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# Impact of Dyselectrolytemia in the Pathogenesis of Diabetic Cataract

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**Abstract:**

**Background** Derangements in serum electrolytes concentration play an important role in the pathogenesis of diabetic cataract is unclear.

**Objectives** The objective of the present study is to estimate electrolytes such as sodium, potassium, chloride and magnesium levels in serum and its association with diabetic cataract.

**Subjects and methods** The present study includes 60 Diabetic cataract (DC) patients, 60 Type 2 DM patients without cataract and 60 normal healthy individuals without cataract in the age group from 40-75 years of both genders. Serum electrolytes were estimated by advanced Ion Selective Electrode method. Serum magnesium was determined by xylidyl blue method.

**Results** The study shows significant decreased in the concentration of serum magnesium ($p<0.001$) and increased in the concentration of serum sodium, potassium and chloride ($P<0.001$) in diabetic cataract patients when compared with diabetic and non-diabetic without cataracts. Pearson's correlation analysis showed Glycemic status had negative correlation with serum magnesium ($r= -0.321$, $r= -0.458$). HbA1c had positive correlation with serum sodium ($r=0.223$) and potassium ($r=0.166$) were observed. Serum sodium ($p<0.001$), serum magnesium ($p<0.001$) and duration of DM ($p=0.001$) were significantly associated with diabetic cataract by using Multivariate logistic regression analysis.

**Conclusion**

Dyselectrolytemia leads to electrolyte imbalance in lens which plays a significant role in the development of cataract formation in diabetes patients.

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**Keywords:** Dyselectrolytemia, Diabetic Cataract, Type 2 Diabetes mellitus, Magnesium

## Introduction

Cataract is a major cause of visual impairment in diabetes mellitus patients and cataract formation occurs early and progression much faster in diabetic than non-diabetic individuals [1–4]. Multiple pathogenic mechanisms, such as increased oxygen free radical formation, abnormal glycosylation of lens proteins, advanced glycation process, and increased tissue sorbitol concentration, have been proposed the cataractogeneic effect in diabetes, but the exact pathogenesis is not known yet [5–10].

Electrolytes are essential for human health and have diverse metabolic characteristics and functions[11,12].They are electrically charged molecules with various functions, including fluid balance, tissue function,[12]maintaining homeostasis in the body, protecting cellular function, acid-base balance and so on.[11,13] The aqueous humor is the central component of lens metabolism, which is produced from plasma secretions. The electrolytes concentration of aqueous humor is directly related to the serum electrolytes concentration. Alteration in serum electrolytes which cause electrolyte imbalance in aqueous humor that may leads to cataract formation [14]. We are planned to understanding the imbalance of serum electrolytes in diabetic cataract patients and their association with cataract.

## Materials and Methods

This comparative study population consisted of three groups where, Group I- 60 Type 2 DM patients with cataract, Group II-60 type 2 diabetes mellitus patients without cataract and Group III - 60 non-diabetic subjects without cataract of both the genders in the age group between 40-75 years. The Sample size was calculated by using the formula $n \geq (Z1\text{-}\alpha/2\sigma/d)$ 2. The average value of serum magnesium among diabetic patients was taken as $1.79 \pm 0.15$ from the previous review of literature [15] by assuming alpha = 0.05; absolute error as 4% and a sample size was calculated as each group. Therefore, the total sample size for each group minimum needed is 55. However, sample size was fixed as 60 each group and the total sample size for three groups is $60 \times 3 = 180$.The present study was conducted from August 2018 to September 2019 in the Department of Biochemistry collaboration with the Department of Ophthalmology in a tertiary care hospital. The study protocol was approved by the Institutional Human Ethics Committee and informed consent form was obtained from all participants. . The study subjects were selected based on inclusion and exclusion criteria from Ophthalmology OPD as follows. All subjects were underwent complete eye examination in the ophthalmology OPD. The cataract was confirmed by using slit-lamp examination and Lens Opacities Classification System III (LOCS III) was used for grading the cataract by consultant ophthalmologist.

