1 Study of the histopathological changes of lacrimal sac and nasal mucosa in patients

2 undergoing external DCR

3 Abstract-

Introduction-The most frequent histopathologic findings in individuals having
dacryocystorhinostomy (DCR) for acquired nasolacrimal duct obstruction are chronic
inflammation and fibrosis of the lacrimal sac. Although uncommon, various pathologic
alterations such infections, systemic inflammatory conditions, and neoplasms like primary
lacrimal system cancers, secondary invasion from neighbouring tissues, or even distant
metastases, may be detected in the lacrimal sac.

Aim- To study the histopathological changes of lacrimal sac and nasal mucosa in patients
undergoing external DCR.

Material and Methods- Observational prospective study conducted at Department of
 Ophthalmology, JNU Hospital Jaipur on 43 patients with PANDO undergoing External DCR
 surgery.

Results- On basis of symptoms out of 43 patients, 40 patients have symptom of watering and 3 patients have 15 16 Non tender swelling and watering as symptom. In present study Left side [69.8% (n= 30) 17 involvement was seen more than right side 30.2% (n=13). In present study HPE findings of 18 Lacrimal Sac Mucosa revealed Chronic Non-granulomatous Inflammation of mild grade in 19 18 patients, Chronic Non-granulomatous Inflammation of moderate grade in 17 patients, and 20 Chronic Non-granulomatous Inflammation of severe grade in 8 patients. In present study HPE 21 findings of nasal Sac Mucosa revealed Chronic Non-granulomatous Inflammation of mild 22 grade in 15 patients, Chronic Non-granulomatous Inflammation of moderate grade in 20 23 patients, and Chronic Non-granulomatous Inflammation of severe grade in 8 patients.

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25 Conclusion- Histopathological evaluation of the lacrimal sac in patients undergoing DCR

26 surgery for PANDO revealed chronic non-granulomatous inflammation. Although, no

27 specific pathology other than inflammation was noted, routine histopathological analysis may

28 confirm a diagnosis and also aid in diagnosis of unsuspected pathology.

30	Keywords- dacryocystorhinostomy (DCR), Chronic Non-granulomatous Inflammation.
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Introduction- Acquired nasolacrimal duct obstruction (ANDO) is a common disease of the lacrimal passages that is most frequently caused by local nonspecific inflammation of the lacrimal sac and the nasolacrimal duct, resulting in occlusive fibrosis [<u>1</u>, <u>2</u>]. The clinical symptoms include chronic lacrimation that is aggravated by exposure to sun, wind, or cold.[3]

42 Obstruction of the nasolacrimal drainage system can cause orbital infection, medial 43 angular uncomfortable swelling, mucoid or mucopurulent discharge, epiphora, and recurrent 44 inflammation of the lacrimal sac. [5] The majority of the time, they are either primary or 45 secondary acquired illnesses. Lacrimal sac neoplasia, inflammatory conditions, some 46 infections, mechanical obstruction, and trauma are secondary causes of ANDO [6]. Most 47 lacrimal sac tumours are malignant and originate from the glandular epithelium or squamous 48 cells [7]. A palpable mass near a lacrimal sac and bloody discharge from a lacrimal duct are 49 indicators of a malignant tumour. Nonetheless, it is possible that up to 40% of all nasolacrimal duct tumours go undetected and are mistaken for chronic dacryocystitis or 50 51 primary ANDO [8].

52 Clinically suspected main acquired nasolacrimal duct blockage is associated with idiopathic
53 persistent inflammation, either with or without fibrosis (PANDO). Secondary acquired
54 lacrimal drainage system obstruction can have a wide range of reasons, including specific
55 inflammatory, traumatic, mechanical, or neoplastic conditions (SALDO). [9]

The most effective treatment for nasolacrimal duct (NLD) obstruction is external dacryocystorhinostomy (DCR), with a success rate of 86.4% and failure rates ranging from 4% to 13%, one such study sought to determine the reasons for external DCR failure using postoperative endoscopic and pathological assessment. [10]

