Prevalence of dry eye diseases in a rural and urban population in West Bengal and the role of air pollution.

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I. Introduction

Dry eye represents a multifactorial, heterogeneous disorder of the preocular tear film, which results in ocular surface disease. The tear film and ocular surface form a complex and stable system that can lose its equilibrium through numerous disturbing factors. ^[1] Reduction in quality of life is inevitable when symptoms of dry eye occur. These symptoms range from mild transient irritation to persistent dryness, burning, itchiness, redness, pain, ocular fatigue and visual disturbance. In the United States alone, approximately 7–10 million Americans require artificial tear preparations, with consumers spending over \$100 million/year. ^[2]

Reported prevalence of dry eye is diverse, with questionnaire based surveys documenting rates ranging from 14.4% to 33% of the population sampled. ^[3,4,5] Studies which also involve tests of tear function including Schirmer's test, tear break up time, fluorescein staining, or rose bengal staining for determination of dry eye have found generally lower prevalence rates. ^[6,7]

Our study aims to study the prevalence of dry eye in a rural and urban population from West Bengal and analyse the role of air pollution as a causative agent of the same.

II. Materials and Methods

This research work is a population based cross sectional study and has two arms, the rural arm and the urban arm. The urban arm has a tertiary eye hospital in Kolkata as the clinical examination centre, whereas an eye care centre in Kuliapara village (P.O. Dhobapara, P.S. Balagarh) of Hooghly district is the rural examination centre.

Study area:

Rural: The rural study area consists of 13 Gram Panchayats in the Balagarh Block of the Chinsurah Sub Division of Hugli district in West Bengal.^[8] The total population of Balagarh sub district is 214,784 and this block has 46,022 households. 45,019 households having a population of 210,065 are classified as rural in the 2011 census.^[9] The patients from the rural study area were transported to our rural Examination Centre which is located in village Kuliapara of Hooghly district. Social workers and volunteers belonging to Kuliapara village distributed leaflets throughout Balagarh regarding the Eye Check Up camps and also helped in word of mouth publicity with active participation of corresponding panchayats.

Urban: Kolkata District under the Kolkata Metropolitan Area(KMA) in West Bengal is our urban study area. KMA is the largest urban agglomeration in eastern India, extends over 1851.41 sq. km. and envelopes three Municipal Corporations including Kolkata Municipal Corporation, Howrah Municipal Corporation and Chandannagore Municipal Corporation; and 38 Municipalities. ^[10] KMA has a population of 14,112,536, according to 2011 Census. ^[11]Kolkata District is bordered by Howrah District, North 24 Parganas District and has 11 Assembly Constituencies. ^[12] Kolkata District has a population of 4,572,876 and it has 929,586 households, all of whom are classified as urban in the 2011 Census. ^[13] Subjects residing in Kolkata District coming for ophthalmologic check up at the out patient department (OPD) of the tertiary eye hospital in Kolkata and fulfilling the laid down inclusion criteria were enrolled into the study.

Institutional Ethics Committee approval was obtained before conducting this cross sectional research work. The clinical examination and data collection lasted from July to December 2013. All patients were examined by an ophthalmologist. The dry eye questionnaire was administered by a social scientist. The examinations, in brief, were as follows :

(a) Ocular and medical history -- A detailed history pertaining to medical and ophthalmic problems was elicited. History elicited includes use of glasses and its duration, history of previous trauma or surgery or laser in the eyes, family history of glaucoma, history of ocular and oral medication, significant systemic illness with special reference to diabetes or hypertension, significant family history and addiction history.

(b) Refraction and recording of uncorrected and best-corrected visual acuity

(c) Torch light external ocular examination including ocular movements and any other obvious strabismus / eyelid pathology.

(d) Pupillary evaluation – Carried out in dim light conditions. The patient is asked to focus on a distant object and the strength and the direct and indirect reaction of each pupil noted. The presence or absence of an afferent pupillary defect is also checked for.

