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ORIGINAL ARTICLE

Assessing the Impact of Chronic Rhinosinusitis on Intraocular Pressure and Glaucoma Progression, A Clinical Study

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ABSTRACT

Background: Chronic rhinosinusitis (CRS) is a chronic inflammatory condition of the paranasal sinuses with systemic effects outside the sinonasal cavity. There is emerging evidence of a possible association between CRS and ocular disorders, including elevated intraocular pressure, and glaucoma progression.

Aims and Objectives: The purpose of this study was to determine the effect that chronic rhinosinusitis has on intraocular pressure and glaucoma progression. It wanted to assess ocular parameters between CRS patients and healthy controls. The aim was to find clinical correlation and risk implication in CRS cases for glaucoma.

Methodology: A prospective, observational study was done in 100 adult participants equally divided into CR and control groups. ENT assessments were performed in detail: nasal endoscopy and CT-based Lund-Mackay scoring. IOP was measured, OCT, visual field testing and optic disc were evaluated. Statistical analysis of data was done using SPSS software and $p < 0.05$ was considered significant. The objective of this study was to see if there are correlations between severity of CRS and ocular changes associated with glaucoma.

Results: Intraocular pressure (IOP) was significantly higher in the CRS group at baseline (18.9 ± 2.1 mmHg) and after six months (20.1 ± 2.4 mmHg) compared to controls (17.3 ± 1.8 and 17.5 ± 2.0 mmHg, $p < 0.05$) respectively. In addition, the early glaucomatous changes were indicated by the CRS group with increased cup to disc ratio and decreased retinal nerve fiber layer (RNFL) thickness. Comparisons of the mean deviation in the visual field showed worse visual field mean deviation in CRS patients ($p < 0.01$). In addition, 16 per cent of controls but 32 per cent of CRS patients required anti-glaucoma medications. These findings may indicate a relation between CRS and glaucoma progression and would call for more frequent ophthalmologic monitoring.

Conclusion: This study showed that chronic rhinosinusitis has a strong association with elevated intraocular pressure and, early, glaucomatous changes. Inflammatory or anatomical mechanisms may contribute to the progression of glaucoma through CRS. Periodic follow up for glaucoma screening in CRS patients is advised.

Keywords: Intraocular pressure, Glaucoma, Chronic Rhinosinusitis, Inflammatory, Glaucomatous

INTRODUCTION

Chronic Rhinosinusitis (CRS) is a chronic inflammatory disorder of the paranasal sinuses that is characterized by symptoms such as nasal congestion, mucopurulent discharge, facial pressure and olfactory dysfunction lasting more than 12 weeks despite medical therapy [1,2]. The upper respiratory tract disease that it is, is increasingly being recognized as far more than a localized sinonasal condition, but rather a systemic inflammatory disease with far reaching implications away from the upper respiratory tract. Recent studies have demonstrated an association between CRS and systemic co morbidities such as asthma, allergic rhinitis and neurocognitive disorders. However, the effect of this on ophthalmologic parameters such as intraocular pressure (IOP) and progression of glaucoma is under-investigated [5].

Elevated IOP is a well-established modifiable risk factor for glaucoma, a progressive optic neuropathy and leading cause of irreversible blindness worldwide, which is closely linked with the disease [6]. Despite numerous studies on the regulation of IOP and its relationship with systemic diseases including hypertension and diabetes mellitus, very little is known regarding how chronic inflammatory diseases such as CRS might influence IOP dynamics and/or cause glaucomatous damage [8,9]. Due to the proximity of the paranasal sinuses to the orbit and the existence of communicating venous and lymphatic drainage systems, it is possible that chronic inflammation of the sinuses might be responsible for changes in the ocular physiology either due to direct spread of inflammation or via systemic inflammatory mediators [10].