### Inclusion criteria

Group I: Type 2 Diabetes mellitus patients having more than 5 years of duration who are under treatment of oral hypoglycemic drugs with cataract,
Group II: Type 2 Diabetes mellitus patients having more than 5 years of duration who are under treatment of oral hypoglycemic drugs without cataract and
Group III: Normal healthy individuals having no history of diabetes and without cataract were recruited who come for routine eye check up in the Ophthalmology OPD and diagnosed by clinical and biochemical examination by ophthalmologist were included in this study.

### Exclusion criteria

Subjects who had history of steroid intake, renal dysfunction, hepatic disease, hypo or hyperthyroidism, traumatic or toxic cataract, Age-related cataract and other systemic diseases and Drugs known to affect magnesium status such as Aminoglycosides, Amphotericin B, Cetuximab, Cyclosporine, Digoxin, Diuretics (loop, thiazide, osmotic), angiotensin converting enzyme inhibitors and angiotensin receptor blockers alcohol and smoking were excluded from the study.

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**Sample collection and processing**

5 ml of fasting venous blood sample was drawn from the subjects and collected in EDTA and sodium fluoride-Potassium oxalate anticoagulant vacutainers. The serum and plasma samples were separated by centrifuging at 3500 rpm for 15-20 minutes. The plasma sample was used for the estimation of glucose by GOD-POD method. The serum sample was used for the estimation of magnesium by xylidyl blue method using Hitachi 902 auto-analyzer and the estimation of sodium, potassium, chloride by advanced Ion Selective Electrode (ISE) method using a fully automated electrolyte analyzer (Easylyte). Whole blood was used for the estimation of Glycated hemoglobin (HbA1c) by HPLC method using Biorad D10 HbA1c analyser.

**Data analysis**

The results were expressed as mean ± standard deviation (SD). Data was analysed by using JASP 8.4 software. The statistical difference between groups were analysed using one-way ANOVA followed by Tukey's HSD post-hoc analysis test. The association between the variables was assessed by using Pearson's correlation coefficient (r). Multiple regression analysis was performed to assess independent relationship between diabetic cataract and electrolyte. A p value of $<0.05$ was considered as statistically significant.

**Results**

The mean age of the diabetic cataract, diabetic without cataract and non-diabetic without cataract were 60.52 ± 6.32, 60.38 ± 6.54 and 58.97 ± 6.48 years old. There was no significant difference observed for age among three groups by using one-way ANOVA ($p=0.347$). Out of 180 subjects, 78 (43%) were males consists of 27 cataracts and 51 without cataracts and 102 were females (57%) which includes 33 cataracts and 69 without cataracts. Among 60 Diabetic Cataract patients, we found 15 (25%) nuclear cataract (NC), 27 (45%) cortical cataract (CC) and 18(30%) posterior sub-capsular cataract (PSC) based on Lens Opacities Classification System III (LOCS III) cataract grading system [16].

Table1 shows the mean concentration of serum electrolyte and glycemic status of the type 2 diabetes mellitus patients with cataract (group I) and diabetic without cataract patients (group II) and normal healthy individual without cataract (group III). Three groups were compared using one way-ANOVA followed by tukey's HSD post hoc analysis test.
Mean fasting plasma glucose and glycated hemoglobin (HbA1c) concentration were significantly elevated in group I (142 ± 65; 8.8 ± 2.6, $p<.001$) when compared to group II [121 ± 26; 7.1 ± 1.2) than group III (95 ± 9.0; 5.5 ± 0.4).

In Diabetic cataract patients, mean serum sodium, potassium and chloride levels were significantly increased ($p<0.001$) whereas mean serum magnesium levels were significantly decreased ($p< .001$) when compared to other groups using one-way ANOVA. When the groups were compared in pairs for serum sodium, Potassium and magnesium using tukey' HSD post hoc analysis test, a significant difference were observed between all paired groups except between group II and III for sodium ($p=0.760$) and for potassium between group I and II ($p=0.076$) and group II and III ($p=0.099$) respectively as depicted in table 1.

There was significantly increased serum chloride level was observed in group I ($p<0.001$) as compared to the other three groups using ANOVA and followed by tukey's HSD post hoc analysis compared in pairs, a significant difference was observed between all paired groups except between group I and II ($p=0.969$) as shown in Table 1.

