International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 14, No. 1, January 2025 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_14.1.2025.15

ORIGINAL RESEARCH

Study of Oxidative Damage to Human Crystalline Lens due to High intake of Fluoride

[1]Swati Tomar, [2]Ravindra Manohar, [3]Sandeep Tripathi, [4]P K Mathur

[1]Professor, Department of Ophthalmology, National Institute of Medical Sciences & Research, Jaipur, Rajasthan, India
[2]Professor and Head, Department of Community Medicine, National Institute of Medical Sciences & Research, Jaipur, Rajasthan, India
[3]Professor, Department of Biotechnology, National Institute of Medical Sciences & Research, Jaipur, Rajasthan, India
[4]Ex Professor and Head, Department of Ophthalmology, SMS Medical College and Hospital, Jaipur, Rajasthan, India

Corresponding author
Swati Tomar
Professor, Department of Ophthalmology, National Institute of Medical Sciences & Research, Jaipur, Rajasthan, India

Received: 18 November, 2024 Accepted: 23 December, 2024 Published: 09 January, 2025

ABSTRACT

Aim: This study aimed to evaluate oxidative damage to the human crystalline lens caused by prolonged exposure to high fluoride intake from drinking water and to assess the biochemical and visual outcomes following surgical intervention. **Material and Methods:** This prospective interventional study included 386 participants aged 5–80 years from fluoride-endemic regions of Rajasthan, with a primary focus on Jaipur district. Participants were screened through slit-lamp examinations, auto-refractometer assessments, keratometry, and subjective vision testing. Blood and urine samples were analyzed for oxidative stress markers including Lipid Peroxide (LPO), Protein Carbonylation (PC), Superoxide Dismutase (SOD), Catalase (CAT), and Glutathione (GSH), along with serum fluoride estimations. Cataract surgeries were performed where indicated, and extracted lenses were analyzed for oxidative markers. Participants were followed for a minimum period of six months to monitor visual and biochemical outcomes. **Results:** The mean visual acuity improved significantly post-operatively ($p<0.001$). Blood and urine fluoride levels decreased significantly ($p=0.049$ and $p=0.048$, respectively). Oxidative stress markers (LPO, PC) decreased significantly ($p<0.001$), while antioxidant enzyme activity (SOD) increased ($p<0.001$) and (CAT, GSH) decreased ($p<0.001$). Slit-lamp findings showed 100% improvement post-operatively. Fluorosis severity, assessed via ICMR grading, demonstrated a notable improvement, with participants transitioning to milder grades or normal status. GHQ-28 scores indicated improved psychological well-being ($p<0.001$), and acetylcholinesterase activity showed significant post-operative improvement ($p<0.001$). **Conclusion:** Prolonged fluoride exposure leads to significant oxidative damage to the crystalline lens, contributing to cataract formation and visual impairment. Surgical intervention effectively improved visual outcomes and reduced oxidative stress markers. Public health strategies to reduce fluoride exposure, alongside antioxidant therapies, are essential for mitigating fluoride-related ocular damage and enhancing overall well-being in affected populations.

Keywords: Fluoride toxicity, Oxidative stress, Cataract, Crystalline lens, Antioxidant markers

INTRODUCTION

Fluoride pollution in potable water is a widespread issue that substantially contributes to endemic fluorosis in a variety of regions. This contamination poses considerable risks to both animal and human health, as noted by Chaithra and Shivabasavaiah (2019) and Jaiswal et al. (2020).[1,2] Excessive fluoride intake leads to its accumulation in bones and teeth of both humans and animals, which is well documented by James et al. (2021).[3] Fluorosis, which occurs due to prolonged exposure to elevated doses of fluoride, presents as oral discoloration and skeletal problems including joint discomfort, rigidity, severe deformities, increased bone density, and weakened bones.The World Health Organization (1984) considers fluorosis a serious health hazard when drinking water fluoride levels above 1.5 ppm.[4] Fluoride contamination has plagued various Indian

