Quantification of Ocular Ultraviolet-B Radiation Exposure in a South Indian Population and its Association with Ocular Surface Disorders, Pseudoexfoliation, Cataract and Age-related Macular Degeneration - A Part of the Chennai Eye Disease Incidence Study

THESIS

Submitted in partial fulfilment

of the requirements for the degree of

DOCTOR OF PHILOSOPHY

by

RASHIMA A

ID. No. 2009PHXF701H

Under the supervision of

Dr Ronnie Jacob George

&

Under the co-supervision of

Prof. Suman Kapur

BITS Pilani

Pilani | Dubai | Goa | Hyderabad

BIRLA INSTITUTE OF TECHNOLOGY AND SCIENCE, PILANI

2016

BIRLA INSTITUTE OF TECHNOLOGY AND SCIENCE, PILANI

CERTIFICATE

This is to certify that the thesis entitled "**Quantification of Ocular Ultraviolet-B Radiation Exposure in a South Indian Population and its Association with Ocular Surface Disorders, Pseudoexfoliation, Cataract and Age-related Macular Degeneration - A Part of the Chennai Eye Disease Incidence Study**" submitted by Rashima A, ID No 2009PHXF701H for award of Ph.D. of the Institute embodies original work done by her under my supervision.

Signature of the Supervisor

Name in capital letters
Dr RONNIE JACOB GEORGE

Designation
Director Research, Vision Research Foundation,
Senior Consultant, Glaucoma Services, Sankara Nethralaya

Place: Chennai
Date: 16.06.2017

Signature of the Co-supervisor

Name in capital letters
Prof. SUMAN KAPUR

Designation
Senior Professor and Dean (University-wide) Head - Department of Biological Sciences, Birla Institute of Technology and Science Pilani, Hyderabad Campus
Smt Sarla Birla and Sh. B. K. Birla Chair Professor

Place: Hyderabad
Date: 15.06.2017

I dedicate this thesis to my parents and gurus, who taught me to think, understand and express. Without their constant motivation and inspiration, I would not been able to pass through the tiring process of research

I dedicate this in memory of my beloved Father

ACKNOWLEDGEMENTS

Immeasurable appreciation and deepest gratitude for the help and support extended to the following persons who in one way or another have contributed in making this thesis possible.

I thank **Dr. S. S. Badrinath**, Chairman Emeritus, **Dr. T. S. Surendran**, Vice-Chairman, Sankara Nethralaya, Chennai, for giving me the opportunity to do this study in this premier institution. My sincere thanks to **Dr. Meenakshi S**, Director, Academics.

I thank **Birla Institute of Technology and Science, Pilani** for continuous support throughout the programme.

My deep sense of gratitude to **Dr Ronnie Jacob George**, my supervisor who was with me at every point in my work; His timely advice and scientific approach with a pleasant smile have helped me to accomplish this task. My sincere thanks for his constant care and motivation through my difficult times.

My sincere gratitude to **Dr. L Vijaya**, Principal Investigator – The Chennai Glaucoma Study, who supported me to perform this research work. Her timely suggestions with kindness and dynamism have enabled me to complete this thesis.

I would like to express my sincere gratitude to **Dr. R. Krishna Kumar**, Principal, Elite School of Optometry and to other optometry department colleagues for their support

My special thanks to the inspirational lady, **Dr Suman Kapur**, Senior Professor and Dean (University-wide) Head - Department of Biological sciences, BITS-Hyderabad campus who had supported me in all small steps in the research works.

I thank the **Research and Consultancy team at BITS** who have helped in processing all the events and answering the queries promptly.

I acknowledge The **Chennai Willingdon Corporate Foundation** for funding the project.

My colleagues **Mr Ramesh S Ve**, and **Ms Lokapavani V** who were supportive in clinical data collection.

Special thanks to all the social workers of the Chennai Glaucoma Study, **Mr Madan Raj, Mr Augustian J, Mr Siva Kumar**, who toiled along with me in the hot sun during data collection and field work. Without them, this study would just be a dream.

I thank the Consultants and the Team members of the Chennai Glaucoma Project, especially **Dr Manish Panday** for his valuable inputs for the manuscripts and their support throughout the project.

Professor Alfio Parisi, University of Southern Queensland, for the discussions about UV radiation measurements. His detailed and critical comments have been of great help during the research. **Dr Catherine A McCarty**, University of Melbourne, for her valuable suggestions in data collection and analysis.

Dr Ronald van der A, Climate Observations, KNMI (Royal Netherlands Meteorological Institute), The Netherlands who tirelessly answered my queries on UV data collection from TEMIS.

I thank my mentors, **Professor Seshasayee** and **Dr Sudharshanam** who instilled the essence of biostatistics. **Mr Shankar Malhari** for his valuable inputs on manuscripts and thesis technical writing.

My sincere pranams to **Dr PP Santanam**, Guru of Occupational optometry for his motivation and **Dr Sumathi Narayanan** for her constant support.

I thank **Dr PR Deepa** and **Ms Bharathi**, Faculty BITS for their continuous support during the research phase. A special note to my collegues **Ms Anuradha** and **Ms Kalpa**, Faculty- ESO, **Ms Uma Paramesh** - Administrator ESO, **Ms Jayasri** – Librarian ESO, **Ms Indhushree,** Faculty - The SN Academy for their constant encouragement throughout the phase of thesis writing.

I thank my sweet students and colleagues **Ms Deepmala, Ms Rekha, Mr Vasanth, Mr Ashim, Ms Najiya** and **Ms Barsha** for their cooperation and moral support for carrying out this work and filled my absence in my routine clinical work.

I thank all my **subjects** for who welcomed me with the smile during home visits in data collection and supported my work. Without their support this work has no relevance.

I thank my beloved **mother**, loving **brother** and **parents in law** who motivated and supported me in all aspects to do this work. I dedicate this work to my beloved **father** who would have been the happiest person to see my work in optometry fraternity.

My goal of doctorate would never been accomplished without the support of my loving **husband** and cute little **son**, who understands all the pain in the stressful periods and support in every step of this new path.

And above all the **Almighty**, who gave me strength and showered his blessings on me to complete this important phase of my career.

- Rashima Asokan

ABSTRACT

Title: Quantification of Ocular Ultraviolet-B Radiation Exposure in a South Indian Population and its Association with Ocular Surface Disorders, Pseudoexfoliation, Cataract and Age-related Macular Degeneration - A Part of the Chennai Eye Disease Incidence Study

Aim and Objectives: 1.To determine the relationship between lifetime ocular ultraviolet radiation exposure and ocular disease. 2. To measure the differences in UV exposure among the urban and rural south Indian population and its impact on ocular diseases.

