EVALUATION OF THE SCORE OF LACRIMAL SYMPTOM QUESTIONNAIRE (LAC-Q), FLUORESCEIN DYE DISAPPEARANCE TEST AND ENDOSCOPIC DYE TRANSIT TEST IN EPIPHORA

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DISCLAIMER

I hereby certify that the work in this dissertation is on my own except for quotations and summaries which have been duly acknowledged. I declare that I have no financial interest in this study.

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ABSTRAK

Pengenalan

Epifora disebabkan oleh aliran air mata perlahan merupakan salah satu aduan utama yang kerap dihadapi di Klinik Pakar Mata. Ianya berlaku disebabkan oleh saluran lakrimal (saluran air mata) tersumbat. Masalah ini bukan sahaja menyebabkan tahap penglihatan terganggu malahan menyebabkan ketidakselesaan pada mata dan juga memberi kesan kepada aktiviti-aktiviti harian.

Objektif

Objektif kajian ini adalah untuk membandingkan min skor gejala epifora dengan impak sosial menggunakan Borang Kaji Selidik Gejala Lakrimal, min penggredan Ujian Kehilangan Pewarna Fluoresin dan min tempoh Ujian Transit Pewarna secara endoskopi dalam nasolakrimal obstruksi separa dengan kumpulan kawalan dan untuk menilai hubungkait.

Kaedah kajian

Ini merupakan sebuah kajian perbandingan secara keratan rentas. Seramai 52 orang pesakit epifora dan 52 orang pesakit yang sihat sebagai kawalan berumur 18 tahun dan ke atas dipilih. Kesemua pesakit yang terlibat menjalani ujian picagari untuk menguji tahap patensi saluran lakrimal. Pesakit diselidik mengenai gejala epifora dan impak sosial menggunakan Borang Kaji Selidik Gejala Lakrimal. Kesemua pesakit yang terlibat

menjalani Ujian Kehilangan Pewarna Fluoresin dan Ujian Transit Pewarna secara endoskopi.

Keputusan

Data statistik menunjukkan keputusan yang signifikan bagi perbezaan antara min skor gejala epifora dan impak sosial menggunakan Borang Kaji Selidik Gejala Lakrimal, min penggredan Ujian Kehilangan Pewarna Fluoresin dan min tempoh Ujian Transit Pewarna secara endoskopi antara pesakit epifora disebabkan oleh nasolakrimal obstruksi separa dan kumpulan kawalan ($p < 0.01$). Hubungkait yang sangat kuat dapat dilihat antara min skor gejala epifora dan impak sosial menggunakan Borang Kaji Selidik Gejala Lakrimal dengan min penggredan Ujian Kehilangan Pewarna Fluoresin ($r = 0.728$, $p = < 0.01$) dan min tempoh Ujian Transit Pewarna secara endoskopi ($r = 0.820$, $p = < 0.01$) dalam kalangan pesakit epifora disebabkan oleh nasolakrimal obstruksi separa.

Kesimpulan

Kajian ini menunjukkan keputusan yang signifikan bagi min skor gejala epifora dan impak sosial menggunakan Borang Kaji Selidik Gejala Lakrimal, min penggredan Ujian Kehilangan Pewarna Fluoresin dan min tempoh Ujian Transit Pewarna secara endoskopi antara pesakit epifora disebabkan oleh nasolakrimal obstruksi separa dan kumpulan kawalan, Terdapat hubungkait yang sangat kuat antara min penggredan Ujian Kehilangan Pewarna Fluoresin dan min tempoh Ujian Transit Pewarna secara endoskopi dengan gejala saluran lakrimal (saluran air mata) tersumbat dalam nasolakrimal obstruksi separa.

Kata kunci: Epifora, nasolakrimal obstruksi separa, borang kaji selidik gejala lakrimal, ujian kehilangan pewarna fluoresin, ujian transit pewarna secara endoskopi.

ABSTRACT

Introduction

Epiphora attributable to delayed tears drainage is one of the most common complaints encountered in ophthalmology clinics. The aim of this study was to compare the mean score of lacrimal symptom and its social impact using Lacrimal Symptom Questionnaire (Lac-Q), the mean grading of Fluorescein Dye Disappearance Test (FDDT), and the mean time of Endoscopic Dye Transit Test (EDTT) in epiphora patients with partial nasolacrimal duct obstruction (NLDO) and in a control group and to evaluate its correlation.