60 The most frequent histopathologic findings in individuals having dacryocystorhinostomy 61 (DCR) for acquired nasolacrimal duct obstruction are chronic inflammation and fibrosis of 62 the lacrimal sac. Although uncommon, various pathologic alterations such infections, 63 systemic inflammatory conditions, and neoplasms like primary lacrimal system cancers, 64 secondary invasion from neighbouring tissues, or even distant metastases, may be detected in 65 the lacrimal sac. It is uncommon, but possibly fatal, when a tumour blocks the lacrimal drainage system. When the lacrimal system is irrigated for diagnostic purposes, patients with 66 67 lacrimal sac tumours may exhibit clinical symptoms such bloody reflux, visible or palpable masses, and bloody tears.[11] According to some authors, to ensure the timely diagnosis of 68 69 tumors involving the lacrimal drainage system, a routine biopsy and histopathological 70 examination of the lacrimal sac should be performed for all patients undergoing 71 dacryocystorhinostomy (DCR) [12]"

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Aim- To study the histopathological changes of lacrimal sac and nasal mucosa in patientsundergoing external DCR.

Material and Methods- Observational prospective study conducted at Department of
 Ophthalmology, JNU Hospital Jaipur on 43 patients with PANDO undergoing External DCR
 surgery.

Informed consents was obtained from the patients enrolled in the study after explaining the procedure to study. This study was conducted in accordance with the ethical performed and the aim of the standards stated by the Ethical Committee and was adhered to the tenets of the Declaration of Helsinki. "

- 82 Complete lacrimal drainage system examination was done including:
- a. Lacrimal sac inspection to assess for the presence of mucocele or pyocele.
- b. Lacrimal sac palpation to assess for the presence of lacrimal sac stones.
- 85 c. ROPLAS Test using cotton tipped applicator.

- 86 d. Fluorescein dye disappearance test (DDT) using a moistened fluorescein strip to instill
- 87 fluorescein into the conjunctival sac of each eye. Patients were instructed not to wipe their
- 88 eyes. Intensity of residual fluorescein stain in the conjunctival sac after 5 minutes was used to
- 89 grade the tear drainage insufficiency. Excess residual stain suggested a delayed clearance and
- 90 lacrimal system obstruction.
- 91 e. Syringing and probing of the lacrimal system to specify the level of lacrimal drainage
- 92 obstruction.
- 93 Full history taking which included medical, surgical and ocular information, all to confirm
- 94 the presence of predisposing conditions, previous history of dacryocystitis and duration and
- 95 grading of epiphora according to Munk scale.

96 f. If irrigation reveals an obstruction in the lacrimal outflow system, diagnostic probing using

- 97 Bowman's lacrimal probes was performed to confirm the level of obstruction.
- 98 Under topical anesthesia, one of the puncta was dilated, and appropriately sized lacrimal
- 99 probe was gently introduced along the canaliculus till it reaches a stop. Hard stop confirmed
- the presence of nasolacrimal duct obstruction (NLDO) while soft stop indicated a canalicularobstruction.
- Slit lamp examination was done for all patients to assess the presence of eye lid disorderscausing epiphora such as entropion as well as to rule out the presence of punctal stenosis.

104 Biopsy specimens (posterior lacrimal sac flap measuring about 4×4 mm and nasal mucosa 5×5 mm) was fixed in 10% formalin solution in a labelled spill proof container along with the 105 106 requisition form for histopathology describing the details of the patient, clinical data, procedure performed and test requested as histopathology was sent for histopathological 107 108 examination in the department of Pathology in JNUIMSRC. Tissue was grossed and 109 processed in Histokinette. Paraffin blocks of the biopsy tissue was made and thin sections of 110 3-5 microns was cut and put over the slides for staining by H&E stain. Sections were 111 examined under the microscope and were evaluated for the degree of inflammation and other 112 relevant microscopic findings.