In addition, CRS is also known to induce pro-inflammatory cytokines such as IL-1β, IL-6, and TNF-α, which play a role in the trabecular meshwork dysfunction and oxidative stress in the anterior chamber, key pathophysiological mechanisms in glaucoma development [3]. Furthermore, corticosteroid therapy, which is considered a mainstay treatment of CRS, is a well-known risk factor for steroid induced ocular hypertension, and therefore offers a potential iatrogenic link between CRS management and glaucoma risk [11].

Sinonasal pathology and ocular health are a clinical area of ambiguity in terms of the interrelation [12]. While there have been previous anecdotal and case based reports suggesting that sinonasal diseases can cause orbital complications, there is a paucity of clinical large scale evidence of the specific impact that CRS has on IOP and progression to glaucoma. Specifically, there is a lack of clarity regarding the impact of long standing sinonasal inflammation on the visual field deterioration, optic nerve health and therapeutic outcomes in glaucoma patients [8].

The purpose of this study is to fill a knowledge gap by systematically evaluating the effect of chronic rhinosinusitis on intraocular pressure and glaucoma progression in a defined clinical cohort. Using a multi modal clinical assessment including endoscopic nasal exam, sinus imaging, ocular tonometry, visual field analysis, and optic nerve examine [16]

MATERIALS AND METHODS

Study Design: Present study was a prospective, observational clinical study conducted at the Departments of Ophthalmology and Otorhinolaryngology of tertiary Care hospitals of Pakistan, over a period of 12 months February 2022 to February 2023. A total of 100 adult patients (aged 30–70 years) were enrolled.

Inclusive and exclusive criteria: The study included 30 to 70 year old adults who gave informed consent and agreed to follow up. The CRS group was confirmed to have chronic rhinosinusitis (CRS) with or without nasal polyps lasting more than 12 weeks based on EPOS 2020 criteria. These controls were age and sex matched individuals with no history of sinonasal disease. Exclusion criteria were: ocular surgery or trauma within 6 months, use of corticosteroids for unrelated conditions, coexisting ocular diseases

affecting intraocular pressure, systemic autoimmune disorders or poor compliance in follow up.

Parameters: All participants age, sex, and laterality of affected eye were recorded as demographic and clinical parameters. The clinical data included the presence or absence of chronic rhinosinusitis, duration of symptoms of CRS, and a history of previous medical or surgical treatment for sinus disease. Baseline and follow-up intraocular pressure (IOP), central corneal thickness (CCT), optic disc (cup to disc ratio), visual field indices (mean deviation and pattern standard deviation), and retinal nerve fiber layer (RNFL) thickness using OCT were the ocular parameters. Additionally, the documentation of use of anti-glaucoma medications, history of glaucoma diagnosis and any observed progression during follow up was also done. In the CRS group, sinonasal disease severity was assessed by the Lund-Mackay CT scoring system and SNOT-22 symptom questionnaire.

Statistical analysis: The data were entered into SPSS version 26.0. The mean ± SD were used to express continuous variables and frequencies and percentage were used to summarize categorical variables. IOP and RNFL thickness was compared between the groups and within groups using paired and unpaired t tests. Changes over time were assessed by applying repeated measures ANOVA. Correlations between CRS severity (Lund-Mackay and SNOT-22 scores) and ocular parameters were explored using Pearson's correlation coefficient. Statistical significance was determined a p value < 0.05.

RESULTS

Demographic profile of the study population is given in Table 1 consisting of 100 subjects, equally divided among Chronic Rhinosinusitis (CRS) group (n=50) and control group (n=50). Participants in the CRS group were 48.6 ± 8.2 years of age, those in control group were 47.9 ± 7.9 years of age, and there was no statistically significant difference between the two groups (p = 0.63). That indicates age matching success and minimal age as a confounding variable. The CRS group was 28 (56%) males and 22 (44%) females, while the control group was 27 (54%) males and 23 (46%) females in gender distribution. There was no difference between groups with respect to proportions of male and female participants, which is confirmed by p values of 0.84 for male and female distributions, and hence no statistically significant sex related difference. Together, these findings support that the two groups were demographically comparable, thereby permitting the disassociation of subsequent differences in clinical parameters to the presence or absence of CRS rather than demographic disparities.