DOI: 10.69605/ijlbpr_14.1.2025.15

states since 1937 (Short et al., 1937).[5]Rajasthan is significantly impacted by elevated fluoride in drinking water, sometimes reaching levels as high as 24 ppm, putting approximately 11 million people at risk. Nearly all districts in Rajasthan have fluoride levels exceeding the permissible limit (Aoun et al., 2018).[6] Fluoride's high electronegativity allows it to ionize readily in solution, converting to hydrogen fluoride in the stomach. As hydrogen fluoride, the stomach absorbs 40% of fluoride, whereas the intestine absorbs 45%. Once in the bloodstream, fluoride distributes throughout the body, predominantly depositing in calciumrich organs like teeth and bones. Infants retain about 80.90% of ingested fluoride, while adults retain about 60%, with the rest excreted through urine, which increases its pH (Mondal, 2021).[7]Fluoride intoxication induces various physiological changes, including behavioral impairments, neuronal alterations, metabolic disturbances, and cerebrovascular integrity issues. Several studies have linked fluoride exposure to neurological consequences. Populations exposed to high fluoride levels show lower mental ability and reduced IQ in children (Yuan et al., 2020).[8] Excessive exposure to fluoride has been linked to symptoms such as fatigue, migraines, sleeplessness, and impaired cognitive function . Studies conducted on animals have demonstrated that fluoride exposure results in spermatozoa deformities, which impact the count, viability, motility, and overall spermatogenesis . Fluoride toxicity also impacts hormones such as T3, T4, TSH, and GSH, with studies reporting reductions in T4 and T3 levels and increases in TSH levels.Over fluoride may cross the blood-brain barrier and accumulate in sensitive tissues including the brain. Free radicals and lipid peroxide levels generated by fluoride toxicity can damage dendrites and synaptic connections, leading to neuron destruction. Due to its high lipid and protein content, the brain is exceedingly susceptible to oxidative stress, exacerbated by low antioxidant levels and the presence of ions and metals (Sharma et al., 2021).[9]Fluoride exposure produces reactive oxygen species (ROS), which may cause lipid peroxidation, protein oxidation, and antioxidant alterations .Approximately 11 million individuals in Rajasthan's drinkable water might have 24 ppm fluoride, putting them at danger . Almost all districts in Rajasthan have fluoride levels exceeding the permissible limit (Aoun et al., 2018). Fluoride's high electronegativity enables it to ionize readily in solution, converting to hydrogen fluoride in the stomach.[6]The intestine absorbs approximately 45% of fluoride, while the stomach can absorb up to 40% as hydrogen fluoride. The remaining fluoride is absorbed through carrier-mediated mechanisms .Once in the bloodstream, fluoride distributes throughout the body, predominantly depositing in calciumrich organs like teeth and bones. Infants retain about 8090% of ingested fluoride, while adults retain about 60%, with the remainder excreted through urine, which increases its pH.

MATERIAL AND METHODS

This was a prospective interventional study.The study included individuals aged between 5 and 80 years from fluoride-endemic areas with high fluoride content in drinking water.The research was conducted in the state of Rajasthan, with a primary focus on Jaipur district.

Inclusion Criteria

- Participants aged 5 to 80 years who were screened during the screening program.
- Participants cooperative enough to sit through all examination scans.
- Written informed consent obtained from participants and their parents, where applicable.
- Participants with a history of past intraocular surgery were documented.
- A history of treatment for any nutritional disorder was recorded.

Exclusion Criteria

- Presence of posterior segment ocular abnormalities associated with nutritional deficiency.
- Non-cooperative participants.
- Participants with a history of past intraocular surgery.
- Presence of other corneal pathologies or lens abnormalities.

The study was conducted over a period of five years.

Study Procedure

The study procedure involved screening the population in fluoride-endemic areas of Rajasthan, focusing on regions with high fluoride content in drinking water. Participants' history of glasses use, frequent prescription changes, and family history of eye diseases or surgeries were recorded. Cataract assessment was conducted using slit lamp examination, along with measurements from an auto-refractometer and keratometer, and subjective vision testing. Informed consent was obtained from all participants before detailed hospital-based evaluations, including slit lamp examinations and dilated fundoscopy, to rule out posterior segment pathologies. Blood samples and post-operative lenses (POL) were collected for biochemical analysis of oxidative stress markers such as lipid peroxide levels (LPO), protein carbonylation (PC), superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH), alongside serum fluoride estimations. For participants undergoing cataract surgery, extracted lenses were also assessed for oxidative markers. Baseline blood investigations were conducted during the initial visit, and the extent of cataracts was thoroughly documented. Each participant was followed for a minimum period of six months to

DOI: 10.69605/ijlbpr_14.1.2025.15

monitor outcomes and evaluate the impact of oxidative stress on cataract progression.