- 113 Correlation between the clinical lacrimal variables including history of acute or chronic
- 114 dacryocystitis, duration of epiphora, grading of epiphora based on Munk score, grading of
- 115 DDT, presence of mucocele or pyocele, regurgitation of sac contents, probing and irrigation,
- 116 intra operative sac appearance and presence of sac calculi and the histopathological findings

- 117 of lacrimal sac and nasal mucosa was done to determine the important clinical parameters
- 118 that may recommend lacrimal biopsy."

119 Results-

Parameter		No.	%
	<40 Years	17	39.5%
	40-49 Years	12	27.9%
Age Category	>=50 Years	14	32.6%
	Total	43	100.0 %
	Female	27	62.8%
Sex	Male	16	37.2%
	Total	43	100.0 %
	Rural	25	58.1%
Residence	Urban	18	41.9%
	Total	43	100.0 %

120 Table:1 - Table showing Demographic distribution of study subjects

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124 **Table-2: Table showing baseline symptoms, signs and eye involvement distribution of**

125 study subjects

	Parameter N		%
	Non tender swelling and watering	3	7.0%
	Watering	40	93.0%
Symptoms	Total	43	100.0 %
Roplas test (Pre- op)	Positive	43	100.0 %

	Total	43	100.0 %
	Regurgitation-Lower Puncta	22	51.2%
Syringing test	Regurgitation-Upper Puncta	21	48.8%
(Pre-op)	Total	43	100.0 %
	Left	30	69.8%
Eve Involved	Right	13	30.2%
	Total	43	100.0 %

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128 Table-3: Table showing post-op symptoms, signs at 1 months of Study Subjects

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	Parameter	No.	%
Symptoms (post-	None	43	100.0 %
op at 1 month)	Total	43	100.0 %
Syringing test	NLD patent	43	100.0 %
month)	Total	43	100.0 %
Fluorescein DDT	Negative	43	100.0 %
month)	Total	43	100.0 %
	None	41	95.3%
Symptoms (post-	Watering	2	4.7%
op at 3 month)	Total	43	100.0 %
Syringing test	None	41	95.3%

(post-op at 3	Regurgitation-Lower Puncta	1	2.3%
month)	Regurgitation-Upper Puncta	1	2.3%
	Total	43	100.0 %
Fluorescein DDT	Negative	41	95.3%
test (nost-on at 3	Positive	2	4.7%
month)	Total	43	100.0 %
	None	41	95.3%
Symptoms (post-	Watering	2	4.7%
op at 6 month)	Total	43	100.0 %
Syringing test	None	41	95.3%
(post-op at 6	Regurgitation-Lower Puncta	1	2.3%
month)	Regurgitation-Upper Puncta	1	2.3%
	Total	43	100.0 %
Fluorescein DDT	Negative	41	95.3%
test (post-op at 6	Positive	2	4.7%
month)	Total	43	100.0 %

134 Table -4: Table showing HPE findings of Lacrimal Sac Mucosa and nasal sac mucosa

		Parameter		No.	%
HPE findings-	Chronic I grade	Non-granulomatous Inf	lammation-mild	18	41.9%
Lacrimal Sac Mucosa	Chronic moderate	Non-granulomatous grade	Inflammation-	17	39.5%
	Chronic severe gra	Non-granulomatous de	Inflammation-	8	18.6%

	Total	43	100.0 %
	Chronic Non-granulomatous Inflammation-mild grade	15	34.9%
HPE findings- Nasal sac mucosa	Chronic Non-granulomatous Inflammation- moderate grade	20	46.5%
	Chronic Non-granulomatous Inflammation- severe grade	8	18.6%

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140 Table-5: Table showing surgical outcome of Study Subjects

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	Parameter	No.	%
	Failure	2	4.7%
Surgical Outcome	Successful	41	95.3%
Surgical Outcome	Total	43	100.0 %

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DISCUSSION "

147 Illnesses of the lacrimal drainage system resulting in epiphora are prevalent in

148 ophthalmology, with the majority being primary instances and a minority being subsequent

149 acquired illnesses. They manifest in maturity and result from non-specific disease. Idiopathic