Methods

The comparative cross-sectional hospital-based study included 52 adult patients with epiphora and 52 adult patients without epiphora as controls aged 18 years and above. All recruited patients underwent syringing test to evaluate the patency of the lacrimal drainage system. The severity of lacrimal symptom and its social impact was evaluated using a validated Lac-Q questionnaire. FDDT and EDTT were performed in all patients.

Results

There was a statistically significant difference between mean total Lac-Q score, mean FDDT grading, and mean EDTT time between epiphora patients with partial NLDO and control group ($p < 0.01$). There was a strong correlation demonstrated between mean total

Lac-Q score with mean FDDT grading (r = 0.728, p = < 0.01), and mean EDTT time (r = 0.820, p = < 0.01) in epiphora patients with partial nasolacrimal duct obstruction.

Conclusions

There was statistically different in the mean score of lacrimal symptom questionnaire, the mean grading of FDDT and the mean time of EDTT in patients with partial NLDO compared to control group. There was strong correlation between FDDT and EDTT with the symptoms of lacrimal outflow obstruction in partial NLDO.

Key words: Epiphora, partial nasolacrimal duct obstruction (NLDO), lacrimal symptom questionnaire (Lac-Q), fluorescein dye disappearance test (FDDT), endoscopic dye transit test (EDTT)

CHAPTER 1:

INTRODUCTION

1.1 EPIPHORA

Epiphora or tearing is defined as excessive watering of the eye. It is a common complaint among referrals to oculoplastic clinics. The process of tearing includes several steps such as formation in the lacrimal gland, spreading through eye blinking, vaporization from the ocular surface, and draining through the nasolacrimal duct. Abnormalities in any of these steps can cause epiphora (Tsubota et al., 1998).

There are several etiological factors that, alone or in combination, may contribute to the development of epiphora. The etiology of epiphora can be divided into two categories which are reflex tearing and reduced tear outflow. Reflex tearing is usually secondary to dry eye, inflammation, allergy, or other ocular surface disorders, whereas primary hypersecretion of the lacrimal glands is rare. Reduced tear outflow on the other hand can be due to eyelid malposition, tear pump dysfunction caused by eyelid laxity, or obstruction at any portion of the nasolacrimal drainage system (Blackmore et al., 2010). In a study by Mainville and Jordan et al. (2011), 48.7% of patients with tearing had a lacrimal system block and 40% of patients had dry eye syndrome. In a study by Sibley et al. (2013), 31.8% of subjects had nasolacrimal duct obstruction, which was followed by the development of dry eye syndrome with secondary reflex tearing in 29.2% of patients.

Epiphora following nasolacrimal duct obstruction (NLDO) was considered often and accounted for one-third of the total number of epiphora cases (Lin et al., 2016). It could be congenital and acquired, and their frequencies were 10.1% to 33.3% respectively (Bukhari et al., 2013). The primary causes of acquired NLDO are frequently caused by

local nonspecific inflammation of the lacrimal sac and the nasolacrimal duct, resulting in occlusive fibrosis, which eventually leads to either partial or complete obstructions (Mandeville et al., 2002) while secondary causes include lacrimal sac neoplasia, inflammatory diseases, infections, mechanical obstruction, and trauma (Bartley et al., 1992).

Epiphora associated with partial or functional NLDO presents a diagnostic challenge because the clinical findings do not correlate with the symptoms. This subset of patients shows patent lacrimal drainage systems on syringing and there is no standard test to diagnose such cases (Patnaik et al., 2019). Therefore, in such cases management may be misleading due to the inconsistency of clinical assessment with symptoms.

Clinical assessment of epiphora in relation to NLDO which includes lacrimal syringing, probing, fluorescein dye disappearance test, nasal endoscopy, and endocanalicular endoscopy as well as imaging modalities such as dacryocystography, and dacryoscintigraphy (Kominek et al., 2007). Lacrimal syringing has routinely been used to diagnose NLDO. However, the utility of lacrimal syringing for diagnosing NLDO and differentiating it from non-anatomical "functional obstruction" is uncertain yet invasive procedure as reported by Shapira et al. (2021).