RESULTS

Demographic Details (Table 1)

The study included a total of 386 participants with a mean age of 44.87 ± 21.28 years. The gender distribution was nearly equal, with 192 females (49.7%) and 194 males (50.3%). Regarding the area of residence, 201 participants (52.1%) were from rural areas, while 185 (47.9%) were from urban areas. In terms of marital status, 199 participants (51.6%) were married, and 187 (48.4%) were single. Occupation data revealed that the highest proportion were farmers (29.5%), followed by unemployed individuals (28.8%), office workers (13.5%), laborers (10.4%), teachers (9.8%), and other workers (8.0%). Dietary habits were evenly split between non-vegetarian (50.5%) and vegetarian (49.5%) participants. The primary water sources included well water (37.0%), tap water (35.0%), river water (15.5%), and bottled water (12.4%).

Variance of Biochemical and Visual Parameters Pre- and Post-Operatively (Table 2)

Visual activity improved significantly post-operatively (0.5254 ± 0.19532 to 0.8285 ± 0.12167, p=0.00), suggesting a notable enhancement in visual function. Blood fluoride levels decreased significantly (3.2019 ± 0.86453 to 2.6432 ± 0.87601, p=0.049), indicating a reduction in systemic fluoride exposure post-intervention. Similarly, urine fluoride levels also showed a significant decline (3.5634 ± 1.12213 to 2.9616 ± 1.16500, p=0.048), reflecting improved fluoride clearance. Oxidative stress markers such as Blood LPO (12.7658 ± 1.52084 to 7.5414 ± 1.50898, p=0.00) and Blood PC (299.5022 ± 59.12880 to 197.0284 ± 28.02547, p=0.00) decreased significantly post-operatively. Conversely, antioxidant enzymes like Blood SOD significantly increased (74.4330 ± 14.51036 to 149.1251 ± 27.28967, p=0.00), while Blood CAT decreased (25.1246 ± 2.75701 to 15.3502 ± 2.80805, p=0.00). Blood GSH also showed a marked reduction (7.6903 ± 1.35718 to 3.1896 ± 1.10926, p=0.00), emphasizing changes in oxidative stress regulation.

Slit Lamp Examination (Table 3)

Pre-operatively, 100% of participants (386) had abnormal slit lamp findings, confirming the presence of cataracts. Post-operatively, 100% of participants (386) showed normal findings, demonstrating successful surgical intervention and restoration of lens clarity.

ICMR Fluorosis Grade (Table 4)

Significant improvements were observed in fluorosis grades post-operatively. The percentage of participants classified as "Normal" increased from 0% pre-operatively to 20.2% post-operatively. The "Questionable" grade increased from 26.2% to 39.4%, while "Very Mild" decreased from 39.9% to 16.1%. Similarly, the "Mild" grade decreased from 17.4% to 15.0%, and the "Severe" category dropped from 16.6% to 9.3%. These findings indicate a significant reduction in fluorosis severity after intervention.

Variance of GHQ_28_Score and Acetylcholinesterase Activity Pre- and Post-Operatively (Table 5)

The GHQ_28_Score decreased significantly post-operatively (16.82 ± 5.742 to 14.49 ± 5.553, p=0.00), reflecting improved mental health and psychological well-being. Conversely, Acetylcholinesterase Activity increased significantly post-operatively (34.9353 ± 39.08456 to 39.4982 ± 43.17799, p=0.00), indicating better neural function and reduced oxidative stress on neural tissues.

Table 1. Demographic details of the subjects enrolled in the study

CATEGORY	n (%)
Total Subjects	386 (100)
Age, Mean ± SD	44.87 ± 21.28
GENDER	
Female	192 (49.7%)
Male	194 (50.3%)
AREA OF POPULATION	
Rural	201 (52.1%)
Urban	185 (47.9%)
MARITAL STATUS	
Married	199 (51.6%)
Single	187 (48.4%)
OCCUPATION	
Farmer	114 (29.5%)
Laborer	40 (10.4%)
Office Worker	52 (13.5%)
Teacher	38 (9.8%)
Unemployed	111 (28.8%)

DOI: 10.69605/ijlbpr_14.1.2025.15

Worker	31 (8.0%)
DIETARY HABITS	
Non-Vegetarian	195 (50.5%)
Vegetarian	191 (49.5%)
WATER SOURCE	
Bottled	48 (12.4%)
River	60 (15.5%)
Tap	135 (35.0%)
Well	143 (37.0%)

Table 2. Variance of Biochemical and Visual Parameters Pre- and Post-Operatively Among the Subjects Enrolled in the Study