150 chronic inflammation, with or without fibrosis, is seen in clinically suspected primary

- 151 acquired nasolacrimal duct obstruction (PANDO). A diverse array of factors, including
- 152 particular inflammatory, traumatic, mechanical, or neoplastic conditions, may resemble
- 153 idiopathic inflammation in secondary acquired lacrimal drainage system obstruction
- 154 (SALDO). The prevalence of unrecognised pathological abnormalities in the lacrimal sac
- during DCR has been documented to range from 0% to 12.5%. Assessing the prevalence of

- 156 primary lacrimal sac-specific pathology that resembles primary acquired lacrimal duct
- 157 obstruction is crucial, as it influences the necessity of routine biopsy during
- 158 dacryocystorhinostomy (DCR) and the potential risk of overlooking a clinically unsuspected
- and intraoperatively non-visible underlying specific non-neoplastic or neoplastic condition
- 160 affecting the lacrimal sac in patients who do not receive routine biopsy during DCR.[13]
- 161 The risk of overlooking a spectrum of lacrimal sac originated specific pathologies
 162 particularly neoplastic malignant lesions that cause nasolacrimal system obstruction, although
 163 low still exists.
- 164 The mean age of presentation in present study study was 44.02±8.33 years. Majidaee et al [14] in
- their study found that mean age of patients was reported to be 48.22 years and Harshika
- 166 **Rauniyar et al [13]** in their study found that mean age of patients was reported to be 46 years
- 167 which is comparable to the present study. In the study done by Badhu et al[15] the mean age of
- 168 patients was reported to be 27.4 ± 13.7 years and in the study by Tuladhar et al [16] the reported
- 169 mean age was 34.4 ± 12.12 years.
- In present study 62.8 % (n=27) were female whereas 37.2% (n=16) were male with female 170 171 i.e. majority of patients were females. This result correlates with the study conducted by Dagleish et 172 al[17], Bharathi et al[18], Badhu et al[15], by Tucker et al[19], Anderson et al[20], and Lee-Wing 173 et al[21]. The preponderance of female patients of PANDO could be explained by fact that females 174 have nasolacrimal ducts of smaller length and size while the males have long and wide nasolacrimal 175 duct . Also, the angulation of the nasolacrimal canal is more in females . Thus the chance of 176 obstruction is more likely in females than males due to the above anatomical variation in both the 177 gender. These anatomical factors might be a reason why this condition is more common in 178 females.[13]
- In present study Left side[69.8% (n= 30) involvement was seen more than right side[30.2%
 (n=13) which is in agreement with the study by Prakash et al[22], Taban et al[23]. The nasolacrimal
 duct and the lacrimal fossa forms a greater angle on the right side than on the left side.
- 182 The most common presenting symptom in present study was watering which is in agreement 183 to the study done by Lee Wing et al[21], and Tucker et al[19] where epiphora was the most 184 common presenting complain.

185 In present study all of lacrimal sac and nasal sac specimens revealed chronic non granulomatous 186 inflammation which is similar to results of Mauriello et al^[24], Lee Wing^[21], Bernardini et al^[25], 187 Merkonidis et al[26], Salour et al[27], Nash et al[28]. Malignancy of Lacrimal sac is very rare 188 and is also less likely detected, however, if the finding is missed may lead to serious consequences. 189 190 Conclusion-Histopathological evaluation of the lacrimal sac in patients undergoing DCR 191 surgery for PANDO revealed chronic non-granulomatous inflammation. Although, no specific pathology other than inflammation was noted, routine histopathological analysis may 192 193 confirm a diagnosis and also aid in diagnosis of unsuspected pathology. 194 195 196 REFERENCES

1977.Weber RK, Keerl R, Schaefer SD, Della Rocca RC. Atlas of Lacrimal Surgery, Vol. 10. Springer 1988cience & Business Media; 2007. [Google Scholar]

1929Mandeville JT, Woog JJ. Obstruction of the lacrimal drainage system. Curr Opin Ophthalmol. 202002;5:303–309. doi: 10.1097/00055735-200210000-00003. [DOI] [PubMed] [Google Scholar]