Methodology:

The Chennai Glaucoma study (CGS) was a population-based study which was followed by the Chennai eye disease incidence study (CEDIS). Participants of both studies were included in the current study. A detailed ocular examination, including lens opacity classification and dilated fundus photography, was done for all subjects. The standardized questionnaire on lifetime migration (place of residence) was administered by a single person. The collected information from the personal UV exposure estimation questionnaire and the UV dose for the respective location calculated based on geographic location details from tropospheric emission monitoring internet service were fitted in the Melbourne visual impairment model. The relationship between lifetime ocular UV exposures and the prevalence and rate of progression of ocular pathology were analysed.

Results:

There were 2091 subjects included in the study (1080 rural and 1011 urban subjects). There were significant differences in the proportion of males and females in the current study. We found a significant difference of median lifetime ocular UV exposure levels among the rural (3.35, IQR: 1.98) and urban population (0.33, IQR: 0.11) (p value, <0.001) and also among rural males 3.56, IQR (2.24) and females 3.21 (IQR 1.88) (p value, <0.001) and among urban males 0.35 IQR (1.61) and females IQR 0.31 (0.08) (p value <0.001). We also found that the proportion of subjects in the higher quintiles of UV exposure was more among the rural population compared to the urban. Our

study showed that urban females are exposed to lower levels of UV exposure when compared with rural females.

The prevalence of pterygium, pinguecula and spheroidal degeneration were 6.7% (95% CI: 5.6 to 7.8), 10.8% (95% CI: 9.4 to 12.1) and 6.7% (95% CI: 5.6 to 7.8) respectively. The prevalence of pseudoexfoliation and age related macular degeneration were 2.7% (95% CI: 2.0 to 3.4) and 4.2% (95% CI: 3.3 to 5.0) respectively. The prevalence of nuclear cataract, cortical cataract and posterior sub-capsular cataract were 26.7% (95% CI: 24.8 to 28.6), 24.2% (95% CI: 22.3 to 25.9) and 19.5% (95% CI: 17.8 to 21.2) respectively. The risk factors for pterygium and pinguecula were rural residence, smokeless tobacco use and increased lifetime ocular UV exposure. Illiterate individuals were at higher risk of pinguecula and spheroidal degeneration. The other risk factors for spheroidal degeneration were increasing age, rural residence, smokeless tobacco use, non-use of spectacles, presence of diabetes mellitus and increased lifetime ocular UV exposure. The risk factors for pseudoexfoliation were increasing age, illiteracy, increased lifetime ocular UV exposure and presence of nuclear cataract. The current study reported increasing age, female gender, rural residence and higher lifetime ocular UV exposure to be associated with risk for the development and progression of any type of cataract. Other than these factors, use of smokeless tobacco, illiteracy, non-use of spectacles, low BMI (lean) were at higher risk for nuclear and posterior sub-capsular cataract development but not with cortical cataract.

Increasing lifetime ocular UV exposure was found to be associated with greater risk of nuclear cataract OR: 1.3 (95% CI: 1.2 to 1.4), cortical cataract OR: 1.1 (95% CI: 1.0 to 1.2) and for posterior sub-capsular cataract 1.2 (95% CI: 1.2 to 1.3). There was no association with macular degeneration. The risk for developing pinguecula, pterygium and spheroidal degeneration showed an increase from 4th highest quintile of lifetime ocular UV exposure. For other disease such as cataracts (nuclear, cortical and posterior sub-capsular cataract) and pseudoexfoliation it increased from 5th quintile of UV exposure levels.

Conclusion:

Lifetime ocular UV exposure significantly differed in this rural and urban population. Increasing lifetime ocular UV exposure was associated with development of pterygium,

pinguecula, spheroidal degeneration, pseudoexfoliation, nuclear and posterior sub-capsular cataract. No association was noted with macular degeneration. Protection from ocular UV exposure could delay the development of these ageing disorders.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ARMD	Age-related Macular Degeneration
BMI	Body Mass Index
CC	Cortical Cataract
CEDIS	The Chennai Eye Disease Incidence Study
CGS	The Chennai Glaucoma Study
CI	Confidence Interval
CIE	Commission Internationale de l'Éclairage
EUREYE	European Eye Study
EUVD	Erythemal Ultraviolet Dose
HDF	Hierarchical Data Format
IQR	Inter Quartile Range
ISCCP	International Satellite Cloud Climatology Project
LOCS	Lens Opacification Classification System
NS	Nuclear Sclerosis
OR	Odds Ratio
PEX	Pseudoexfoliation
POLA	Pathologies Oculaires Liées à l'Age
PSC	Posterior Sub-capsular Cataract
RPE	Retinal Pigment Epithelium
SPSS	Statistical Package for the Social Sciences
SZA	Solar Zenith Angle
TEMIS	Tropospheric Emission Monitoring Internet System
TOC	Total ozone column
UV	Ultraviolet
UVR	Ultraviolet Radiation
WHO	World Health Organisation

FLOW OF THESIS

The thesis is structured as chapters. The initial chapters are on introducing to the subject with evidence from review of literature. Next it deals on the aim and objectives of the study. Methodology used in the study is described in detail. Thus the chapters 1 to 4 have common information about the study. The results and its relevant discussion are separated as chapters which are shown in the section on organisation of thesis.

Chapter 1

INTRODUCTION
AND
REVIEW OF LITERATURE

1.1 UV Radiation and Ocular Health:

Global atmospheric changes such as depletion of ozone increase the level of ultraviolet radiation (UVR) reaching earth. This can have adverse effects on human health including eye disorders (Lucas et al. 2015). The acute effects of UVR on eye were reported to be photokeratitis, photoconjunctivitis and the long term effects pterygium, pinguecula, pseudoexfoliation, cataract, squamous cell carcinoma, and macular degeneration (Taylor 1989).

Pterygium is one of the most common ocular surface conditions highly prevalent in the equatorial region (commonly known as pterygium belt region(Cameron ME 1965)); this could be because of the high exposure to UVR in those regions (Wong et al. 2001). It is a basophilic degeneration of the subepithelial stroma in the bulbar region of the conjunctiva. It not only affects the cosmesis of the patient, but is also responsible for refractive astigmatism, and can potentially be a blinding disease in its advanced stage due to invasion of the visual axis which may require surgery for visual rehabilitation. The prevalence rate varies from 0.7 to 31% in different geographical regions (C A McCarty et al. 2000; Panchapakesan et al. 1998; Saw & Tan 1999; Wu et al. 1999; Hussain et al. 2004; Wong et al. 2001; Asokan et al. 2012; Nangia et al. 2013). A recent review on the prevalence of pterygium from 20 studies has reported the pooled prevalence rate of pterygium to be 10.2% (95% CI 6.3 to 16.1) in the overall population (Liu et al. 2013). Pinguecula, which is a yellowish growth on the corneal limbus, could be a triggering factor for occurrence of pterygium. The prevalence of pinguecula is more than 40% in people above 40 years of age (Panchapakesan et al. 1998; Viso et al. 2011) in the Blue Mountains Eye Study and in Spain. The reported prevalence was lower in India when compared to western

countries; in South India the reported prevalence was 11.3% (Asokan et al. 2012) and it was 24.4 per thousand elderly in North India (Singh et al. 1997). Spheroidal degeneration is defined as small grey deposits/ droplets beneath the corneal epithelium (Johnson 1981). The prevalence of spheroidal degeneration in South African natives is reported to be 7% (Bartholomew 1977). The increased association with UV radiation is explained well in the study of people residing near coastal regions (Johnson 1981). Studies reported an association of these ocular surface disorders with UV exposure (Threlfall & English 1999; Sekelj et al. 2007; Coroneo 1993; Pham et al. 2005; Newkirk et al. 2007). However, there is a lack of information about these associations in India.

