of nuclear sclerotic cataracts (Klein et al., 2006).

## MATERIALS AND METHODS

The research work was done at the Bio-chemistry department APS university Rewa (M.P). Random sampling method was used. A total of 302 patients were selected for the study after a detailed interview using validated questionnaire about their personal data, health, residence & its surrounding environment & smoking habits, general physical and ophthalmic examination and blood glucose analysis to assess their eligibility based on inclusion and exclusion criteria. As far as it could be ascertained no one selected were occupationally exposed to metals. Out of 302 cataract patients 150 were male and152 were female. Every patient was explained about the study and its usefulness. They were also assured that their participation has nothing to do with their line of management and surgical procedure and their extracted lenses were otherwise going to be discarded. The confidentiality of their particulars was also assured. Those who agreed a written consent was taken. Lens samples were collected by Extra Capsular Cataract Extraction (ECCE) surgical technique. Lens samples were collected in sterilized glass bottles which were washed with nitric acid and then by deionized water.



**Picture**

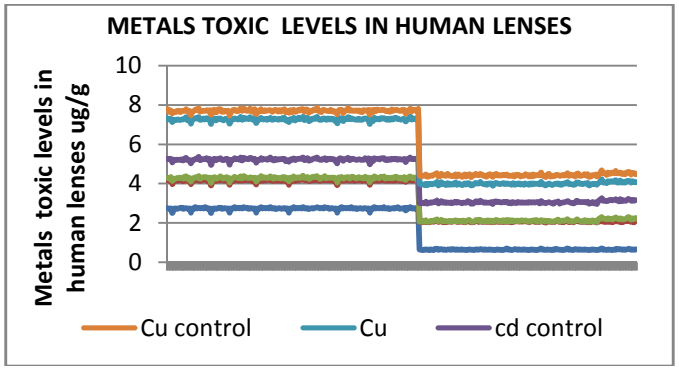
The weights were carefully recorded & then specimens were stored at -20ºC till analyzed. In the lens sample bottle 3 ml of 65 % Conc. Nitric Acid HNO3 was added and left for 30 minutes at ambient temperature. The digested lens material was transferred into a 50 ml beaker. In the sample bottle 2 ml conc. Nitric Acid was again added to remove any leftover & transferred to the beaker. The sample was heated on a hot plate (sand bath) and temperature was gradually increased to 140ºC until decomposition was completed and the mixture was almost dry. The decomposed sample was cooled to ambient temperature. 3-5 ml deionized water was added to beaker and beaker was shaken well to dissolve the decomposed material of lens and then transferred to 25 ml calibrated volumetric Flask. The beaker was again rinsed twice with 10 ml deionized water & then transferred to the volumetric flask. Deionized water was added to the volumetric flask to make it 25 ml, and then used for metal analysis by spectroscopic analysis. Blank samples were also prepared by similar method under identical conditions. Blanks were used to eliminate any possible contamination due to digestion process. The prepared samples of lenses were analyzed for Cadmium, Lead and Copper. Hitachi Atomic Absorption Spectrophotometer (Z-8000) with Zeeman Effect back ground correction was used for analysis equipped with a graphite furnace, a microprocessor and a built in printer (Anzar Ahmad *et al.*).

## RESULTS

The number, frequency and univariate analyses of socio-demographic characteristics of the sample population are given in Table -1.

**Table 1. Univariate analyses of socio-demographic factors of patients based on visual outcomes after cataract surgery**

| | | Visual outcome | | |
|---|---|---|---|---|
| | Variables | Good (n=170) | Poor (n=132) | Total |
| 1- | | Age group, years | | |
| a- | ≤50 | 18 (10.5%) | 13 (7.6%) | 31 |
| b- | 51-80 | 127(74.70%) | 99(58.2%) | 226 |
| c- | ≥80 | 25(14.7%) | 20(11.7%) | 45 |
| 2- | | Residence | | |
| a- | City | 85 (50%) | 35 (27%) | 120 |
| b- | Village | 110 ((65%) | 72 (56%) | 182 |
| 3- | | Occupation | | |
| a- | Employed | 57 (34%) | 40 ( 30%) | 97 |
| b- | Retired | 102 (76%) | 55 (42%) | 157 |
| c- | Unemployed | 35 (21%) | 44 (33%) | 79 |
| 4- | | Material status | | |
| a- | Married | 100 (59%) | 25 (19%) | 125 |
| b- | Un marride | 95 (56%) | 82(62%) | 177 |