2021. Bartley GB. Acquired lacrimal drainage obstruction: an etiologic classification system, case 2022ports, and a review of the literature. Part 1. Ophthal Plast Reconstr Surg. 1992;8:237–242. doi: 2020.1097/00002341-199212000-00001. [DOI] [PubMed] [Google Scholar]

2044 Makselis A, Petroska D, Kadziauskiene A, Jaruseviciene R, Ruzgys A, Cimbalas A, Besusparis 2005 Asoklis RS. Acquired nasolacrimal duct obstruction: clinical and histological findings of 275 2006ases. BMC Ophthalmol. 2022 Jan 5;22(1):12. doi: 10.1186/s12886-021-02185-x. PMID: 20074986808; PMCID: PMC8734260.

20 BTucker N, Chow D, Stockl F, Codère F, Burnier M. Clinically suspected primary acquired 20 Pasolacrimal duct obstruction: clinicopathologic review of 150 patients. Ophthalmology. 21 D97;11:1882–1886. doi: 10.1016/S0161-6420(97)30012-8. [DOI] [PubMed] [Google Scholar] 215LStefanyszyn MA, Hidayat AA, Pe'er JJ, Flanagan JC. Lacrimal sac tumors. Ophthal Plast 21Reconstr Surg. 1994;3:169–184. doi: 10.1097/00002341-199409000-00005. [DOI] [PubMed] 21[Google Scholar]

2164Ni C, D'Amico DJ, Fan CQ, Kuo PK. Tumors of the lacrimal sac: a clinicopathological analysis 216f 82 cases. Int Ophthalmol Clin. 1982;22:121–140. doi: 10.1097/00004397-198202210-2160010. [DOI] [PubMed] [Google Scholar]

2177.Ryan SJ, Font RL. Primary epithelial neoplasms of the lacrimal sac. Am J Ophthalmol. 218973;76:73–88. doi: 10.1016/0002-9394(73)90014-7.

219 Mauriello JA Jr, Palydowycz S, DeLuca J. Clinicopathologic study of lacrimal sac and nasal 220 ucosa in 44 patients with complete acquired nasolacrimal duct obstruction. Ophthalmic Plast 22 Reconstr Surg. 1992;8(1):13-21. doi: 10.1097/00002341-199203000-00002. PMID: 1554647.

222 Heathcote JG. The ocular adnexa. Saudi J Ophthalmol. 2022 Apr 18;35(3):167-169. doi: 2220.4103/SJOPT.SJOPT_43_22. PMID: 35601866; PMCID: PMC9116093.

2240. Parmar DN, Rose GE. Management of lacrimal sac tumors. Eye (Lond) 2009;17(5):599–606. 225oi: 10.1038/sj.eye.6700516.

22KI. Valenzuela AA, McNab AA, Selva D, O'Donnell BA, Whitehead KJ, Sullivan TJ. Clinical 23Features and management of tumors affecting the lacrimal drainage apparatus. Ophthal Plast 22Reconstr Surg. 2010;22(2):96–101. doi: 10.1097/01.iop.0000198457.71173.7b. [DOI] [PubMed] 23[Google Scholar]

2312. Anderson NG, Wojno TH, Grossniklaus HE. Clinicopathologic findings from lacrimal sac 23biopsy specimens obtained during dacryocystorhinostomy. Ophthalmol Plast Reconstr Surg. 232009;19(3):173–176. doi: 10.1097/01.iop.0000066646.59045.5a.

23/33. Harshika Rauniyar. The role of inflammatory biomarkers in predicting primary acquired
23/4asolacrimal duct obstruction and postoperative recurrence. Nagoya J Med Sci. 2021
23/51ay;85(2):289-298. doi: 10.18999/nagjms.85.2.289. PMID: 37346835; PMCID: PMC10281832.