Pseudoexfoliation is a disorder of extracellular matrix which results in the deposition of membrane like materials in the intraocular and extraocular tissues. The prevalence of Pseudoexfoliation in the Indian population ranged from 1.49% to 5.98 % (Krishnadas R, Nirmalan PK 2003; H Arvind et al. 2003; Thomas et al. 2005; Jonas et al. 2013). Stein JD et al have shown an association between sunshine and pseudoexfoliation (Stein et al. 2011). In the Andhra Pradesh Eye Disease Incidence study, those who were engaged in outdoor work were at higher risk for pseudoexfoliation (Thomas et al. 2005). The association of pseudoexfoliation with exposure to UV radiation is reported from a few studies abroad but none from India to the best of our knowledge (Pasquale et al. 2014; Kang et al. 2012).

Cataract is the leading cause for blindness. The WHO estimates showed an increase in cataract blindness from 63 million in 1971 to 125 million in

1995 and predicted that it would increase to 200 million by the year 2011 (Limburg et al. 1996). They estimated that 20% of cataract blindness may be due to sun exposure (WHO 2002). The Chennai Glaucoma Study reported that the prevalence of bilateral blindness in a rural South Indian population was 3.6% of which cataract was responsible for 78.6 % (Vijaya et al. 2006). The incidence of visually significant cataract was first reported from the Chennai Eye Disease Incidence Study as 6.36%, 95% C.I. 5.40 to 7.32 in South India (Panday et al. 2015).

Age-related macular degeneration is associated with increased prevalence among the elderly. Various studies have documented its prevalence from 1.2% to 29.3%. Population based studies have reported its prevalence as 1.7% in US, Beaver Dam eye study (Klein et al. 1992), 1.4% in Australia, Blue Mountains eye study (Mitchell et al. 1995) and 1.2% in Netherlands, Rotterdam study (Vingerling et al. 1995). The prevalence in India is documented to be 1.1% in South India and 4.7% in North India (Krishnan et al. 2010). Studies have shown its association with UV radiation exposure (Khan et al. 2006; Taylor et al. 1990; Pham et al. 2009; Fletcher et al. 2008). There is little available evidence of its association in Indian population.

Timely referral and treatment for those at higher risk of eye disease due to UV exposure will help to reduce the burden of blindness.

1.2 Review of literature:

1.2.1 Ultraviolet radiation:

Ultraviolet radiation (UVR) is divided by wavelength into UVA 400 – 315 nm, UVB 315 – 280 nm and UVC <280 nm. Almost all UVC and substantial amount of UVB is prevented from reaching earth's surface by the ozone layer. Thus the eye is exposed to UVR between 290 nm and 400 nm. The cornea absorbs UV of <300 nm but transmits about 60% of radiation at 320 nm and 80% at 380 nm. The aqueous humour transmits most of the incident UVR. The strongest absorption of UV radiation by the crystalline lens is noted in the 340 nm – 360 nm ranges and is seen to be reduced in the 310 nm – 320 nm ranges. Shorter wavelengths are more damaging than the long ones as higher energy photons are more damaging to the retina. High energy visible and ultraviolet photons produce damage by photochemical mechanism (Taylor 1989).

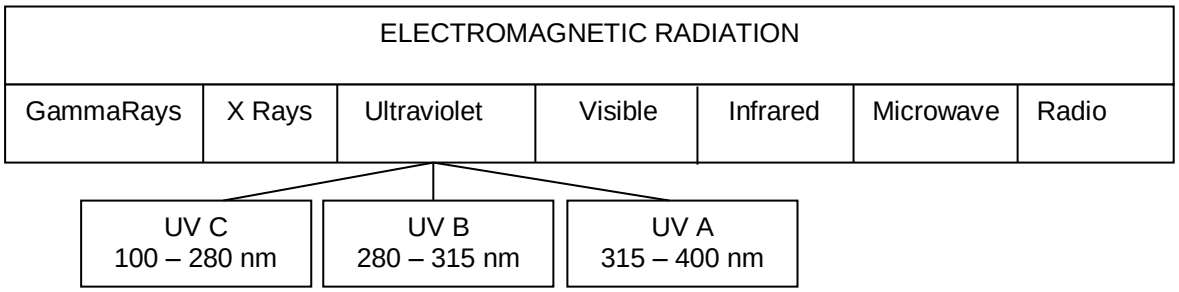


Figure 1.2.1.1: Description on the electromagnetic radiation

Transmission of UV radiation in the eye:

These UV radiations can reach the human eye and can be transmitted to the retina via the ocular media. The transmission property in the ocular media is given in figure 1.2.1.2.

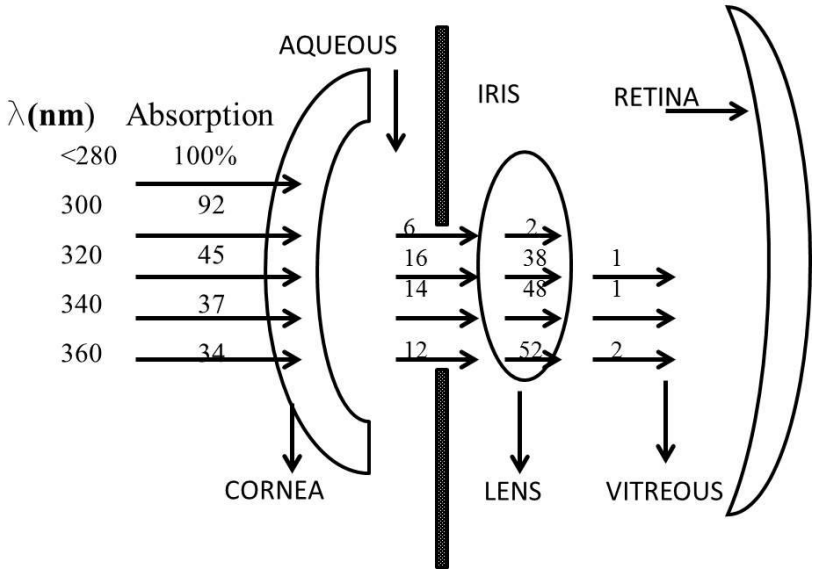


Figure 1.2.1.2: Schematic representation of transmission of UV radiation in eye

Protective mechanisms of the eye against UV radiation:

The human eye does not have inherent protective mechanisms against radiations. The major natural ocular defense mechanisms are the recessed location of the eye in the orbit and partial closing of the eyelids in response to high visible light levels. These are only partially effective and long term incident UVR absorbed may cause degenerative effects. Incident UVR can be lowered by covering, filtering, and shading. In particular, sunglasses and headwear that shade the eyes from direct visible and UVR insolation do not generally provide complete protection from scattered and temporally incident light. This shows that the human

eye is under risk of damage due to UV radiation which passes the ocular media. Thus it is important to measure the long term UV radiation exposure to quantify its adverse effects.

