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Research Article

Association of serum electrolyte imbalance with tear film osmolarity in chronic dry eye syndrome

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Abstract: Dry eye syndrome (DES) represents a multifactorial ocular surface disorder characterised by instability of the tear film and hyperosmolarity, often reflecting systemic and local homeostatic imbalance. Recent evidence suggests that serum electrolytes influence tear film composition through altered lacrimal gland secretion and osmotic gradients. This cross-sectional analytical study investigated the relationship between serum electrolyte levels and tear film osmolarity in patients with chronic DES. A total of 160 participants aged 25–65 years were enrolled—80 clinically diagnosed with chronic DES and 80 age- and sex-matched healthy controls. Tear osmolarity was measured using a TearLab osmometer, and serum sodium, potassium, chloride, and bicarbonate were analysed via automated chemistry analyser. Sample size was calculated in Epi Info™ (expected correlation coefficient 0.30, 90% power, 95% confidence), requiring 146 subjects; recruitment was increased to 160 to compensate for attrition. Mean tear osmolarity was significantly higher in DES patients (322.6 ± 12.8 mOsm/L) than controls (297.4 ± 9.6 mOsm/L; $p < 0.001$). Serum sodium ($r = 0.42$, $p < 0.001$) and chloride ($r = 0.31$, $p = 0.004$) showed positive correlations with tear osmolarity, while potassium and bicarbonate demonstrated negative but non-significant associations. Multivariable regression confirmed serum sodium as an independent predictor ($\beta = 0.37$, $p < 0.001$). These findings highlight systemic electrolyte imbalance—particularly hypernatremia—as a contributing factor to increased tear film osmolarity in chronic DES, suggesting integrated ocular–systemic evaluation could enhance management

strategies.

Keywords: dry eye syndrome, serum electrolytes, tear osmolarity, hypernatremia

Introduction: Dry eye syndrome (DES) is a prevalent ocular surface disorder resulting from a loss of tear film homeostasis, characterised by symptoms of ocular discomfort, visual disturbance, and tear film instability. Chronic DES is now recognised as a systemic as well as local pathology, involving inflammatory, hormonal, and osmotic factors that disrupt lacrimal gland secretion and ocular surface integrity. The tear film, comprising lipid, aqueous, and mucin layers, is maintained through a delicate osmotic balance influenced by both glandular secretion and systemic hydration. When osmotic balance is disturbed, tear hyperosmolarity triggers epithelial stress, inflammatory mediator release, and cell apoptosis—core mechanisms underlying DES progression.1-4

Recent studies emphasise tear hyperosmolarity as a key diagnostic and pathogenic biomarker of DES. Advances in osmometry have allowed accurate quantification of tear osmolarity, establishing it as a direct measure of ocular surface stress. However, the systemic factors that drive hyperosmolarity remain incompletely understood. Serum electrolytes—especially sodium, chloride, and potassium—govern extracellular fluid osmotic pressure, and their imbalance may contribute to altered tear composition. Increased serum osmolarity or hypernatremia can directly increase lacrimal gland osmotic load, reducing aqueous tear output and elevating tear osmolarity. Conversely, electrolyte depletion, dehydration, or metabolic disorders can impair ocular surface hydration, predisposing to chronic DES.5-8

Several systemic conditions, such as diabetes mellitus, renal impairment, and thyroid dysfunction, are known to alter both serum electrolytes and tear film properties. However, most previous research has focused on either ocular or systemic parameters in isolation. Only a few contemporary investigations, primarily from 2022–2024, have begun to elucidate the systemic–ocular osmotic interplay in DES. These studies suggest a potential link between elevated serum sodium and chloride and higher tear osmolarity in patients with chronic dry eye, yet sample sizes have been limited and population-specific data remain scarce. Given regional climatic differences, dietary salt intake, and hydration habits, understanding this association in local populations is critical.9-12.

Pakistan's climatic and socio-behavioural context—characterised by high ambient temperature, low humidity, and widespread high-salt dietary habits—may further amplify susceptibility to osmotic imbalances influencing tear physiology. Urban low-humidity environments, air pollution, and screen-based lifestyles have significantly increased DES incidence in recent years, while serum electrolyte disturbances, particularly mild hypernatremia and hypokalemia, are frequently encountered in general clinical practice. Investigating the link between these parameters may yield important preventive and therapeutic insights.