Table 1: Demographic Characteristics of Study Participants

Parameter	CRS Group (Mean ± SD)	Control Group (Mean ± SD)	p-value
Mean Age (years)	48.6 ± 8.2	47.9 ± 7.9	0.63
Sex (Male)	28	27	0.84
Sex (Female)	22	23	0.84

Key clinical parameters for the Chronic Rhinosinusitis (CRS) group were summarized and compared to those of the control group in Table 2. Multiple ophthalmic measurements showed significant differences, which may point to a role of CRS in ocular changes, especially those related to glaucoma progression. At baseline, the mean IOP (18.9 ± 2.1 mmHg) was significantly higher in the CRS compared to the control group (17.3 ± 1.8 mmHg, p = 0.014). This difference became more apparent later after 6 months of follow up, 6 months, IOP was 20.1 ± 2.4 mmHg in CRS group and 17.5 ± 2.0 mmHg in controls (p = 0.002), possible an IOP progression in patients with CRS.

CCT values were slightly higher in the CRS group (535 ± 22 µm) as compared to controls (530 ± 20 µm) but this difference was not statistically significant (p = 0.46) and therefore did not contribute significantly to the increased IOP observed. The CRS group also had significantly higher cup to disc ratio (0.62 ± 0.07) compared to controls (0.58 ± 0.06, p = 0.031) suggesting a possible association between CRS and optic nerve changes. Additionally, RNFL thickness was decreased in the CRS group (82.4 ± 5.3 µm) compared to the control group (87.2 ± 4.8 µm, p = 0.005), suggesting that CRS patients may have a progressive optic nerve damage.

Table 2: Clinical Parameters in CRS and Control Groups

Parameter	CRS Group (Mean ± SD)	Control Group (Mean ± SD)	p-value
Mean IOP (mmHg) - Baseline	18.9 ± 2.1	17.3 ± 1.8	0.014
Mean IOP (mmHg) - 6 months	20.1 ± 2.4	17.5 ± 2.0	0.002
Central Corneal Thickness (µm)	535 ± 22	530 ± 20	0.46
Cup-to-Disc Ratio	0.62 ± 0.07	0.58 ± 0.06	0.031
RNFL Thickness (µm)	82.4 ± 5.3	87.2 ± 4.8	0.005
Visual Field MD (dB)	-4.2 ± 1.5	-2.1 ± 1.2	0.008
Patients on Anti-Glaucoma Medications	16	8	0.041
Lund-Mackay Score	12.6 ± 3.8	1.2 ± 1.1	<0.001
SNOT-22 Score	42.3 ± 6.1	5.1 ± 2.4	<0.001

Visual field mean deviation (MD), an index of visual function, was also more impaired in the CRS group (-4.2 ± 1.5 dB) than in controls (-2.1 ± 1.2 dB, p = 0.008), suggesting functional deterioration that may relate to structural optic nerve damage. Treatment wise, 16 patients in the CRS group were on anti-glaucoma meds while only 8 patients in the control group (p = 0.041) suggesting higher clinical burden of glaucoma management in CRS patients. Overall, CRS group showed significantly higher Lund Mackay CT score (12.6 ± 3.8) compared to controls (1.2 ± 1.1, p < 0.001) for radiological severity in the CRS specific metrics. Similarly, objective and subjective diagnostic criteria were validated by the fact that the SNOT-22 score (42.3 ± 6.1) was significantly elevated in the CRS group compared to controls (5.1 ± 2.4, p < 0.001).

DISCUSSION

In contrast, the present study presents novel insights into a potential association of chronic rhinosinusitis (CRS) with ocular health, specifically in regards to IOP dynamics and glaucoma progression. We compared a well matched CRS cohort of patients to healthy controls and observed statistically significant elevations in IOP, optic nerve changes and visual field deterioration in CRS patients over a six month follow up period [13]. These findings suggest that CRS may contribute to a degree that has been underappreciated in modulating intraocular physiology and accelerating glaucomatous changes [14].