1.2.2. Methods of measurement of UV radiation:

The measurement of ultraviolet radiation (UVR) on humans is a complex task. It is not practical to place large measuring devices all over a human. But lifetime ocular UV exposure assessment is very important to calculate the adverse effects of UV radiation on eye. There are many ways to assess UV radiation on humans.

Questionnaire based assessment:

This helps to get cumulative lifetime ocular UV exposure. Studies have shown good correlation with questionnaire estimation in relation to activity-based questionnaire when compared to time-based questionnaire. Thus knowing the activity is an important cue for the subject to recollect and provide information about their sun exposure activity (McCarty et al. 1996).

Dosimeters:

Dosimeters are small, light-integrating UV detectors. They contain materials that undergo photo-degradation and a resulting change in optical absorbance when exposed to UV radiation (Diffey et al. 1977; Turnbull & Parisi 2010). Spectrophotometers are employed to quantify the degree of degradation, by measurement of the change in optical absorbance (ΔA) at a specific wavelength. Some of the dosimeters are

made from polysulphone, allyl diglycol carbonate (CR-39), nalidixic acid and polyphenylene oxide (Turnbull & Parisi 2010).

Polysulphone dosimeters:

Polysulphone has been used in many of the researches on UV exposure studies. The effectiveness of use of cotton clothing, tree shade, hats and the timing of outdoor activities has been investigated with polysulphone dosimeters. These dosimeters have also been employed in the form of polysulphone fabricated into contact lenses in the measurement of biologically damaging UV exposures to the surface of the eye. Exposure of the film to UV wavelengths up to approximately 340 nm causes a change in the optical absorbance (ΔA) of the film (Lester et al. 2003; Parisi et al. 2004).

It is not possible to measure the UV exposure for lifetime using these dosimeters. It can only be used to estimate for a day or on hourly basis. Due to the limitations such as erroneous results with thickness variations, irregularities on surface and pre-exposure, it limits the usage in large epidemiological studies.

Meteorological station information:

Ground-based measurements of the UV Index and simultaneously measured total ozone column (TOC) values have resulted in a specification of the UVI as function of TOC and Solar Zenith Angle (SZA), both at local solar noon. The TOC at local solar noon is determined from satellite observations in combination with data assimilation which uses meteorological fields (wind, temperature,

pressure) to obtain a global ozone field at local solar noon. The SZA at local solar noon depends on the latitude and the day of the year (Parisi et al. 2001; Wong et al. 1995).

These measurements of UV index with its archival data would provide valuable information and can help in estimating the lifetime personal exposure from the questionnaire based assessment for epidemiological studies (Asokan et al. 2016).

1.2.3 Studies on UV radiation and ocular disorders:

1.2.3.1 Ocular Surface Disorders:

McCarty et al found that the lifetime ocular sun exposure was an independent risk factor for pterygium (OR: 1.63, 95% CI: 1.18 to 2.25) and the attributable risk of sunlight and pterygium was estimated to be 43.6% (95% CI: 42.7 to 44.6) (C A McCarty et al. 2000). They also found that rural residence is a risk factor for pterygium (OR: 5.28, 95% CI: 3.56 to 7.84). The Blue Mountains eye study found that pterygium was significantly associated (OR: 3.3, 95% CI: 1.1 to 10.3) with the incidence of late ARMD (Panchapakesan et al. 1998). Studies have reported the association of these ocular surface disorders with UV exposure (Threlfall & English 1999; Sekelj et al. 2007; Coroneo 1993; Pham et al. 2005; Newkirk et al. 2007).

1.2.3.2 Pseudoexfoliation:

Pseudoexfoliation (PEX) syndrome is a generalized disorder of the extracellular matrix characterized by the production of abnormal

basement membrane-like material. The material gets deposited in several intraocular and extra ocular tissues. In the eye, material gets deposited at the pupillary margin, angle, anterior lens capsule, zonules and the anterior vitreous. On the anterior capsule it has a characteristic distribution of a central disc surrounded by a clear zone, followed by a peripheral ring-like deposit of the material (Naumann et al. 1998). The prevalence of PEX has been reported from different populations (Viso et al. 2010; Arnarsson et al. 2007; Anastasopoulos et al. 2011; You et al. 2013; Allingham et al. 2001; Forsman et al. 2007) and is known to be high in Scandinavian countries and Greece (Forsman et al. 2007; Anastasopoulos et al. 2011; Allingham et al. 2001). Cross sectional population based studies have reported the prevalence of PEX in the Indian population and it varied from 2% to 6% in subjects aged 40 years and older (H Arvind et al. 2003; Thomas et al. 2005; Krishnadas R, Nirmalan PK 2003).

1.2.3.3 Cataract:

There are studies which document the ultraviolet radiation to evaluate the relationship between cataract and UV B radiation. They differed in their way of evaluating the risk. Geographical correlation study measures exposure based solely on the place of residence. The study by Hiller et al in the United States showed that the prevalence of cataract was higher among the people with greater annual hours of sunlight (Hiller et al. 1977). Another study in Nepal by Brilliant et al showed that the prevalence of cataract was higher among people living in lower altitude than higher altitude (Brilliant et al. 1983). These studies do not account for the personal or individual exposure to UV radiation.

Thus it gives a generalized view about the exposure at the place of residence and not the actual individual exposure.

The Chesapeake Bay study was a cross-sectional study of watermen in United States (Taylor et al. 1988). Quantification of individual ocular UV B exposure was done using an exposure model questionnaire developed by Rosenthal and colleagues (Rosenthal et al. 1988). Questionnaire information on occupational and leisure exposure to UVB since the age of 15 years, types of work terrain and use of headwear and eyewear were combined with measures of ambient UVB flux and field and laboratory data to estimate cumulative exposure and average annual exposure to solar UVB.

The Beaver Dam study was a cross-sectional survey of the adult population in Wisconsin (Cruickshanks et al. 1992). Exposure to UVB was assessed using a similar questionnaire based information and exposure model as the Chesapeake Bay study. The average annual ambient UVB light exposure was constructed for each individual, based on years of residence in a region weighted by the total ambient UVB light present in that area, as a ratio of the level of such light present for one year in Wisconsin.

The POLA study was a prospective population based study at Sete, France. The exposure was assessed using ambient solar radiation exposure in the place of residence adjusted for the use of protective devices (Delcourt, Carrière, et al. 2000; Delcourt et al. 2014).