Pearson's correlation analysis showed a significant negative correlation of glycemic status (FBS, HbA1C) with magnesium($r= -0.321$; $r=-0.458$, $p<0.001$) and positive correlation of HbA1c

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with serum sodium (r=0.223, p=0.003) and potassium (r=0.166, p=0.026), were observed as shown in table 2. In addition, there was a significant positive correlation of serum sodium with serum potassium (r=0.159, p=0.033) and negative correlation of duration of DM with Magnesium (r= -0.588) were observed respectively.

Tables 3 represent the Multivariate logistic regression analysis also revealed that the serum sodium (OR= 1.742; 95% CI= 0.294-0.816, P<0.001), serum magnesium (OR= 0.001; 95% CI = -9.765 to -4.039, P<0.001) and duration of DM (OR= 1.311; 95% CI= 0.106-0.436, P=0.001) were significantly associated with diabetic cataract.

**Table 1: Comparison of glycemic status, serum electrolyte levels among groups (One Way ANOVA)**

| Parameters | Group I - Type 2 DM with cataract N=60 (Mean±SD) | Group II -Type 2 DM without cataract N=60 (Mean±SD) | Group III- Normal healthy individuals N=60 (Mean±SD) | ANOVA p value |
|---|---|---|---|---|
| **Fasting plasma glucose (mg/dL)** | $142 \pm 65_{a}‡_{b}†$ | $121 \pm 26_{c}‡$ | 95 ± 9.0 | <.001* |
| **HbA1c (%)** | $8.8 \pm 2.6_{ab}†$ | $7.1 \pm 1.2_{c}†$ | 5.5 ± 0.4 | <.001* |
| **Serum Sodium (mg/dL)** | $140.7 \pm 2.36_{ab}†$ | 138.2 ± 2.60 | 137.9 ± 2.41 | <.001* |
| **Serum Postassium (mg/dL)** | $4.64 \pm 0.44_{b}†$ | 4.46 ± 0.30 | 4.29 ± 0.58 | <.001* |
| **Serum Chloride (mg/dL)** | $105.0 \pm 3.35_{b}†$ | $104.8 \pm 3.23_{c}†$ | 102.7 ± 2.51 | <.001* |
| **Serum Magnesium (mg/dL)** | $1.35 \pm 0.21_{ab}†$ | $1.62 \pm 0.25_{c}†$ | 1.93 ± 0.24 | <.001* |

*p<0.05 significant; HbA1c=Glycosylated haemoglobin,
A-comparison of group-1vs group-2; b- comparison of group-1vs group-3;
c- Comparison of group-2vs group-3, † Tukey's post hoc test, P < 0.001; ‡Tukey's post hoc test, P < 0.01.

**Table 2: Association between serum electrolyte and glycemic status**

| Parameter | Pearson's correlation coefficient (r value) | p Value |
|---|---|---|
| **FBS Vs Magnesium** | -0.321 | <0.001* |
| **HbA1c Vs Sodium** | 0.223 | 0.003* |
| **HbA1c Vs Potassium** | 0.166 | 0.026* |
| **HbA1c Vs Magnesium** | -0.458 | <0.001* |

* p<0.05 significant

**Table 3: Multiple logistic regression analysis to assess independent relationship between diabetic cataract and electrolyte (Dependent variable: Diabetic cataract)**

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| Predictors | Standard error | Odds ratio | z | p Value | 95% CI Lower bound | 95% CI Upper bound |
|---|---|---|---|---|---|---|
| **Sodium** | 0.133 | 1.742 | 4.169 | <0.001* | 0.294 | 0.816 |
| **Potassium** | 0.771 | 9.189 | 2.877 | 0.004* | 0.707 | 3.729 |
| **Magnesium** | 1.461 | 0.001 | -4.726 | <0.001* | -9.765 | -4.039 |
| **Duration of DM** | 0.084 | 1.311 | 3.221 | 0.001* | 0.106 | 0.436 |