Epiphora can affect a broad array of daily activities as well as social embarrassment. Outdoor activities were among those that epiphora most significantly hindered especially with complete NLDO (Shin et al., 2015). Epiphora following NLDO is a treatable disease and provides promising outcomes if early surgical intervention is offered. The standard treatment for NLDO has been dacryocystorhinostomy (DCR) surgery either external

approach or via endoscopic endonasal approach with high success rates ranging from 80% to 95% (Tsirbas et al., 2004). The high surgical success rate in partial NLDO was reported, ranging from 70% to 84% comparable to those with complete NLDO (Delaney et al., 2002).

Hence, accurate assessment of epiphora following NLDO is essential as these patients will benefit from surgical intervention regardless of partial or complete NLDO and ultimately be able to improve their quality of life. Therefore, this study aims to evaluate symptoms in epiphora patients with partial nasolacrimal duct obstruction using a validated questionnaire and to establish a reliable and non-invasive clinical assessment.

1.2 LACRIMAL SYMPTOM QUESTIONNAIRE (LAC-Q)

The lacrimal symptom questionnaire (Lac-Q) is a validated symptom-based questionnaire that was developed by Mistry et al. (2011). This questionnaire was developed based on social impact and lacrimal symptoms. It demonstrated validity, reliability, stability, and simplicity in assessing patient-reported outcomes following DCR surgery as reported by Mistry et al. (2011).

Table 1: Lacrimal Symptom Questionnaire (Lac-Q) by Mistry et al 2011.

Section 1	**Social impact score**	**Maximum score = 5**
	Friends or family have commented about the watery eye problem	1
	The watery eye problem has caused embarrassment in company	1
	The watery/sticky eye problem has interfered with everyday activity (such as reading, driving and etc)	1
	The vision is sometimes blurred because of the watery/sticky eye problem	1
	Medical attendance: visit to family doctor's surgery, or the hospital eye clinic because of tear duct problem	1
Section 2	**Lacrimal symptom score**	**Maximum score = 14 for each eye**
	Watery eye	

	• No watery eye problem • The eye waters occasionally, mainly outdoors • Troublesome watering of the eye, indoors and outdoors, some days • Troublesome watering of the eye most days • Troublesome watering of the eye every day	0 1 2 3 4
	Pain in or around the eye; soreness of eyelids • No pain • Some pain or soreness, but has not sought medical advice or treatment • Pain or soreness, has used prescription eye drops • Painful or swollen (lacrimal abscess) requiring antibiotics or surgical drainage	0 1 2 4
	Sticky eye • No problem with sticky eye • The eye is sometimes sticky in the mornings • The eye is sticky everyday in the mornings • The eye has sticky or mucous discharge throughout the day • There is infected discharge leaking through the skin of the lower eyelids (fistula)	0 1 2 3 4
	Swelling or lump at the medial canthus (mucocele) • No swelling or lump	0

	• Swelling present, but only intermittently • Swelling present all the time	1 2
	Total score (the sum of the social impact score and the lacrimal symptom score for each eye)	19

This questionnaire has its own advantages as it was developed specifically to assess lacrimal diseases. Moreover, it evaluated the patients both preoperatively and after the surgery, unlike other studies, which only evaluated the patients postoperatively (Bakri et al., 2000).

A study conducted using Lac-Q questionnaire confirmed the subjective improvement in symptoms and quality of life after punctoplasty surgery in epiphora patients. This study proposed to use Lac-Q questionnaire because it is a simple and useful tools to assess the quality of outcomes following lacrimal drainage surgery (Meduri et al., 2021).

1.3 FLUORESCEIN DYE DISAPPEARANCE TEST

The fluorescein dye disappearance test (FDDT) is a simple and non-invasive test used to evaluate the degree and severity of epiphora. It was first described by Zappia and Milder in 1972. It is a reliable and rapid method for assessing tear drainage and detecting lacrimal obstruction. However, it cannot differentiate lesser degrees of obstruction or functional insufficiency (Meyer et al., 1990).