The tear film's osmolarity depends on the balance between tear production and evaporation, both of which can be modulated by systemic electrolyte concentration. Sodium and chloride ions, the primary contributors to extracellular osmolarity, increase osmotic pressure when elevated, while potassium and bicarbonate maintain epithelial ion balance and buffering. Alterations in these ions can therefore impact tear osmolarity directly or through secondary inflammatory and secretory mechanisms. Experimental studies have shown that hyperosmolar stress leads to upregulation of inflammatory cytokines such as IL-1β and TNF-α, further disrupting tear secretion.

Despite these mechanistic insights, there remains a paucity of robust clinical data linking serum electrolyte profiles to tear film osmolarity in chronic DES. Most prior studies have used small, hospital-based samples or lacked standardized tear osmolarity measurement. The present study was therefore designed as a community-based, cross-sectional analytical investigation to quantify the association between serum electrolyte imbalance and tear osmolarity in chronic DES. It was hypothesised that serum sodium and chloride levels would show a positive correlation with tear osmolarity, independent of age, sex, and hydration status. By identifying systemic predictors of tear hyperosmolarity, this study aims to contribute to a more integrated approach to DES management that addresses both ocular and systemic components.

Methodology: This cross-sectional analytical study was conducted in the Ophthalmology and Clinical Pathology Departments at Ophthalmology Department, Mayo Hospital, Lahore from January 2023 to June 2023. Ethical approval was obtained from the institutional review board, and all participants provided written and verbal informed consent. Participants aged 25–65 years presenting with symptoms of chronic DES (≥6 months) were recruited consecutively. Diagnosis was based on the Tear Film and Ocular Surface Society (TFOS DEWS II) criteria: OSDI score

>13, Schirmer's test <10 mm/5 min, and tear breakup time <10 seconds. Exclusion criteria included acute ocular infection, contact lens use, history of ocular surgery, autoimmune disease, renal dysfunction, diuretic use, and systemic dehydration.

A control group of age- and sex-matched healthy volunteers with no ocular surface disease and normal tear function was recruited from hospital staff and attendants. Sample size was estimated using Epi Info™ (StatCalc) for a correlation study: expected correlation (r) = 0.30, 90% power, α = 0.05, two-tailed test. The calculated sample size was 146; after accounting for 10% nonresponse, 160 participants were enrolled (80 DES cases, 80 controls).

Venous blood samples were collected in the morning after fasting for 8 hours. Serum sodium, potassium, chloride, and bicarbonate were analysed using an automated electrolyte analyser based on ion-selective electrode technology. Tear osmolarity was measured using a TearLab osmometer by collecting 50 nL tear samples from the inferior meniscus of each eye. Mean values of both eyes were taken for analysis. All measurements were conducted in controlled temperature and humidity conditions to minimise environmental bias.

Data were analysed using SPSS version 26. Descriptive statistics were expressed as mean ± SD. Group comparisons were made using independent t-tests for continuous variables and chi-square tests for categorical variables. Pearson correlation and multivariable linear regression were performed to assess relationships between serum electrolyte levels and tear osmolarity after adjusting for confounders including age, sex, BMI, and hydration status. Statistical significance was defined as $p < 0.05$.

Results

Table 1. Demographic and Clinical Characteristics

Variable	DES (n=80)	Controls (n=80)	p-value
Age (years)	46.8 ± 10.2	45.9 ± 9.6	0.58
Female (%)	58.7%	55.0%	0.64
BMI (kg/m²)	26.4 ± 3.1	25.7 ± 3.3	0.19

Variable	DES (n=80)	Controls (n=80)	p-value
Mean OSDI score	38.7 ± 9.1	9.3 ± 2.8	<0.001
Schirmer's (mm/5 min)	6.2 ± 2.4	14.9 ± 3.1	<0.001

Tear function was markedly impaired in DES patients compared to controls ($p < 0.001$).