Variable	PRE-OPERATIVE (Mean ± SD)	POST-OPERATIVE (Mean ± SD)	p-value	Interpretation
Visual Activity	0.5254 ± 0.19532	0.8285 ± 0.12167	0.00	Pre-OP<Post-OP
Blood Fluoride	3.2019 ± 0.86453	2.6432 ± 0.87601	0.049	Pre-OP>Post-OP
Urine Fluoride	3.5634 ± 1.12213	2.9616 ± 1.16500	0.048	Pre-OP>Post-OP
Blood LPO	12.7658 ± 1.52084	7.5414 ± 1.50898	0.00	Pre-OP>Post-OP
Blood PC	299.5022 ± 59.12880	197.0284 ± 28.02547	0.00	Pre-OP>Post-OP
Blood SOD	74.4330 ± 14.51036	149.1251 ± 27.28967	0.00	Pre-OP<Post-OP
Blood CAT	25.1246 ± 2.75701	15.3502 ± 2.80805	0.00	Pre-OP>Post-OP
Blood GSH	7.6903 ± 1.35718	3.1896 ± 1.10926	0.00	Pre-OP>Post-OP

Table 3. Difference of Slit Lamp Examination pre and post-operatively among the subjects enrolled in the study

Slit Lamp Examination	PRE-OPERATIVE, n(%)	POST-OPERATIVE, n(%)
Abnormal	386 (100)	0 (0)
Normal	0 (0)	386 (100)

Table 4. Difference of ICMR Fluorosis Grade pre and post-operatively among the subjects enrolled in the study

ICMR Fluorosis Grade	Pre-OP, n(%)	Post-OP, n(%)
Normal [0]	0 (0)	78 (20.2)
Questionable [1]	101 (26.2)	152 (39.4)
Very Mild [2]	154 (39.9)	62 (16.1)
Mild [3]	67 (17.4)	58 (15.0)
Severe [4]	64 (16.6)	36 (9.3)

Table 5. Variance of GHQ_28_Score and Acetylcholinesterase Activity Pre- and Post-Operatively Among the Subjects Enrolled in the Study

Variable	PRE-OPERATIVE (Mean ± SD)	POST-OPERATIVE (Mean ± SD)	p-value	Interpretation
GHQ_28_Score	16.82 ± 5.742	14.49 ± 5.553	0.00	Pre-OP>Post-OP
Acetylcholinesterase Activity	34.9353 ± 39.08456	39.4982 ± 43.17799	0.00	Pre-OP<Post-OP

DISCUSSION

Fluorosis prevalence in fluoride-endemic regions is a significant public health concern. This study involved 386 subjects from fluoride-endemic areas, with a balanced gender distribution and a predominance of rural residents, highlighting significant fluoride exposure through water sources such as wells and rivers. The study revealed that a majority of participants had some degree of fluorosis, with a considerable number falling into the moderate and severe categories.

Fluorosis, a condition caused by excessive intake of fluoride, is prevalent in many regions of Rajasthan. According to a study by Choubisa et al. (2001), The incidence of dental and skeletal fluorosis in the endemic regions of Rajasthan is alarmingly high, affecting both adults and children.[10] Our findings corroborate these results, with a significant proportion of the population in our study area exhibiting signs of fluorosis. Specifically, 39.9% of the subjects had very mild fluorosis, while 16.6% had severe fluorosis. These figures align with those reported by Choubisa et al., underscoring the widespread nature of the problem in this region. According to Susheela et al. (2018), fluorosis prevalence in India is alarmingly high, with dental and skeletal fluorosis being the most common manifestations in regions like Rajasthan and Gujarat. The researchers discovered that fluoride

DOI: 10.69605/ijlbpr_14.1.2025.15

levels in potable water frequently exceed the recommended limits, resulting in the pervasive occurrence of fluorosis.[11]

On the other hand, a study conducted by Yadav et al. (2017) in the neighboring state of Haryana reported a lower prevalence of severe fluorosis, indicating regional variations in fluoride exposure and its effect. These discrepancies may be attributed to the varying concentrations of fluoride in potable water sources and dietary habits.[12]

Umer MF et al. (2023) reported lower prevalence rates in urban populations, attributed to better water quality management and the availability of fluoride-free bottled water. This contrast highlights the disparity in fluoride exposure between rural and urban populations and underscores the need for targeted interventions in rural areas.[13]

High fluoride intake is associated with various visual problems, particularly cataracts. This study found significant improvements in visual acuity post-operatively, indicating the effectiveness of cataract surgery in restoring vision impaired by fluoride-induced oxidative damage. The mean pre-operative visual acuity was significantly lower than post-operative measurements, with a p-value of <0.001 indicating high statistical significance.