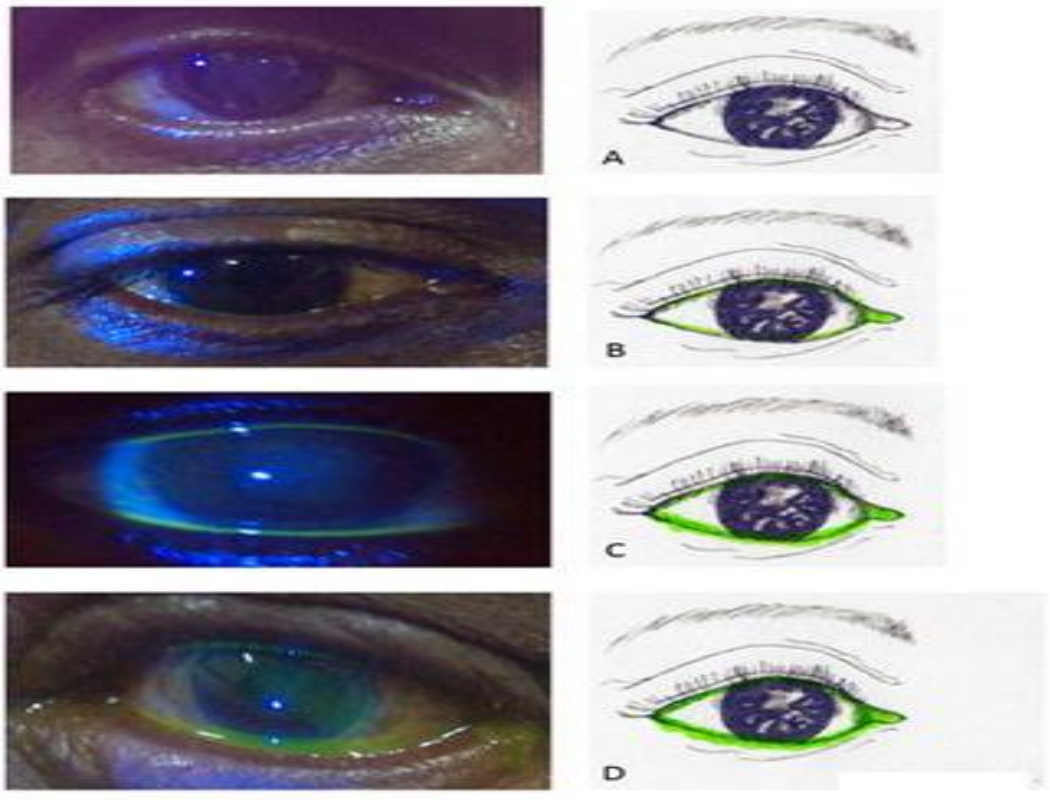
Another study showed FDDT is a rapid, simple, reproducible, and practical clinical test in diagnosis of lacrimal drainage system (Toprak et al., 2002). The reliability of this tests was reported in many studies. A study conducted by MacEwen and Young et al. (1991) showed a high sensitivity (82.3%) and specificity (85.2%) in confirming the presence of lacrimal drainage abnormality in infants. Other authors previously found a 92% sensitivity and 82.7% specificity for five minutes FDDT in lacrimal drainage system obstruction associated with topical antiglaucoma medications (Kashkouli et al., 2008).

The procedure is performed by instilling a drop of fluorescein into the lower fornix of the conjunctival sac. The amount of remaining stained tear meniscus is evaluated by cobalt blue light of a slit-lamp in five minutes. Results will be graded as per Zappia and Milder Classification as shown in Table 2 and Image 1 (Zappia and Milder et al., 1972).

Table 2: Zappia and Milder Grading of Fluorescein Dye Disappearance Test by Zappia and Milder et al 1972.

GRADE	DESCRIPTION	INTERPRETATION
Grade 0 (Image 1A)	No fluorescein remaining in the conjunctival sac	Negative (No obstruction)
Grade 1 (Image 1B)	Thin fluorescing marginal tear strip only	
Grade 2 (Image 1C)	Between Grade 2 and Grade 3	Positive (Obstruction present)
Grade 3 (Image 1D)	Brightly fluorescing tear strip	

Image 1: Zappia and Milder Grading of Fluorescein Dye Disappearance Test by Zappia and Milder et al. 1972



1.4 ENDOSCOPIC DYE TRANSIT TEST

An endoscopic dye transit test (EDTT) is a procedure that allows direct visualization of the fluorescein flows into the nasal cavity. This procedure is performed by instilling a drop fluorescein into the lower fornix of the conjunctival sac and the flow of fluorescein stained tears into the nasal cavity is observed using nasal endoscope.