The Salisbury Eye Evaluation Project examined relationships between annual ocular UVB doses and cataract in white and African-American

populations in Maryland (Sheila K West, Duncan, Muñ Oz, et al. 1998). It used a detailed model of sun exposure to assess sun exposure since age 30, with adjustment for wearing of hats and glasses, average UVR and cloud cover.

1.2.3.3a Specific Type of Cataract and their association with UV radiation:

a. Nuclear cataract:

Valero et al have found an association between the duration of outdoor exposure at younger age and risk for nuclear cataract (OR 3.05, 95% CI 1.25–7.42) (Pastor-Valero et al. 2007). Other studies have not shown any relationship with the sunlight exposure and nuclear cataract.

b. Posterior sub-capsular cataract (PSC):

Collman et al found an association between sunlight exposure and posterior subcapsular cataract that was similar in strength to that between cortical cataract and sunlight exposure (OR= 1.52, 95% CI 0.28 to 5.44 for the highest exposure) (Collman et al. 1988). Despite high ocular UVR exposure in the Chesapeake Bay watermen study there were a few PSC cataracts to analyze associations with UVR exposure (Taylor et al. 1988).

The India-US Case-control Study on age-related cataract showed a decreased risk of all types of cataract with increased lifetime cloud cover at the place of residence (OR = 0.78, 95% CI 0.68 to 0.9) (Mohan et al.

1989). Increase in cloud cover reduces the UV exposure. They did not assess personal exposure to Ultraviolet radiation.

In the Italian-American Cataract Study, UVR exposure was assessed by occupational exposure, use of a hat in the summertime and leisure activities in the sunlight (Italian-American Cataract Study Group 1991). Analysis of the results revealed a decreased risk of PSC cataract with increasing occupational exposure and leisure time exposure to sunlight, but a positive association with the use of a hat in summer. The observation of increased risk of PSC cataract with the wearing of a hat in summer is counterintuitive but could be explained if wearing a hat in summer was more common among those who spent longer hours in the sun.

The Lens Opacities Case-Control study (Leske et al. 1991), The Beaver Dam Eye study (Cruickshanks et al. 1992) and The Salisbury Eye Evaluation Project (S K West et al. 1998) did not find association between UVB exposure and PSC with occupational exposure, sex and race.

This lack of association was also supported in the Melbourne Visual Impairment Study (McCarty et al. 1999). Cortical cataract showed a significant association with increased average annual ocular UVB exposure and PSC cataract was associated with increased age, rural location, and use of thiazide diuretics, vitamin E intake and myopia.

The POLA study found no significant association between PSC and average annual ambient solar radiation exposure (Delcourt, Cristol, et al.

2000). Professional exposure to sunlight was associated with an excess risk of PSC cataract (OR = 1.75, 95% CI: 1.10 to 2.80).

c. Cortical cataract

The Chesapeake Bay study found that men in the highest quartile of exposure were at 3.3 times higher risk for cortical cataract. (RR: 3.3, 95% CI: 0.9 to 10.0) but this was not statistically significant (Taylor et al. 1988).

The Beaver Dam Study found an association between UVB exposure and cortical cataract for males (RR 1.4, 95% CI: 1.0 to 1.8) but not for females (RR 0.9, 95% CI: 0.7 to 1.3). Both were not statistically significant (Cruickshanks et al. 1992).

The POLA study found an association between the ambient solar exposure and cortical cataract (OR 2.48; 95 % CI: 1.24 to 4.99) and mixed cataract (OR 3.98; 95% CI: 1.98 to 7.98) (Delcourt 2001).

West SK et al reported a higher prevalence of cortical opacity with higher UVR exposure (OR (highest quartile of UV exposure of lowest) = 1.57, 95% CI: 1.04 to 2.38) (Sheila K West, Duncan, Mun, et al. 1998). Smoking, education and alcohol use were not significantly related to cortical opacity. The association of UVR with cortical cataract was further supported by the findings of McCarty et al in the Visual Impairment study in Victoria, Australia (C. A. McCarty et al. 2000). There was a statistically significant increased risk of cortical cataract (OR = 1.44, 95% CI: 1.21 to 1.73).

1.2.3.4 Age-related Macular Degeneration:

Studies have shown that ARMD results from a photosensitizing injury to the choriocapillaris; chronic low level exposure of reactive oxygen to the choriocapillary endothelium induces Type IV collagen synthesis which in turn thickens Bruch's membrane and choriocapillary septa. Compromised blood supply to the retina has been postulated by others to play a role in drusen formation and the development of ARMD (Winkler & Boulton 1999).

Gottsch et al. have developed an animal model of a chronic low level photosensitizing injury to the choriocapillaris (Gottsch et al. 1993). In the mouse model of protoporphyria, with an approximately 10-fold increase in protoporphyrin IX and exposure to blue light (380-430 nm, 14μW/cm^2), a time and light dependent increase in choriocapillary and subretinal RPE basal laminarlike deposits was demonstrated. After seven months protoporphyric mice exposed to blue light exhibited a 100% thickening of Bruch's membrane when compared to controls. The thickening was extended around entire basement membrane of the choriocapillary endothelium. The ultrastructure of the RPE and the rod outer segments demonstrated no evidence of light-induced degeneration or other abnormalities in experimental animals or the light and dark controls.

The POLA study (Delcourt 2001) did not find any association with sunlight exposure and the presence of pigmentary changes or ARMD. In the Beaver Dam study (Tomany et al. 2004; Klein et al. 2015), the data on sun exposure and indicators of sun sensitivity were obtained from a standardized questionnaire. They found that the subjects exposed to the summer sun for more than five hours a day during their teens, in their

30s, and at the baseline examination were at a higher risk of developing early ARMD (RR, 2.20, 95% CI: 1.02 to 4.73). They also found a protective effect in subjects using hat and sunglasses.

In Blue Mountains Eye Study (Pham et al. 2009) standardized questionnaires were used for data collection. They did not find any relationship between sunlight and ARMD.

In the European eye study (EUREYE study) (Fletcher et al. 2008), subjects with low levels of antioxidants were vulnerable to low levels of protection against blue light and thus were at higher risk for ARMD.

1.2.4 Gaps in existing research

There is little evidence about ultraviolet radiation in the South Indian population and its effects on the eye. Various studies done elsewhere reported the association between ultraviolet radiation and the eye but they differed in the methodology in their measurement of UV radiation and disease; and hence it is difficult to extrapolate their results because of the geographical variations in UV exposure and racial differences in disease risk.

There are also no data on the rural and urban differences in the UV exposure levels from south India. This information would be helpful in understanding the difference in prevalence of ocular condition among these populations.

The current study was a part of the Chennai Eye Disease Incidence Study. The main outcome of this study was to understand the relationship between UV radiation exposure and ocular disease and also to study its effect on the progression of the disease. The information collected in this study would form a knowledge base for the prevention of adverse effects of UV exposure that is achievable with known and accessible interventions.