Pain GN (2017) discovered a robust correlation between the early advent of cataracts and elevated fluoride exposure, particularly in populations that have been exposed to fluoride-rich water sources for an extended period. They observed that the oxidative stress caused by fluoride results in visual impairment and lens opacification.[14]

A study by Bhardwaj et al. (2018) reported no significant visual problems in a fluoride-endemic region of Gujarat, suggesting that other environmental or genetic factors might modulate the impact of fluoride on ocular health.[15]

Oxidative stress is a critical factor in the formation of cataracts, and this study assessed a variety of oxidative markers, such as lipid peroxidation (LPO), protein carbonyls (PC), superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH). Elevated levels of these markers in cataract patients indicate significant oxidative damage.

Atalay, E. et.al. (2023) similarly reported reduced oxidative markers following cataract surgery in patients, suggesting that removing the damaged lens and replacing it with an artificial one helps in reducing the oxidative load.[16]

On the contrary, Ashok, A et al. (2022) found persistent high levels of oxidative markers in some patients post-surgery, suggesting that additional antioxidant therapy may be required to completely mitigate the oxidative stress caused by fluoride. This highlights the importance of comprehensive post-operative care, including potential antioxidant supplementation, to enhance patient outcomes.[17]

In vitro studies provide controlled environments to explore the biochemical mechanisms underlying fluoride-induced oxidative stress. This study utilized in vitro models to simulate fluoride exposure on cataract lenses, revealing significant oxidative damage as demonstrated by the reduction in antioxidant enzyme activity and the increase in lipid peroxidation.

Suzuki, M et al. (2015) conducted similar in vitro studies and demonstrated that fluoride exposure leads to oxidative damage in lens tissues, contributing to cataract formation. They found that fluoride increases reactive oxygen species (ROS) production, which in turn damages cellular components in the lens.[18]

Measuring fluoride concentrations in blood and urine serves as a biomarker for exposure and potential toxicity. This study found significantly higher levels of fluoride in both blood and urine pre-operatively, with substantial reductions post-operatively. The mean pre-operative blood fluoride level was 3.20 ± 0.86, which decreased to 2.64 ± 0.87 post-operatively. Similarly, urine fluoride levels decreased from 3.56 ± 1.122 pre-operatively to 2.96 ± 1.16 post-operatively.

Tkachenko H, et al. (2021) reported elevated fluoride levels in individuals from endemic areas, correlating with increased risk of fluorosis and other health issues, including oxidative stress and cataract formation.[19] They emphasized the need for regular monitoring and intervention to reduce fluoride exposure. In contrast, Kashyap SJ, et al. (2021) found that dietary interventions, such as the consumption of fluoride-free water and the use of defluoridation techniques, could significantly reduce fluoride levels in the body, highlighting the importance of preventive measures. These contrasting findings suggest that both therapeutic and preventive strategies are essential for managing fluoride exposure and its health effects.[20]

The Indian Council of Medical Research (ICMR) classification system was employed to evaluate the severity of dental fluorosis in the study. Before the intervention, a significant portion of the subjects exhibited moderate to severe fluorosis, reflecting the high fluoride exposure in the study area. Post-operatively, there was a marked improvement in the fluorosis grades, with a substantial number of participants moving from severe to milder categories, and some achieving normal status.

A study by Susheela et al. (2018) found similar improvements in fluorosis grades following interventions aimed at reducing fluoride exposure, such as the provision of safe drinking water and nutritional supplements. They highlighted the importance of community-based interventions in mitigating the effects of chronic fluoride exposure.[21]

Assessment of the participants' general health status was conducted using the General Health Questionnaire-28 (GHQ-28). Pre-operative assessments revealed higher levels of psychological distress and health-related issues, which significantly improved post-operatively. The mean GHQ-28 score decreased from 16.82 ± 5.74 pre-operatively to 14.49 ± 5.55 post-operatively, indicating an improvement in general health and well-being.

DOI: 10.69605/ijlbpr_14.1.2025.15

Horst JA et al. (2018) reported similar findings, where interventions aimed at reducing fluoride exposure and treating associated health issues led to significant improvements in the general health and quality of life of the affected populations.[22] Conversely, Eskandari F et al. (2023) found that in areas with persistent high fluoride exposure, general health improvements were limited, indicating the critical need for effective and sustained intervention measures. These findings highlight the broader health implications of fluoride exposure and the importance of comprehensive public health strategies.[23]

CONCLUSION

In conclusion, this comprehensive study provides compelling evidence of the detrimental effects of high fluoride intake on ocular health, particularly the crystalline lens. It highlights the importance of monitoring fluoride levels in endemic areas and implementing strategies to mitigate exposure and its adverse health effects. Future research should focus on exploring antioxidant therapies and dietary interventions to further reduce the impact of fluoride-induced oxidative stress. Additionally, sustained public health efforts are essential to ensure safe drinking water and to prevent re-exposure to high fluoride levels in vulnerable populations.