**Graph 1. Metals toxic levels in human lenses**

The sample of 302 Adults. The age at surgery ranged from 23 to 98 years. The age at surgery was calculated from having recorded (58.2%). Most of the patients resides in village area 110 ((65%). One hundred fifty seven patients were retired. According to the Table -2, Five variables were used like good operative VA 42(25%), Border line pre –operative VA 60(35%) in Good visual out comes. Cataract were increased with diabetes mellitus good visual out comes was 49 (29%) and Poor visual out comes was 62 (46%).

**Table 2. Univariate analyses of clinical and surgical factors of patients based on visual outcome after cataract surgery**

| Visual outcome | | | | |
|---|---|---|---|---|
| Variables | | Good(n=170) | Poor (n=132) | Total |
| 1- | Preparative –visual activity | | | |
| a- | Poor | 68 (40%) | 79(60%) | 147 |
| b- | Good | 42 (25%) | 20 (15%) | 62 |
| c- | Border line | 60 (35%) | 33 (25%) | 93 |
| 2- | Diabetes | | | |
| a- | Absent | 121 (71%) | 70 (54%) | 191 |
| b- | Present | 49 (29%) | 62 (46%) | 111 |
| 3- | Hypertension | | | |
| a- | absent | 95 (56%) | 82(62%) | 177 |
| b- | present | 75(44%) | 50 (38%) | 125 |
| 4- | Intra ocular pressure | | | |
| a- | Normal | 150 (88%) | 110 (83%) | 260 |
| b- | High | 20 (12%) | 22 (17%) | 42 |
| 5- | Surgical procedure | | | |
| a- | Phaco | 125 (74%) | 50(38%) | 175 |
| b- | ECCE | 45 (26%) | 82( 62%) | 127 |

125 patients had hypertension, the good visual outcome was 75 (44%) and Poor visual outcome was 50(38%). intraocular pressure high in 42 patients. Good visual out comes was 20 (12%), and Poor visual outcome was 22(17%). Phacoemulsification process were used in 175 patients. Good visual out comes were 125(44%) and Poor visual outcome was 50(38%).

Table-3, Shows concentrations (ppm) of Cu, Cd, and Pb in lenses of study participants in relation with age, sex and frequency of cigarette smoking. Mean concentration of copper, cadmium and lead level were higher in age group of >50 years. Mean concentration of copper, lead and cadmium level were higher in male, the mean concentration of these elements was also higher among those smoking more than 20 cigarettes/day. Table – 4, Shows mean and standard deviation of Cu, Cd and Pb, levels in smokers and non-smokers lenses of study participants. Among smoker, mean concentrations of lead, cadmium and copper were 2.723, 0.1380 and 2.34 µg/gm of wet tissue weight respectively. Among non-smokers mean concentration of lead, cadmium and copper were 0.635, 0.4943 and 0.9327 µg/gm of wet tissue respectively.