236

238	14. Majidaee M, Mohammadi M, Sheikh MR, Khademlu M, Gorji MH. Patients undergoing
239	dacryocystorhinostomy surgery in northern iran: an epidemiologic study. Ann Med Health
240	Sci Res. 2014 May;4(3):365–8
241	
242	15. Badhu B,Dulal S, Kumar S, Thakur SKD,Sood A, Das H. Epidemiology of chronic
243	dacryocystitis and success rate of external dacryocystorhinostomy in Nepal. Orbit Amst Neth.
244	2005 Jun;24(2):79–82.
245	
246	16. Tuladhar S, Adhiari S. Effectiveness of sedation in dacryocystorhinostomy surgery. Nep J
247	Oph. 2009;1(1):25–31.
248	
249	17.Dalgleish r. Incidence of Idiopathic acquired Obstructions in the lacrimal Drainage
250	apparatus*. Br j Ophthalmol. 1964 jul;48(7):373–6. 11.
251	
252	18. Bharathi MJ, Ramakrishnan R, ManekshaV, Shivakumar C, Nithya V, Mittal S.
253	Comparative bacteriology of acute and chronic dacryocystitis. Eye Lond Engl. 2008
254	Jul;22(7):953–60. 12.
255	
256	19. Tucker N, Chow D, Stockl F, Codère F, Burnier M. Clinically suspected primary acquired
257	nasolacrimal duct obstruction: clinicopathologic review of 150 patients. Ophthalmology.
258	1997 Nov;104(11):1882–6.
259	
260	20. Anderson NG, Wojno TH, Grossniklaus HE. Clinicopathologic Findings From Lacrimal
261	Sac Biopsy Specimens Obtained During Dacryocystorhinostomy: Ophthal Plast Reconstr
262	Surg. 2003 May;19(3):173-6. 15.
263	
264	21. Lee-Wing MW, Ashenhurst ME. Clinicopathologic analysis of 166 patients with primary
265	acquired nasolacrimal duct obstruction. Ophthalmology. 2001 Nov;108(11):2038-40.
266	
267	22. Prakash R, Babu RJ, Nagaraj ER, Prashanth HV, Shah JS. Bacteriological study of
268	dacryocystitis. J Clin Diagn Res 2012;6:652-5.
269	

270	21. Taban M, Jarullazada I, Mancini R, Hwang C, Goldberg RA. Facial asymmetry and nasal
271	septal deviation in acquired nasolacrimal duct obstruction. Orbit Amst Neth. 2011
272	Oct;30(5):2269.
273	
274	24. Mauriello JA, Palydowycz S, DeLuca J. Clinicopathologic study of lacrimal sac and nasal
275	mucosa in 44 patients with complete acquired nasolacrimal duct obstruction.
276	OphthalPlastReconstr Surg. 1992;8(1):13–21.
277	
278	
279	25. Bernardini FP, Moin M, Kersten RC, Reeves D, Kulwin DR. Routine histopathologic
280	evaluation of the lacrimal sac during dacryocysto rhinostomy: how useful is it?
281	Ophthalmology. 2002 Jul;109(7):1214–7.
282	
283	26.Merkonidis C, Brewis C, Yung M, Nussbaumer M. Is routine biopsy of the lacrimal sac
284	wall indicated at dacryocystorhinostomy? A prospective study and literature review. Br J
285	Ophthalmol. 2005 Dec;89(12):1589–91.
286	
287	27. Salour H, Hatami MM, Parvin M, Ferdowsi AA, Abrishami M, Bagheri A, Aletaha M,
288	Yazdani S. Clinicopathological study of lacrimal sac specimens obtained during DCR. Orbit.
289	2010 Oct;29(5):250-3. doi: 10.3109/01676830.2010.485720. Epub 2010 Sep 2. PMID:
290	20812824.
291	
292	28. Nash M, Skippen B, Gal A, Benger R. The Role of Routine Biopsy of the Lacrimal Sac.
293	2015;34(6):320-3. doi: 10.3109/01676830.2015.1078370. Epub 2015 Oct 19. PMID:
294	26479081.
205	
293	
296	\mathbf{v}