Chapter 2

AIM AND OBJECTIVES

Aim:

The aim of the current study is to investigate the association between lifetime ocular UV exposure and ocular disorders such as ocular surface disorders, pseudoexfoliation, cataract and macular degeneration in the South Indian population.

Objectives:

a. To estimate the lifetime ocular UV exposure among subjects from rural and urban South India
b. To measure the difference in lifetime ocular UV exposure among the urban and rural population.
c. To determine the relationship of lifetime ocular UV radiation exposure and ocular disease such as ocular surface disorders, pseudoexfoliation, cataract and macular degeneration.
d. To understand the relationship between lifetime ocular UV exposure and ocular disease progression.

Chapter 3

METHODOLOGY

3.1 Overview on the Chennai Glaucoma study and the Chennai Eye Disease Incidence Study

3.1.1 The Chennai Glaucoma study:

The Chennai Glaucoma study (Arvind et al. 2003) was a population-based study, designed with a view to gather information on the prevalence of glaucoma and other eye diseases in a rural and urban South Indian population. The study was funded by Chennai Willingdon Corporate Foundation. A total of 7785 persons, above 40 years of age, from rural Tamil Nadu and Chennai city were examined at a special facility created at Sankara Nethralaya, Chennai. About 3924 subjects representing the rural south Indian population participated from 27 contiguous villages of Thiruvallur and Kancheepuram districts of Tamil Nadu. About 3850 Urban subjects participated from five randomly chosen divisions from Chennai city. Every patient underwent a detailed ophthalmic evaluation which including dilated fundus evaluation and grading of lens opacities using The Lens Opacities Classification System (LOCS II) (Chylack et al. 1989). The details of the clinical procedures are described in Appendix I. All abnormal features were recorded using standard international classifications. Data collection also included assessment of socio-economic status, systemic and ocular history.

3.1.2 The Chennai Eye Disease Incidence Study:

All subjects who had participated in the Chennai Glaucoma Study (2001-2004) from both the rural and urban arm underwent a repeat history, detailed ophthalmic examination and administration of instruments assessing the socio-economic status, demographic and personal history

(smoking and smokeless tobacco, alcohol consumption and food habits). All the study participants were re-enumerated and re-examined from 2007 to 2010. A total of 4421 subjects participated. The incidence of new diseases from the baseline and changes from the first examination were studied.

Written informed consent was obtained from all subjects for both studies and they were performed in accordance with the tenets of the Declaration of Helsinki. The study was approved by the institutional review board, Vision Research Foundation, Chennai.

3.2 Ultraviolet Radiation Exposure (UVR) Study:

The current study was done as a part of The Chennai Eye Disease Incidence Study. Participants who satisfied the inclusion and exclusion criteria were taken up for the study. This study had the following phases.

1. Selection of subjects and their demographics from the CGS
2. Collection of personal UV exposure details
3. Estimation of UV dose for each geographical location
4. Estimation of Personal Lifetime Ocular UV Exposure from Melbourne Visual Impairment model
5. Clinical data compilation of subjects from CGS and CEDIS
6. Data Analysis

3.3 Process of the study

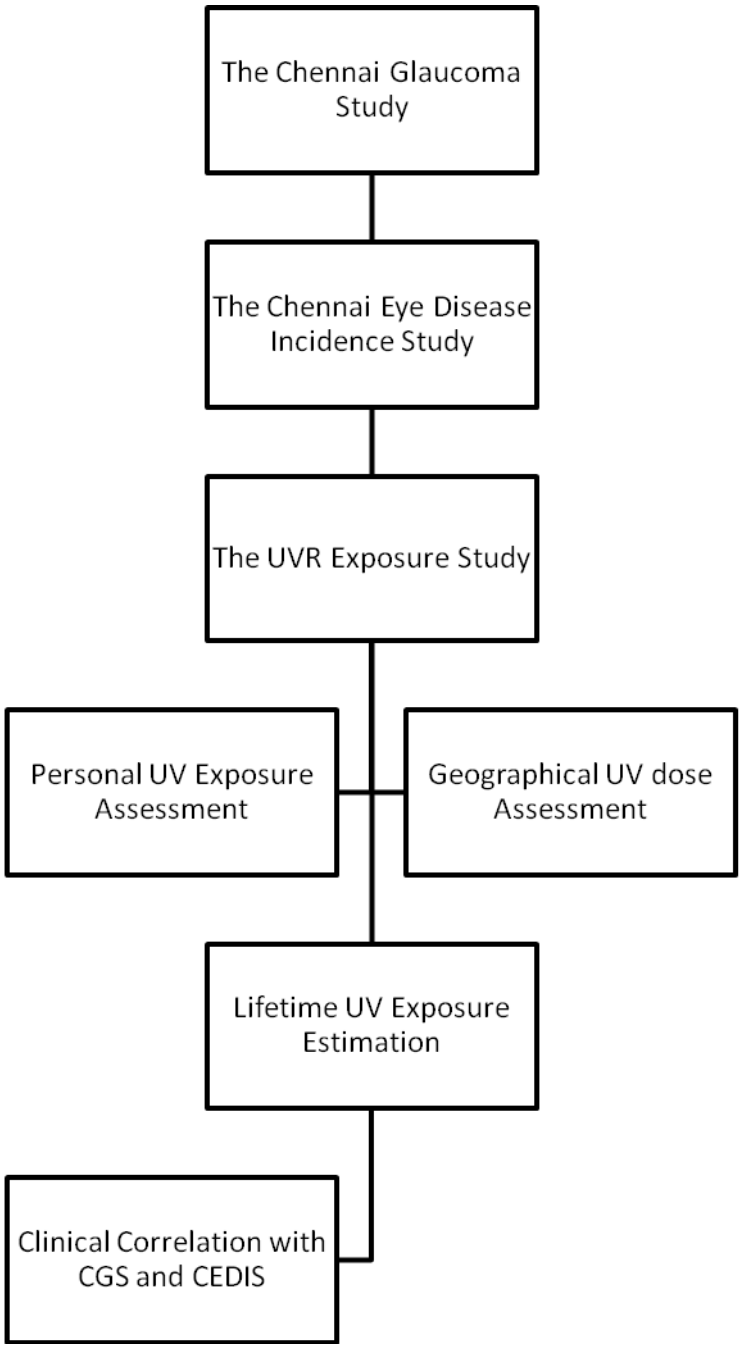


Figure 3.3.1 Description of flowchart of methodology

3.4 Study Design, Sampling and Subject selection:

Study design:

The current UVR exposure study is part of the population based study of The Chennai Glaucoma Study (n=7774). This is a retrospective cohort study (Population based: The Chennai Glaucoma Eye Disease Incidence study, n=4421). The data from CGS was taken as baseline and the follow-up data from CEDIS were studied. The Investigator was masked to the clinical findings.