Table 2. Serum Electrolytes and Tear Osmolarity

Parameter	DES (Mean ± SD)	Controls (Mean ± SD)	p-value
Serum Na^+ (mmol/L)	142.8 ± 3.9	138.4 ± 2.6	<0.001
Serum K^+ (mmol/L)	3.7 ± 0.4	3.9 ± 0.3	0.01
Serum Cl^- (mmol/L)	107.2 ± 4.2	102.8 ± 3.6	<0.001
Serum HCO_3^- (mmol/L)	22.1 ± 2.9	23.5 ± 2.7	0.02
Tear osmolarity (mOsm/L)	322.6 ± 12.8	297.4 ± 9.6	<0.001

Tear osmolarity was significantly higher in DES patients and showed strong correlation with serum sodium and chloride.

Table 3. Correlation and Regression Analysis

Variable	Pearson's r	p-value	Adjusted β (Regression)	p-value
Serum Na^+	0.42	<0.001	0.37	<0.001
Serum K^+	-0.19	0.09	-0.14	0.12
Serum Cl^-	0.31	0.004	0.26	0.01
Serum HCO_3^-	-0.12	0.23	-0.09	0.29

Serum sodium remained the strongest independent predictor of tear osmolarity after adjusting for confounders.

Discussion: This study demonstrated a significant association between serum electrolyte imbalance—particularly elevated sodium and chloride levels—and increased tear osmolarity in patients with chronic DES. The findings substantiate the hypothesis that systemic electrolyte status

influences ocular surface homeostasis through osmotic coupling between plasma and tear film. The observed mean tear osmolarity of >320 mOsm/L among DES patients aligns with established diagnostic thresholds for moderate-to-severe dry eye, confirming tear hyperosmolarity as a core feature of disease pathogenesis.13-14

Elevated serum sodium emerged as the most robust independent predictor of increased tear osmolarity. This relationship is physiologically plausible, given sodium's central role in extracellular osmotic regulation. Hypernatremia increases plasma osmolarity, driving fluid redistribution and altering lacrimal gland secretion dynamics, which may decrease tear aqueous volume and increase osmotic concentration. The concurrent elevation in serum chloride further compounds this osmotic load, resulting in ocular surface desiccation and inflammation.15-17

Mild hypokalemia observed in DES patients is consistent with reports suggesting that potassium deficiency impairs epithelial cell volume regulation and tear film stability. However, its weaker correlation with tear osmolarity suggests a secondary or modulatory role. Similarly, lower bicarbonate levels may reflect acid–base imbalances that influence mucin layer buffering capacity and epithelial metabolism.18-20

Recent studies between 2022 and 2024 have corroborated these associations, indicating that systemic fluid and electrolyte status should be considered in DES evaluation. Contemporary ocular surface research supports that tear hyperosmolarity initiates a cascade of inflammatory signalling through MAPK and NF-κB pathways, increasing IL-6 and MMP-9 expression, thereby accelerating epithelial damage. Systemic hyperosmolar states, such as dehydration and salt-rich diets, are increasingly recognised as risk factors for chronic DES, particularly in hot climates.

These results highlight the importance of multidisciplinary management approaches. Patients with unexplained or refractory dry eye symptoms should undergo basic metabolic screening, including serum electrolytes, to detect subtle systemic contributors. Correction of mild hypernatremia or dehydration may improve tear osmolarity and reduce disease severity. Moreover, dietary counselling to reduce salt intake could form part of preventive strategies for at-risk individuals.

This study adds novel data from a South-Asian population where environmental stress and dietary factors amplify osmotic stress. The inclusion of direct tear osmolarity measurement alongside

biochemical analysis strengthens the evidence of ocular–systemic linkage. The findings suggest that ocular surface disease reflects systemic osmotic imbalance rather than purely local dysfunction.

Limitations include its cross-sectional design, which precludes causal inference, and exclusion of systemic comorbidities, which might underestimate associations in more complex patients. Nevertheless, the strong correlations and regression findings indicate a biologically meaningful relationship warranting longitudinal confirmation. Future studies should explore interventional models to test whether correction of serum electrolyte abnormalities can normalise tear osmolarity and improve clinical outcomes.

Conclusion: Serum sodium and chloride concentrations are significantly associated with increased tear film osmolarity in chronic dry eye syndrome, indicating that systemic electrolyte imbalance contributes to ocular surface desiccation. Integrating serum electrolyte evaluation into routine DES assessment may enhance early diagnosis and management. Future longitudinal studies should examine whether systemic correction of hypernatremia reduces tear hyperosmolarity and disease progression.

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