(e) Slit lamp biomicroscopy : The results recorded included condition of eye lid margins including meibomian gland status, conjunctival heyperemia, eversion of eye lids to check for hyperaemia/follicle/papillae. Telangiectasias at lid margin and/or plugging of lid orifices on slit lamp examination were the major determinants of presence of Meibomian Gland Dysfunction. Presences of filaments/strands were also looked for. (f) A single observer who is a social scientist administered the dry eye questionnaire. The pre-designed dry eye questionnaire was based on models suggested by Hikichi, ^[14] Toda, ^[15] and Rocheand et al ^[16] and consisted of yes/no responses to 13 symptoms, namely: ocular fatigue, non-sticky eye discharge, foreign body sensation, heavy sensation, discomfort, ocular pain, watering, temporary blurred vision (improved on blinking), itching, photophobia, redness and burning/stinging sensation. A response was defined as positive when the subject reported a symptom to occur sometimes, often or all the time and as negative when reported to occur rarely or never. After ascertaining the responses to each of the questions, the symptom score was calculated. Exposure to sunlight/high temperatures, excessive winds, air pollution, smoking and drugs was inquired for.

(g) Objective tests (under room temperature conditions with airconditioners switched off and/or fan speed minimised) comprised of Schirmer's test and tear film breakup time (TBUT). Schirmer's test is mainly used to assess the aqueous component of the pre corneal tear film. A Whatman filter paper no 41 with dimensions of 5mm by 35 mm is used. Without application of any topical anesthesia (Schirmer's I), the paper is placed at the junction of outer 1/3rd and middle 1/3rd of the lower lid. The amount of wetting after 5minutes is measured. TBUT gives us an idea about stability of the tear film. After staining the conjunctival film fluorescein, the patient is asked to blink and keep the eyes open. The time (in seconds) between the last blink and the first appearance of a dry spot is measured. Presence of strands/filaments was also looked for before and after the tests. In those already using tear substitutes, dry eye tests were performed after overnight discontinuation of medication.

For the present research work, subjects with active ocular infection, any corneal disease and opacities, history of ocular trauma, one eyed patients, subjects using computers for >6 hours/day and those with any histories of ocular surgery in either eye were excluded. Subjects were also excluded if they had a best corrected visual acuity <20/200, spherical refraction outside -5.0 diopters, cylinder correction outside 3.0 diopters, or a combination thereof, or any other ocular or systemic disease for which regular medications had to be taken.

All subjects over forty years or turning forty in the calendar year of examination and having none of the exclusion criteria were included for enumeration and analysis. Only those residing in the study areas for atleast the preceding five years were enumerated.

A symptom score of more than 3, Schirmer's test value ≤ 5 mm in 5 minutes on

Whatman's filter paper No. 41, TBUT value <10 seconds and presence of strands and/or filaments and/or Meibomian Gland disease in either/both eyes were taken as indicators of dry eye. If three or more of the above tests were positive, the subject was deemed to be suffering from dry eye.

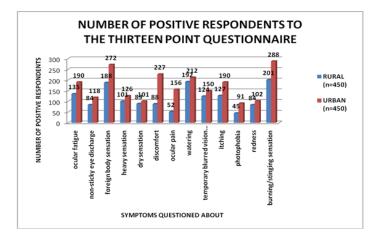
III. Results:

Four hundred and fifty subjects fulfilling the laid down inclusion criteria were included for analysis in each of the two arms, rural and urban. The average age of subjects examined in the rural group was 54 years (range 40 years to 75 years) and that in the urban group was also 54 years (Range 40 years to 76 years), with no statistically significant age difference in the two groups. In the rural group, 257 (57.11%) were males and in the urban group 234 (52%) were males.