The most prominent modifiable risk factor for glaucoma development and progression is elevated IOP. Baseline IOP and the six months IOP elevation were significantly higher in CRS patients than in control group [19]. Orbital venous congestion or change in episcleral venous pressure due to chronic inflammation in the paranasal sinuses results in aqueous outflow impairment and elevated IOP. Additionally, it is well known that long standing sinonasal inflammation also upregulates cytokines such as interleukin 1β (IL-1β), tumor necrosis factor alpha (TNF-α), and matrix metalloproteinases, all of which have been implicated in trabecular meshwork dysfunction and oxidative stress, which are pathophysiological mechanisms involved in the development of open angle glaucoma [18, 15].

In addition, we observe a large increase in cup-to-disc ratio and reduction in retinal nerve fiber layer (RNFL) thickness in the CRS group compared to controls. In combination with observed visual field defects, these structural markers support the idea that CRS may cause damage to the optic nerve beyond the effects of increased IOP alone [14]. This suggests important considerations for the pathogenesis of glaucoma related to systemic inflammation, and local anatomical changes. Sustained inflammation signaling

from adjacent sinus structures may extend or via common vessels and lymphatics to the optic nerve head, thus it is plausible [20].

A higher proportion of CRS patients were already on anti-glaucoma medications as compared to controls but despite this, they still had progressive changes in IOP and optic nerve parameters. This observation might suggest the existence of resistance to standard IOP lowering therapies or non IOP dependent mechanism of glaucomatous damage, mediated through inflammatory or neurotoxic pathways related to CRS [19].

Finally, the severity of CRS, as determined by the Lund-Mackay CT score and the SNOT-22 symptom questionnaire, also had a trend of correlation with worsening ocular parameters, but further studies in larger cohorts and using multivariate regression analysis are needed to confirm causality [18]. These findings emphasize the clinical importance of an interdisciplinary approach that focuses ophthalmologists' attention on glaucomatous changes in patients with chronic sinonasal disease, particularly patients who are receiving long term corticosteroid therapy, a known risk factor for steroid induced ocular hypertension [13].

The absence of significant difference between groups of central corneal thickness (CCT) indicates that the observed IOP changes are not likely to be due to artefacts related to corneal biomechanics. This serves to strengthen the trustworthiness of IOP measurements and further corroborate the hypothesis of true physiological change in aqueous humor dynamics in CRS patients. Although this study is robust with respect to its prospective design and multi-modal assessment, it is not without limitations [11,18]. Although six months is a sufficient follow up time to detect early changes, it might not completely capture the long term progression of glaucoma in CRS patients. Furthermore, a sample size sufficient to demonstrate power for primary outcomes does not allow generalizability of findings to different CRS subtypes, such as CRS with nasal polyposis versus those without [12].

Without inflammatory biomarker profiling, we also have limited ability to make mechanistic inferences. Longitudinal follow up beyond one year should also be considered, as should inflammatory cytokine assays, and the effect of specific CRS treatments (e.g., endoscopic sinus surgery vs. medical therapy) on ocular outcomes. Additionally, studies are warranted to determine the potential role of systemic anti-inflammatory agents or immunomodulatory therapies to prevent glaucoma risk in CRS patients in view of integrated disease management [11,15].

CONCLUSION

Our study concludes with a strong association between chronic rhinosinusitis and ocular parameters associated with progression of glaucoma. This also confirmed the need for proactive ocular monitoring in CRS patients as CRS patients were more likely to have elevated IOP, optic nerve changes and visual field deterioration. These findings support closer cooperation between otolaryngologists and ophthalmologists in order to expedite diagnosis, prevention, and management of vision threatening complications in patients with chronic sinonasal inflammation.

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