* P<0.05 significant,

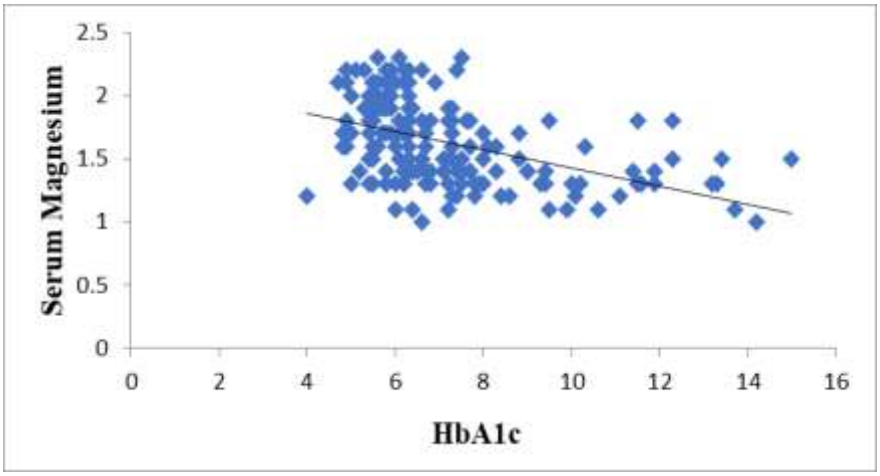


**Figure 1: Correlation between HbA1c and serum magnesium**

**Discussion**

Alteration in serum electrolytes observed in the present study (Table 1) suggests an important role of electrolytes disturbances in the pathogenesis of diabetic cataract. In our study, we found that mean serum sodium, potassium and chloride levels were significantly elevated whereas serum magnesium levels was significantly decreased in type2 DM with cataract subjects compared to type 2 DM without cataract and normal healthy individuals without cataract. Our findings are in accordance with the previous studies reported by Klein et al., Choudhury et al., and Ederer et al. showed two to four fold increase risk of cataract in diabetes patients as compared to non-diabetics [3, 17, 18]. Our report is close resemblance with the study reported by Pollreisz et al [19] where there was Positive correlation of serum sodium and potassium levels with the duration of diabetes. The result suggests that increased risk of cataract development with longer duration of diabetes mellitus.

In our study, mean serum magnesium concentration was significantly decreased in diabetic cataract patients than type 2 DM without cataract and normal healthy individuals without cataract subjects. Our reports are consisted with the studies reported by Badyal et al, Chambers et al, Kundu et al and Kaliaperumal et al [20–23] where mean serum magnesium in diabetic study group was lower when compared to control group.

In addition, there was significant negative correlation of serum magnesium with glycaemic status and duration of diabetes which indicates that diabetic cataract subjects are more prone to hypomagnesaemia than controls. By using multivariate logistic regression analysis, our study shows that high concentration of serum sodium, potassium and low concentration of magnesium play potential risk factors of cataract genesis in diabetes mellitus subjects.

**Conclusion**

The cardinal concept portrayed in the present study is that dyselectrolytemia cause fluid imbalance in lens leading to cataract formation in diabetes.