Questions Asked	No. Of POSITIVE respondents in the RURAL Group (n=450)	No. Of POSITIVE respondents in the URBAN Group (n=450)
ocular fatigue	135 (30%)	190 (42.22%)
non-sticky eye discharge	84 (18.67%)	118 (26.22%)
foreign body sensation	188 (41.78%)	272 (60.44%)
heavy sensation	101 (22.44%)	126 (28%)
dry sensation	89 (19.78%)	101 (22.44%)
Discomfort	88 (19.56%)	227 (50.44%)
ocular pain	52 (11.56%)	156 (34.67%)
Watering	192 (42.67%)	212 (47.11%)
temporary blurred vision	124 (27.56%)	150 (33.33%)
Itching	127 (28.22%)	190 (42.22%)
Photophobia	45 (10%)	91 (20.22%)
redness	84 (18.67%)	102 (22.67%)
burning/stinging sensation	201 (44.67%)	288 (64%)

The following answers were obtained to the dry eye questionnaires:

The following figure (Figure 1) graphically depicts the positive responses in the two groups. Subjects with a positive response to three or more questions were 225 (50%) in the rural group and 299 (66.44%) in the urban group.



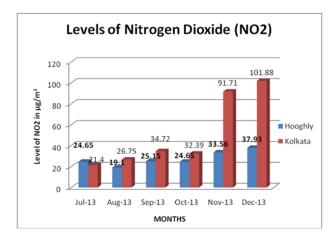
The following results were obtained on ophthalmological examination:

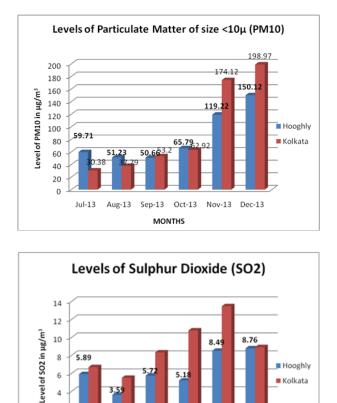
Parameter Tested	Positive in Either/Both eyes in RURAL	Positive in Either/Both eyes in	
	group (n=450)	URBAN group (n=450)	
Schirmer's Test value <5mm after	161 (35.78%)	232 (51.56%)	
5mins			
TBUT <10seconds	182 (40.44%)	267 (59.33%)	
Presence of Filaments/Meibomian	74 (16.44%)	129 (28.67%)	
Gland Dysfunction			

As per our operational definition, subjects with three or more of the following positive criteria were deemed to have dry eye :

- a) Three or more positive responses to the thirteen point dry eye questionnaire
- b) Schirmer's I test value of <5mm after 5minutes in either or both eyes
- c) Tear film Break Up Time (TBUT) <10seconds in either or both eyes
- d) Presence of filaments or Meibomian Gland Dysfunction in either or both eyes.

By the above criteria, 180 subjects (40%) had dry eye disorder in the Rural Group (122 males:58 females) whereas 247 subjects (54.89%) had dry eye disorder in the Urban Group (135 males:112 females). As a second aspect of our research work, the air pollution levels in the districts of Kolkata and Hooghly were collected from the official website of West Bengal Pollution Control Board ^[17]. The three parameters considered were the levels of Nitrogen Dioxide(NO2) in μ g/m³, levels of particulate matter in air with a size of less than 10 microns (PM10) and the level of Sulphur Dioxide (SO2) in the air. According to the website, the air quality stations are operated manually, twice every week, as per directions of the Central Pollution Control Board. The following average daily values were obtained for the period July 2013 to December 2013 :







Sep-13 MONTHS

Oct-13 Nov-13 Dec-13

Kolkata

Dry eye, or keratoconjunctivitis sicca (KCS), is a distressing problem for both subjects and treating ophthalmologists. The actual prevalence of this condition in the community is unknown because patients present for assessment and treatment when the condition is moderate to severe and the symptoms have become intolerable. Even at this stage, the diagnosis may not be made if the ophthalmologist does not perform the diagnostic tests required to detect dry eye. The condition of dry eye is therefore often overlooked and hence underdiagnosed in the population. Available prevalence data have originated from clinics or hospitals and thus comprise a select group of patients who are not representative of the population in general.^[18]