**Tabel 3. Socio –demographic characteristics of study participants**

| characteristics | | Copper(Cu) Mean (S.D) PPm | Lead (pb) Mean (S.D) PPm | Cadmium (cd) Mean (S.D) PPm |
|---|---|---|---|---|
| 1- | Age (years) | | | |
| a- | ≤50 | 2.034±0.02011 | 2.710± 0.07176 | 0.1384±0.02146 |
| b- | 51-80 | 1.571±0.5452 | 1.847±1.036 | 0.09257±0.05693 |
| c- | ≥80 | 0.9333±0.02078 | 0.6378±0.02021 | 0.09044±0.05819 |
| 2- | Gender | | | |
| a- | Male | 2.034 ± 0.01947 | 2.723 ±0.05628 | 0.1381± 0.0216 |
| b- | Female | 1.020±0. 2987 | 0.8008 ±0.5663 | 0.05638 ±0.05004 |
| 3- | Frequency of Cigarettes smoking | 2.034±0.01982 | 2.719 ±0.06131 | 0.1380 ±0.02110 |
| a- | 10-20 cigarettes/day(n=90) | 2.34±0.01982 | 2.719±0.06131 | 0.1380±0.02110 |
| b- | >20 cigarettes/day(n=72) | 2.033 ±0.01921 | 2.729±0.04592 | 0.1381±0.02167 |

**Table 4. Cu, Pb and Cd Concentrations (mean & SD) in ppm with respect of age, gender and frequency of cigarette smoking**

| Groups | Lead Mean (SD) (Lens) µ g/gm | Cadmium Mean (SD) (Lens) µ g/gm | Copper Mean (SD) (Lens) µ g/gm |
|---|---|---|---|
| Group 1 Smoker(162) | 2.723 ± 0.05507 | 0.1380±0.02129 | 2.034±0.01950 |
| Group 2 Non smoker (140) | 0.6356 ± 0.01878 | 0.04943 ±0.04559 | 0.9327 ±0.01985 |

## DISCUSSION

The WHO recommends that a clinical audit record be maintained for all cases of cataract surgery. It mandates that with available correction, acceptable visual outcomes post cataract surgery are good outcome (6/18 or better) in >80% of cases, borderline outcome (<6/18 to 6/60) in <15%, and poor outcome (<6/60) in <5% of cases (Pararajasegaram, 2002). Our data set did not meet these criteria's with the figures falling short in each of the categories. The results from population-based surveys elsewhere have shown that 40% or greater of postoperative eyes have a presenting VA of worse than 6/18 (He *et al.,* 1999). Place of residence has limited effect on visual outcomes. Some studies report poor outcomes among rural patients (Dandona *et al.,* 1999), while others ascribe no significant association (Nirmalan *et al.,* 2002). Similarly Our data shown that more of the patients belonging to the village. Despite the association between ocular co-morbidity and cataract surgery, (Lundström *et al.,* 2012) state that it is not a contraindication for cataract surgery. Analyses of systemic co-morbidities such as diabetes mellitus, hypertension, cardiovascular disease and high cholesterol revealed that only hypertension is significantly associated with poor visual outcomes. Several studies identify diabetes mellitus as a risk factor for cataract (Harding *et al.,* 1993). Although diabetes mellitus is not significantly associated with poor outcomes in this study, univariate analyses showed evidence that the odds of poor outcome are increased on having diabetes mellitus. Study imply that hypertension gives rise to conformational changes in the lens capsule (Leon *et al.,* 2000). My study shows that 44% patients had hypertension. Phacoemulsification, a procedure developed by Charles D. Kelman (Goldstein, 2004), is the preferred surgical procedure while ECCE is performed depending on the condition of the anterior chamber, iris, and lens (Lundström *et al.,* 2012). Phacoemulsification requires a smaller incision and is suture-less which can lead to significant reduction in surgically-induced astigmatism (Kshitiz *et al.,* 2012). In this study, the odds of a poor outcome are increased when the surgical procedure was ECCE which is consistent with previous studies (Desai *et al.,* 1999). Study data reveals the potential role of cigarette smoking in the development of cigarette smoking in the development of cataract. The smokers are increasing in developing countries Two thirds of blindness cases in the world is reported in women (Abou-Gareeb *et al.,* 2001).

### Conclusion

The gathering of copper, lead, and cadmium occurs in cataract. The probable source of cadmium in humans is cigarettes. Lenticular cadmium accumulation also increases copper and lead precipitation in the lens. Cigarette smoking might be cataractogenic. Cigarette is composed of tobacco, paper, additives and filter. Smoking causes deposition of many metals in human tissues and lead to harmful effects even at lower levels.

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