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**References**

[1] Harding JJ, Egerton M, van Heyningen R, Harding RS. Diabetes, glaucoma, sex, and cataract: analysis of combined data from two case control studies. Br J Ophthalmol 1993;77:2–6.
[2] Kahn HA, Leibowitz HM, Ganley JP, Kini MM, Colton T, Nickerson RS, et al. The Framingham Eye Study. II. Association of ophthalmic pathology with single variables previously measured in the Framingham Heart Study. American Journal of Epidemiology 1977;106:33–41. https://doi.org/10.1093/oxfordjournals.aje.a112429.
[3] Klein BE, Klein R, Moss SE. Prevalence of cataracts in a population-based study of persons with diabetes mellitus. Ophthalmology 1985;92:1191–6. https://doi.org/10.1016/s0161-6420(85)33877-0.
[4] Nielsen NV, Vinding T. The prevalence of cataract in insulin-dependent and non-insulin-dependent-diabetes mellitus. Acta Ophthalmol (Copenh) 1984;62:595–602. https://doi.org/10.1111/j.1755-3768.1984.tb03972.x.
[5] Yildirim Z, Yildirim F, Ucgun NI, Kilic N. The evaluation of the oxidative stress parameters in nondiabetic and diabetic senile cataract patients. Biological Trace Element Research 2009;128:135–43. https://doi.org/10.1007/s12011-008-8258-9.
[6] Gul A, Rahman MA, Salim A, Simjee SU. Advanced glycation end-products in senile diabetic and non-diabetic patients with cardiovascular complications. Age (Dordr) 2008;30:303–9. https://doi.org/10.1007/s11357-008-9072-1.
[7] Crabbe MJ. Cataract as a conformational disease--the Maillard reaction, alpha-crystallin and chemotherapy. Cellular and Molecular Biology (Noisy-Le-Grand, France) 1998;44:1047–50.
[8] Ahmed N. Advanced glycation endproducts--role in pathology of diabetic complications. Diabetes Res Clin Pract 2005;67:3–21. https://doi.org/10.1016/j.diabres.2004.09.004.
[9] Lee AY, Chung SS. Contributions of polyol pathway to oxidative stress in diabetic cataract. FASEB J 1999;13:23–30. https://doi.org/10.1096/fasebj.13.1.23.
[10] Spector A. Oxidative stress-induced cataract: mechanism of action. FASEB Journal: Official Publication of the Federation of American Societies for Experimental Biology 1995;9:1173–82.
[11] Ahmed S, Nur F, Shahjahan M. Factors influencing electrolyte imbalance in diabetic patients. 2013. https://doi.org/10.13140/RG.2.1.4882.4164.
[12] Gn D, Cherian S, Lakshmi K. A comparative study of electrolyte imbalances in controlled and uncontrolled diabetes mellitus. International Journal of Clinical Biochemistry and Research 2017;4:22–4.
[13] Goldberg A, Hammerman H, Petcherski S, Zdorovyak A, Yalonetsky S, Kapeliovich M, et al. Prognostic importance of hyponatremia in acute ST-elevation myocardial infarction. The American Journal of Medicine 2004;117:242–8.
[14] Davies PD, Duncan G, Pynsent PB, Arber DL, Lucas VA. Aqueous humour glucose concentration in cataract patients and its effect on the lens. Experimental Eye Research 1984;39:605–9. https://doi.org/10.1016/0014-4835(84)90060-5.
[15] Kauser MM, Afreen A, M KJ. Study of Serum Magnesium Levels in Diabetic Retinopathy. Journal of Research in Medical and Dental Science 2014;2:19–22.
[16] Chylack LT, Wolfe JK, Singer DM, Leske MC, Bullimore MA, Bailey IL, et al. The Lens Opacities Classification System III. The Longitudinal Study of Cataract Study Group. Archives of Ophthalmology (Chicago, Ill: 1960) 1993;111:831–6. https://doi.org/10.1001/archopht.1993.01090060119035.

[17] Choudhury RB, Gayan PS, Das B. Comparative Study Of Serum And Aqueous Humour Electrolytes In Diabetic And Non-Diabetic Cataract Patients n.d.:6.
[18] Ederer F, Hiller R, Taylor HR. Senile lens changes and diabetes in two population studies. American Journal of Ophthalmology 1981;91:381–95.
[19] Pollreisz A, Schmidt-Erfurth U. Diabetic Cataract—Pathogenesis, Epidemiology and Treatment. Journal of Ophthalmology 2010;2010:1–8.

[20] Badyal A, Sodhi KS, Pandey R, Singh J. Serum magnesium levels: A key issue for diabetes mellitus. Jk Science 2011;13:3.

[21] Chambers EC, Heshka S, Gallagher D, Wang J, Pi‐Sunyer FX, Pierson RN Jr.Serum magnesium and type‐2 diabetes in African Americans and Hispanics: A NewYork cohort. J Am Coll Nutr 2006;25:509‐13.

[22] Kundu D, Osta M, Mandal T, Bandyopadhyay U, Ray D, Gautam D. Serum magnesium levels in patients with diabetic retinopathy. Journal of Natural Science, Biology, and Medicine 2013;4:113–6. https://doi.org/10.4103/0976-9668.107270.

[23] Kaliaperumal R, Venkatachalam R, Nagarajan P, Sabapathy SK. Association of Serum Magnesium with Oxidative Stress in the Pathogenesis of Diabetic Cataract. Biological Trace Element Research 2020. https://doi.org/10.1007/s12011-020-02429-9.