A population based study(subjects aged 40 years or more) in Melbourne, Australia, pulished in 1998 found the prevalence of dry eye as follows: 10.8% by rose bengal, 16.3% by Schirmer's test, 8.6% by tear film breakup time, 1.5% by fluorescein staining, 7.4% with two or more signs, and 5.5% with any severe symptom not attributed to hay fever. Women were more likely to report severe symptoms of dry eye.^[19]

In a population based study from Indonesia, a validated six item questionnaire of ocular symptoms relating to dry eye was used which included the following questions (1) Do your eyes ever feel dry? (2) Do you ever feel a gritty or sandy sensation in your eye? (3) Do your eyes ever have a burning sensation? (4) Are your eyes ever red? (5) Do you notice much crusting on your lashes? and (6) Do your eyes ever get stuck shut? The study found the prevalence of one or more of the six dry eye symptoms often or all the time adjusted for age was 27.5% (95% confidence interval (CI) 24.8 to 30.2).[20]

Dry-eye symptoms were very common in a population based sample of Chinese ≥65 years of age in Taiwan. Of 1361 participants, 459 (33.7%) reported having 1 or more dry eye symptoms often or all the time, and 96% of them (441/459) had at least 1 positive sign, including tear film breakup time <10 seconds, positive fluorescein stains of the cornea,

Schirmer score of <5 mm, or abnormal anatomic features of meibomian glands. ^[21]

6

4 2 0

Jul-13

Aug-13

The only prominent past population based dry eye study from India examined 500 patients aged above 20 years presenting to a tertiary eye care centre with various ocular problems. This study, pulished in 2004, found that 18.4% patients had dry eye $^{[22]}$. However, the prevalence was 16.2% in 41-50 years age group and increased to 36.1% in those aged more than 70 years.

Our study design is unique in that it compares dry eye prevalence in a rural and urban population from West Bengal and 450 subjects have been analysed in each of the two arms. In our study, 68% of those with dry eye in the rural population are males, whereas 55% of those with dry eye in the urban population are males. The much higher percentage of males can be attributed to the fact that majority of the males (73%) with dry eye in the rural group are farmers, who spend long hours in the sun. 86% of the females with dry eye in the rural group were post menopausal as compared to 54% in the urban group, which can be possibly attributed to poor knowledge and usage of hormone replacement therapy in the rural group.

Our study, which included those above 40 years, has a dry eye prevalence (by study criteria) of 40% in the rural group and 55% in the urban group. The prevalence of dry eye is much higher compared to the other studies probably due to our criteria used to define dry eyes. Another very important fact is that all the previously mentioned studies were held in the early part of the twenty first century. Since then, the level of air pollution has increased by leaps and bounds, and so has global warming, leading to the higher prevalence in both the rural and urban groups. Infact in the questionnaire, burning/stinging sensation in one/both eyes was seen in 45% respondents in the rural group and 64% in the urban group, which substantiates the effect of air pollution on dry eye disorders.

When the various parameters were compared between the two groups using t Test, a p value of 0.009 was obtained, which proves that there is a statistically significant higher prevalence of dry eye in the urban group as compared to the rural group. This wide rural urban difference can definitely be attributed to the higher level of air pollution in our urban study area. The six month (July 2013 to December 2013) average values of NO2, PM10 and SO2 in Kolkata (our urban study area) is 51.48, 92.9 and 8.92 while the corresponding values in Hooghly District (rural study area) are 27.51 (p=0.1 compared to Kolkata), 82.79(p=0.5) and 6.27 (p=0.03; statistically significant).