Duration of the Study: 4 years: August 2012 to March 2016

Inclusion Criteria:

i. Participants of both the Chennai Glaucoma Study and The Chennai Eye disease incidence study
ii. Unilateral or bilateral phakic subjects

Exclusion criteria:

i. Subjects who had undergone bilateral cataract surgery at the time of the baseline study
ii. Subjects with more than 15 life periods (migrations) in their lifetime

Sample Size Estimation:

All the subjects who satisfied the inclusion criteria were included for the study. Of the 4421 subjects who participated in the CEDIS, 4101 subjects (2028 Rural and 1651 urban) were eligible for UVR exposure study satisfying the inclusion and exclusion criteria. In the current study we included 2091 subjects (1080 rural subjects and 1011 urban subjects). Post hoc power analysis revealed 96.8% power in estimating the difference of UV dose levels between rural and urban population.

3.5 UVR Exposure Study - Methodology Description:

I Personal UV exposure Assessment:

For UV exposure data collection to be comparable, the published questionnaire from the Melbourne Visual Impairment model was used (McCarty et al. 1996). This standardized questionnaire on lifetime migration (place of residence) was administered by a single person to all the eligible subjects (Appendix II). The information from birth till date of questionnaire administration was elicited. The place of living with the year or period was noted for each subject. The job or task performed at each location was also documented. The number of hours of exposure to sunlight with respect to each task was also documented.

II Geographical UV Dose Calculation:

UV index is an estimation of the UV levels that are important for the effects on the human skin, where one unit = 25 mW/m^2. It is estimated for local solar noon when the sun is highest in the sky. It is valid for clear sky condition and does not account for cloud shielding (www.temis.nl). A sample of UV dose levels are shown in figure 3.5.1

It is estimated that, of the global UV radiation at the ground, 94% is UV-A, 6% is UV-B. Of the erythemal UV irradiance, however, 17% is UV-A, 83% is UV-B.

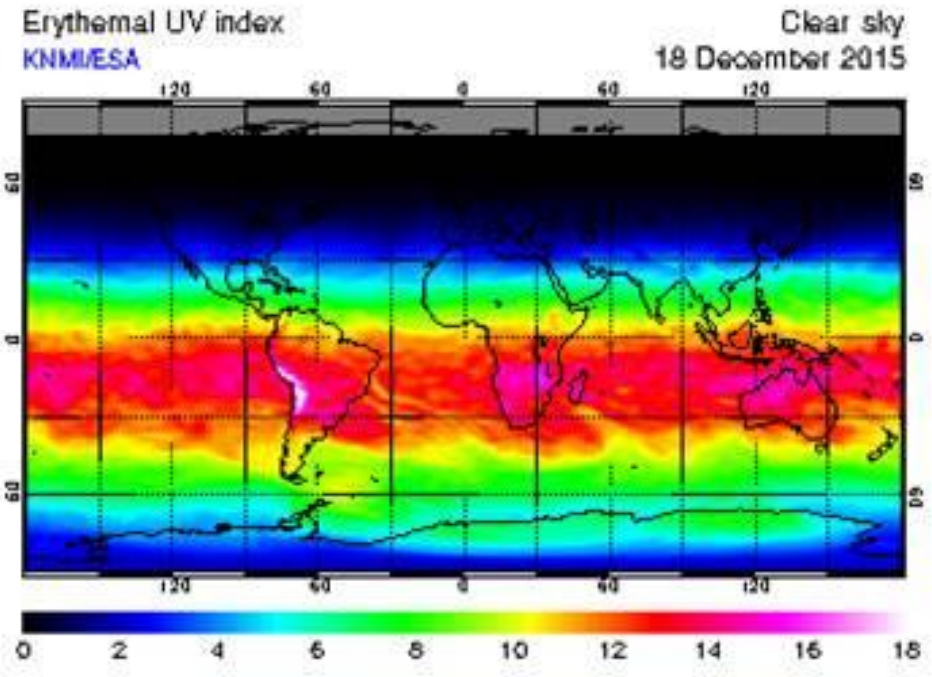


Figure 3.5.1. The sample of UV dose levels from Tropospheric Emission Monitoring Internet System for a particular day

The UV dose is the effective UV irradiance (given in kJ/m^2) reaching the Earth's surface integrated over the day. The UV dose is based on the CIE action spectrum for the susceptibility of the Caucasian skin to sunburn (erythema). UV dose is the integration of the erythemal UV index, as derived from satellite observations, from sunrise to sunset, with a time step of 10 minutes (www.temis.nl). The integration takes the cloud cover into account and thus leads to an estimate of the daily erythemal UV dose: the total amount of UV radiation absorbed by the human skin during the day, expressed in kJ/m^2. But practically it is not possible to estimate the cloud cover minute by minute and hence UV dose is estimated for clear sky situation.

The respective UV dose (J/cm^2) for each place was computed for each month. Information extracted from www.temis.nl is provided in table

3.6.1. The files are saved in HDF format and then extracted to Microsoft Excel 2013. The extracted information is saved as per month data for all the latitudes and longitudes. The annual UV dosage for each location is calculated based on cumulative UV dosage levels at those latitudes and longitudes. This process is time consuming as it involves data capturing, file transferring and location identification (place of living for each subject on each migration). The latitude and longitude of each place of living (including migration) was noted for each life period. The UV dose over a twelve month period was recorded from www.temis.nl for the 28th day of every month.

Table 3.5.1: Information from Tropospheric Emission Monitoring Internet System on the UV dose levels.

Product	**Erythemal UV dose (kJ/m^2)**
Number_of_longitudes	720
Longitude_range	-179.75, 179.75
Longitude_step	0.50
Number_of_latitudes	360
Latitude_range	-89.75, 89.75
Latitude_step	0.50
Iuvfield	UV dose field
Iuvfield	UV dose field
Iuverror	Error in UV dose due to error in ozone field
Units	UV dose unit kJ/m^2

Thus annual UV dose for the respective location was calculated. The data at each place will be taken as the location factor for each location in the Melbourne visual impairment model.

Lifetime ocular UV exposure estimation:

The collected information from the personal UV exposure estimation questionnaire and the UV dose for the respective location calculated based on geographic location details are fitted in the Melbourne visual impairment model as given below:

$$OE_{eff} = \sum_{s=1}^{n} years_s \times LF_s +$$
$$\sum_{p=1} years_p \{[hrsday_p \times 5/7 \times LF_p] \times [hatday_p \times 0.53 + (1-hatday)]_p] \times [sungday_p \times 0.07 + (1-sungday)]_p] \times [glsday_p \times 0.21 + (1- glsday)]_p] \} +$$
$$\{[hrsleis_p \times 2/7 \times LF_p] \times [hatleis_p \times 0.53 + (1-hatleis)]_p] \times [sungleis_p \times 0.07 + (1- sungleis)]_p] \times [glsleis_p \times 0.21 + (1-glsleis)]_p] \}$$

Where

OE_{eff} = lifetime effective ocular exposure

$years_s$ = number of school years in period s

LF_s = Location factor, constant value for s location

$years_p$ = number of years in life period p

$hrsday_p$= number of hours spent outside in weekday, period p

LF_p = Location factor, constant value for p location

$hatday_p$= % of time that the person worn hat in weekday, period p

$sungday_p$= % of time that the person worn sunglasses in weekday, period p

$glsday_p$= % of time that the person worn glasses in weekday, period p

$hrsleis_p$= number of hours spent outside in leisure time, period p

$hatleis_p$= % of time that the person worn hat in leisure time, period p

$sungleis_p$= % of time that the person worn sunglass in leisure time, period $_p$

$glsleis_p$= % of time that the person worn glasses in leisure time, period $_p$

The use of protective devices such as hat, umbrella, spectacles or sun glasses during outdoor exposure of work was graded and weighted as 0- Never, 0.25 - Less than half of the time, 0.50 - Half of the time, 0.75 – More than half of the time, 1- always.