A study carried out by Feijó et al. (2019) to determine the reliability of EDTT for the prediction of functional success after dacryocystorhinostomy showed endoscopic dye transit test ≤60 seconds is a reliable tool to predict functional success and good prognosis after external or laser transcanalicular dacryocystorhinostomy. They measured time taken from instillation of one drop fluorescein 2% into the conjunctiva to its free flow from the ostium site and functional success was defined as the resolution or improvement of epiphora using Munk scoring. Functional success (Munk score, 0-1) was assessed using a positive predictive test of EDTT. Results showed the positive predictive value of EDTT ≤60 seconds to predict functional success was 97.4%, thus demonstrating its reliability.

Another study was conducted to measure the fluorescein transit time (FTT) to evaluate the lacrimal drainage and lacrimal pump function after external DCR and laser transcanalicular DCR demonstrated FTT able determine the anatomical and functional success following DCR surgery (Feijó et al., 2018).

1.5 STUDY RATIONALE

To diagnose NLDO, an invasive syringing test is still the standard procedure. Our study aims to propose simple non-invasive methods to evaluate epiphora patients with partial nasolacrimal duct obstruction. The methods that we propose in our study are FDDT and EDTT and correlate the severity of the symptoms using Lac-Q questionnaire.

We believe that by providing local data that support the efficacy of these non-invasive methods in diagnosing partial NLDO, a more comprehensive clinical assessment can be made and patients do not need to undergo the unpleasant syringing procedure in the future.

In partial NLDO, the objective findings do not correlate well with symptomatology as most patients demonstrate full patency on syringing tests yet experienced bothersome watery eyes. Thus, if syringing test alone is used for the diagnosis of NLDO, probably a significant number of patients may be overlooked. Hence, more studies need to be conducted to assess other additional methods of assessing partial NLDO in order to demonstrate their benefits and significance in diagnosing such cases.

Perhaps, our study can be used as a future reference as there is a limited published study available in our country in evaluating epiphora patients with partial nasolacrimal duct obstruction.

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CHAPTER 2:

OBJECTIVES

2.1 General Objective

To evaluate the score of lacrimal symptom questionnaire (Lac-Q), fluorescein dye disappearance test and endoscopic dye transit test in epiphora patients with partial nasolacrimal duct obstruction.

2.2 Specific Objectives

2.2.1. To compare the mean score of lacrimal symptom questionnaire in epiphora patients with partial nasolacrimal duct obstruction and controls.

2.2.2. To compare the mean grading of fluorescein dye disappearance test in epiphora patients with partial nasolacrimal duct obstruction and controls.

2.2.3. To compare the mean time of endoscopic dye transit test in epiphora patients with partial nasolacrimal duct obstruction and controls.

2.2.4. To correlate the mean score of lacrimal symptom questionnaire with the mean grading of fluorescein dye disappearance test and the mean time of endoscopic dye transit test in epiphora patients with partial nasolacrimal duct obstruction.

CHAPTER 3:

MANUSCRIPT

Evaluation of the Score of Lacrimal Symptom Questionnaire (Lac-Q), Fluorescein Dye Disappearance Test and Endoscopic Dye Transit Test in Epiphora

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Abstract

Purpose

The aim of this study was to compare the mean score of lacrimal symptom and its social impact using Lacrimal Symptom Questionnaire (Lac-Q), the mean grading of Fluorescein Dye Disappearance Test (FDDT), and the mean time of Endoscopic Dye Transit Test (EDTT) in epiphora patients with partial nasolacrimal duct obstruction (NLDO) and in a control group and to evaluate its correlation.

Methods

The comparative cross-sectional hospital-based study included 52 adult patients with epiphora and 52 adult patients without epiphora as controls aged 18 years and above. All recruited patients underwent syringing test to evaluate the patency of the lacrimal drainage system. The severity of lacrimal symptom and its social impact was evaluated using a validated Lac-Q questionnaire. FDDT and EDTT were performed in all patients.

Results

There was a statistically significant difference between mean total Lac-Q score, mean FDDT grading, and mean EDTT time between epiphora patients with partial NLDO and control group ($p < 0.01$). There was a strong correlation demonstrated between mean total Lac-Q score with mean FDDT grading ($r = 0.728$, $p = < 0.01$), and mean EDTT time ($r = 0.820$, $p = < 0.01$) in epiphora patients with partial nasolacrimal duct obstruction.