The main effect of breathing in raised levels of nitrogen dioxide is the increased likelihood of respiratory problems. Nitrogen dioxide inflames the lining of the lungs, and it can reduce immunity to lung infections. This can cause problems such as wheezing, coughing, colds, flu and bronchitis. Similar effects are seen on ocular surface as well. The effects of inhaling particulate matter that have been widely studied in humans and animals now include asthma, lung cancer, cardiovascular issues, respiratory diseases, ocular surface disorders, birth defects, and premature death. The size of the particle is a main determinant of where in the respiratory tract the particle will come to rest when inhaled. Because of their small size, particles on the order of ~10 micrometers or less (PM10) can penetrate the deepest part of the lungs such as the bronchioles or alveoli. ^[23] Larger particles are generally filtered in the nose and throat via cilia and mucus, but particulate matter smaller than about 10 micrometers, can settle in the bronchi and lungs and cause health problems. Similarly, particles smaller than 2.5 micrometers, PM2.5, tend to penetrate into the gas exchange regions of the lung, and very small particles (< 100 nanometers) may pass through the lungs to affect other organs. Coarse particulate matter (PM) has an aerodynamic diameter of 2.5 to 10µ and is derived from abraded soil, road dust or aggregation of smaller combustion particles. Sulfur dioxide (SO2) is a gas primarily emitted from fossil fuel combustion at power plants and other industrial facilities, as well as fuel combustion in mobile sources such as locomotives, ships, and other equipment. Current scientific evidence links SO2 exposure with adverse impacts on the respiratory system and other body systems by triggering various allergic reactions. SO2 also reacts with other chemicals in the air to form tiny sulfate particles, contributing to levels of PM 2.5. SO2 also reacts with other chemicals in the air to form acids, which fall to the earth as acid rain. Acid rain damages forests and crops, changes the makeup of soil, and makes lakes and streams acidic and unsuitable for fish ^[24]. Overall these and other environmental pollutants have been demonstrated to augment histamine release from allergen activated mast cells and thereby to aggravate clinical symptoms of red eyes, watering and irritation of eyes, and various respiratory ailments in humans.

Dry eye is now defined as "a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface." ^[25] Ocular surface inflammation plays a key role in the pathogenesis and symptomatology of both dry eye disease and allergic conjunctivitis. Depending on the geographic area, the signs and symptoms of allergic conjunctivitis often overlap with those of aqueous deficient dry eye and MGD. The lack of an adequate tear film and the presence of ocular surface inflammation aggravate the irritation caused by allergens and mast cell products such as histamine. The tear film serves as a barrier to allergens and dilutes them, as well as washes away inflammatory mediators. If eyes are dry, more allergens reach the conjunctiva and mast cells. In addition, inflammatory mediators have an increased residence time and enhanced concentration in the tear film. ^[26]

Dr Anat Galor et al in a 2013 study found that environmental factors play an important role in dry eye diseases. Among these, air pollution and atmospheric pressure emerged as the most influential predictors. The study further states that veterans especially in Chicago and New York City were 3 to 4 times more likely to be diagnosed with dry eye diseases compared with less urban areas such as Ukiah, California.^[27] Versura et al also

concluded that ocular surface subclinical inflammation and ocular dryness are related to high concentrations of atmospheric polluters, in both sexes.^[28]

Our study also similarly demonstrates the detrimental effect of air pollution on dry eye disease. Ophthalmologists and general physicians need to be aware of this association between environmental conditions and dry eye disease and elicit an environmental history when assessing patients with dry eyes. Topical lubricants and topical anti inflammatory agents are generally used by ophthalmologists for the treatment of dry eye. Our study emphasises that environmental manipulations, such as increasing local humidity and decreasing exposure to air pollution, should be considered as part of the overall management of patients with dry eyes. Infact a close liaison between ophthalmologists and environmental social scientists are necessary to draw up an action plan to address this burning issue. A population based study of this magnitude will also raise the awareness of the general population, which is probably the most important step towards containing this serious ocular health problem.

Acknowledgement

The West Bengal University of Health Sciences, Kolkata 64.

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