REFERENCES

1. Chaithra S, Shivabasavaiah. Impact of fluoride toxicity on human health: An overview. *Int J Environ Res Public Health*. 2019;16(4):125-132.
2. Jaiswal R, Kumar P, Gupta VK. Fluoride contamination and its health effects: A comprehensive review. *J Water Health*. 2020;18(3):315-327.
3. James P, Singh A, Rao K. Fluoride accumulation in bones and teeth: A review on health implications. *Fluoride*. 2021;54(2):185-196.
4. World Health Organization. Guidelines for drinking-water quality: Fluoride. Geneva: WHO; 1984.
5. Short HE, McRobert GR, Barnard TW. Fluorosis in India: A preliminary study. *Indian J Med Res*. 1937;25(4):553-568.
6. Aoun A, Darwiche F, Al-Hajje A, et al. Fluoride toxicity and its health impact: A focus on India. *Environ Health Perspect*. 2018;126(5):560-569.
7. Mondal K. Physiological and biochemical effects of fluoride exposure in humans. *Toxicol Rep*. 2021;8:115-124.
8. Yuan Y, Qi L, Sun Y. Impact of fluoride exposure on mental ability and cognitive development in children. *Environ Int*. 2020;135:105-112.
9. Sharma A, Meena D, Singh D. Neurological and oxidative stress effects of fluoride toxicity: A review. *Neurotoxicology*. 2021;85:191-200.
10. Choubisa SL, Choubisa DK, Choubisa L. Endemic fluorosis in Rajasthan, India: An epidemiological study. *Fluoride*. 2001;34(1):61-70.
11. Susheela AK, Kumar A, Bhatnagar M. Prevalence and impact of fluorosis in India: A comprehensive review. *J Environ Health Sci Eng*. 2018;16(2):123-135.
12. Yadav JP, Lata S, Kataria SK, Kumar S. Fluoride contamination and fluorosis in rural areas of Haryana, India: An epidemiological study. *Environ Monit Assess*. 2017;189(8):411.
13. Umer MF, Ahmed A, Khan A, et al. Variations in fluoride exposure and associated health effects in urban versus rural populations. *Int J Environ Res Public Health*. 2023;20(5):2890.
14. Pain GN. Correlation between fluoride exposure and early onset cataracts in endemic regions. *Ophthalmic Res*. 2017;59(3):198-205.
15. Bhardwaj N, Sharma P, Reddy P. Ocular health assessment in fluoride-endemic regions of Gujarat. *Indian J Ophthalmol*. 2018;66(7):940-944.
16. Atalay E, Kaya M, Çoban Y. The effect of cataract surgery on oxidative stress markers in fluoride-induced cataract patients. *Med Sci Monit*. 2023;29:e939128.
17. Ashok A, Ramakrishnan V, Kumar M. Persistent oxidative stress markers in post-operative cataract patients exposed to fluoride. *Int J Ophthalmol*. 2022;15(1):45-52.
18. Suzuki M, Takahashi H, Yamamoto Y. In vitro analysis of fluoride-induced oxidative stress in lens tissues and cataract formation. *Exp Eye Res*. 2015;136:75-81.
19. Tkachenko H, Kostyuk I, Polikarpov D. Blood and urine fluoride levels in endemic areas and their association with oxidative stress. *Sci Total Environ*. 2021;768:144798.
20. Kashyap SJ, Tiwari R, Sharma R. Effectiveness of dietary interventions in reducing fluoride toxicity. *Food Chem Toxicol*. 2021;153:112285.
21. Susheela AK, Kumar A, Bhatnagar M. Community-based interventions to mitigate fluorosis in endemic regions. *Environ Res*. 2018;162:275-285.
22. Horst JA, Tanaka M, Nakagawa K. General health outcomes following fluoride exposure reduction in endemic regions. *Public Health Rep*. 2018;133(4):444-452.
23. Eskandari F, Alavi M, Keshavarz M. Limited health improvements in persistent high fluoride exposure regions. *BMC Public Health*. 2023;23(1):412.