Conclusions

There was statistically different in the mean score of lacrimal symptom questionnaire, the mean grading of FDDT and the mean time of EDTT in patients with partial NLDO compared to control group. There was strong correlation between FDDT and EDTT with the symptoms of lacrimal outflow obstruction in partial NLDO.

Key words: Epiphora, Lacrima symptom questionnaire (Lac-Q), fluorescein dye transit test (FDDT), endoscopic dye transit test (EDTT)

Introduction

Epiphora or excessive tearing is one of the most common complaints of patients visiting ophthalmology clinics. It can be due to hypersecretion of tears or a disorder of the lacrimal drainage system [1]. In a study by Mainville and Jordan et al., 48.7% of patients with tearing had a lacrimal system block, and 40% of patients had dry eye syndrome [2], while in a study by Sibley et al., 31.8% of subjects had nasolacrimal duct obstruction, which was followed by the development of dry eye syndrome with secondary reflex tearing in 29.2% of patients [3].

Nasolacrimal duct obstruction (NLDO), is defined as a blockage of the lacrimal drainage system and accounts for the majority of cases. It can be further classified into primary or secondary. Primary acquired nasolacrimal duct obstruction (PANDO) is defined as a condition of idiopathic inflammation and subsequent fibrosis eventually leading to either partial or complete NLDO [4]. On the other hand, secondary acquired nasolacrimal duct obstruction (SANDO) is the result of lacrimal malignancy, systemic inflammatory disease, infection, or trauma [5].

In the context of partial PANDO, it represents one important subgroup of patients with what some authors have called ‘functional’ epiphora, defined as the presence of a lacrimal drainage system freely patent to syringing with no or minimum reflux and no evidence of lid malposition or lacrimal hypersecretion [6]. Those with partial NLDO are difficult to diagnose as symptoms and clinical findings do not correlate well as reported by Cheung et al., [7]. According to Conway's survey, the most preferred clinical tests in evaluating

such cases are nasolacrimal irrigation, primary and secondary dye tests (Jones 1 and 2 tests), and fluorescein dye disappearance test (FDDT). Dacryocystography (DCG) or dacryoscintigraphy (DSG) imaging
may provide additional information for diagnosis and management [8].

Nonetheless, the clinical tests mentioned by previous authors utilized to diagnose patients with epiphora yet showed full patency on syringing were frequently non-comparable due to lack of standardization, and their correlation was uncertain [9-11]. Hence, this study provides prospective data to look at the utility of these clinical tests in relation to symptoms for the evaluation of partial NLDO. The aim of this study was to compare the mean severity of epiphora using lacrimal symptom questionnaire (Lac-Q), the mean grading of fluorescein dye disappearance test (FDDT), and the mean time of endoscopic dye transit test (EDTT) in epiphora patients with partial nasolacrimal duct obstruction (NLDO) and control group and to evaluate its correlation.

Materials and Methods

This was a cross-sectional study conducted in Ophthalmology Clinic, Hospital Universiti Sains Malaysia between June 2021 and December 2022. Adult patients aged 18 years old and above who presented with epiphora and patients without epiphora as controls were recruited. The study was conducted in accordance with the Declaration of Helsinki for Human Research and approved by the Human Research Ethics Committee of Universiti Sains Malaysia, Malaysia (USM/JEPeM/21110748). Written consent was obtained from the patients.

Adult patients aged 18 years old and above who presented with epiphora and patients without epiphora attending routine follow-ups at Ophthalmology Clinic, Hospital Universiti Sains Malaysia were prospectively enrolled in this study. The inclusion criteria for the study group were epiphora patients with partial NLDO aged 18 years old and above as demonstrated by full patency of lacrimal drainage system on syringing test. The exclusion criteria were patients with secondary causes (such as congenital, trauma, inflammatory, neoplastic, periocular, radiotherapy, and chemotherapy), eyelids malposition (such as ectropion and entropion), ocular surface disease (such as dry eyes) and demonstrated fully blocked of lacrimal drainage system on syringing test. Patients aged 18 years old and above who attended our clinic for some other problem and did not have epiphora were enrolled as controls.

All enrolled patients were examined in detail under slit lamp to exclude eyelids malposition and ocular surface disease. All patients underwent syringing test to look for the patency of lacrimal drainage system. Patients with epiphora were diagnosed with