3.6 Clinical Data-Disease diagnostic definitions:

The clinical examination was done for the subjects at the base hospital. It includes detailed history and comprehensive eye examination (Elaborated in Appendix I). The collected data was drawn from both CGS (Baseline) and CEDIS (Follow-up) database. All these was cleaned and analysed according to the needed information.

Ocular Surface Disorder:

Pterygium was diagnosed by the presence of characteristic raised fleshy growth that crossed the limbus and encroached on clear cornea. (Figure 3.6.1)

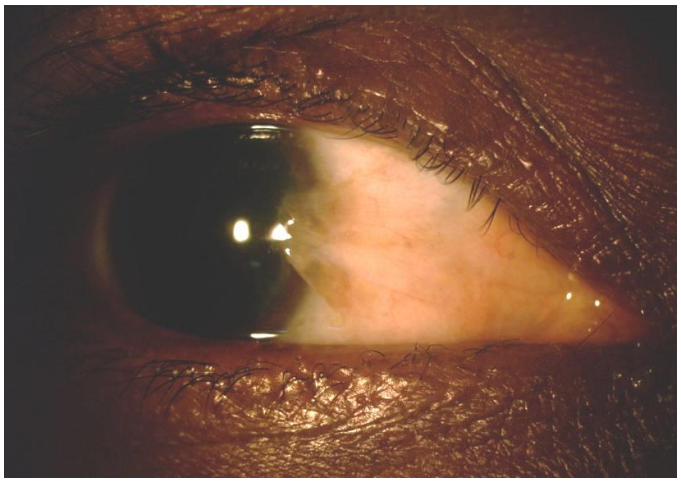


Figure 3.6.1 Pterygium

Pinguecula was diagnosed by the presence of characteristic fleshy lesions in the nasal or temporal bulbar conjunctiva. (Figure 3.6.2)

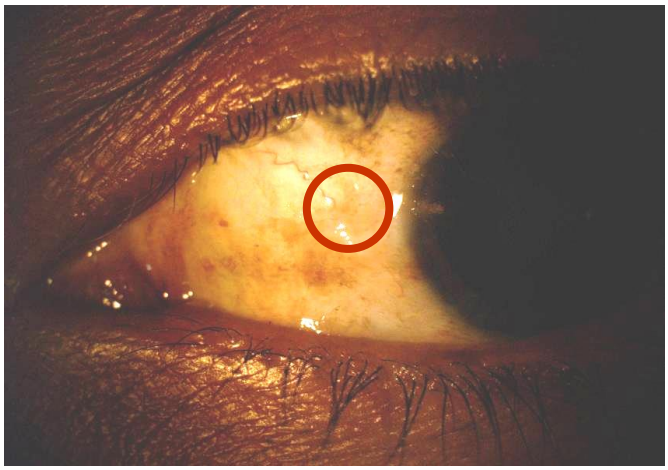


Figure 3.6.2 Pinguecula

Spheroidal degeneration or Climatic Droplet Keratopathy was defined as nodules like structures grown onto the cornea. This has shiny luster and can cause diminution of vision. (Figure 3.6.3).

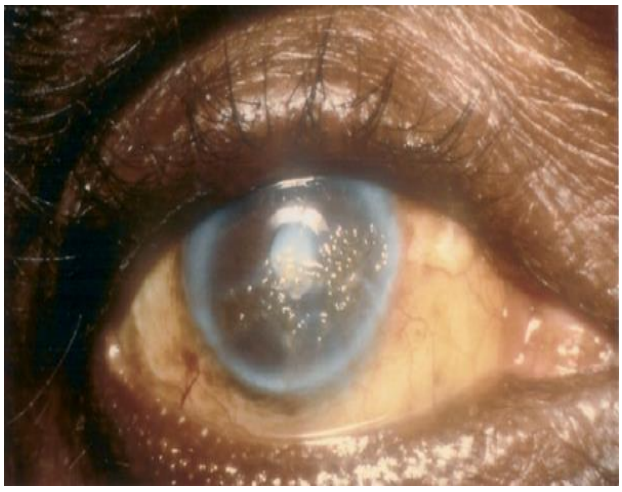


Figure 3.6.3: Spheroidal degeneration

Pseudoexfoliation:

The subject was classified as having pseudoexfoliation (PEX) syndrome if PEX material was present in either or both eyes at one or more locations, namely pupillary margin, anterior lens capsule, anterior chamber angle, corneal endothelium anterior vitreous phase and zonules. (Figure 3.6.4)

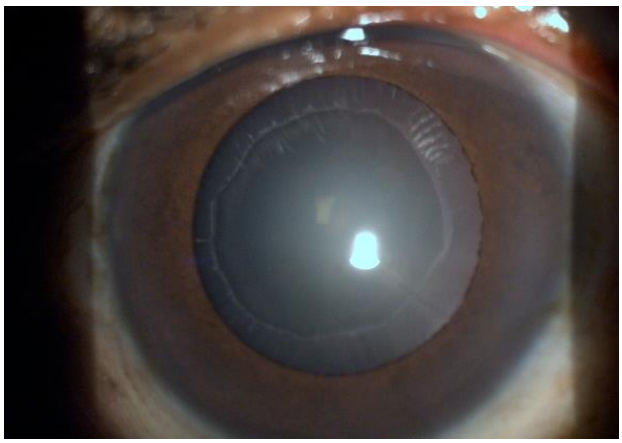


Figure 3.6.4: Pseudoexfoliation over anterior lens capsule

For pterygium, pinguecula, spheroidal degeneration and pseudoexfoliation, we have only assessed the incidence of cases as the assessment of progression was not possible without any baseline measurements.

Cataract:

Cataract Status was assessed based on Lens opacification classification system II and III (Chylack et al. 1989; Chylack et al. 1993).It is classified as Nuclear Sclerosis (NS 0 to NS IV), Posterior Sub-capsular Cataract (PSC 0 to PSC IV) and CorticalCataract (C0 to C V). Any change in cataract grade by one step was classified as progression. (Figure 3.6.5)

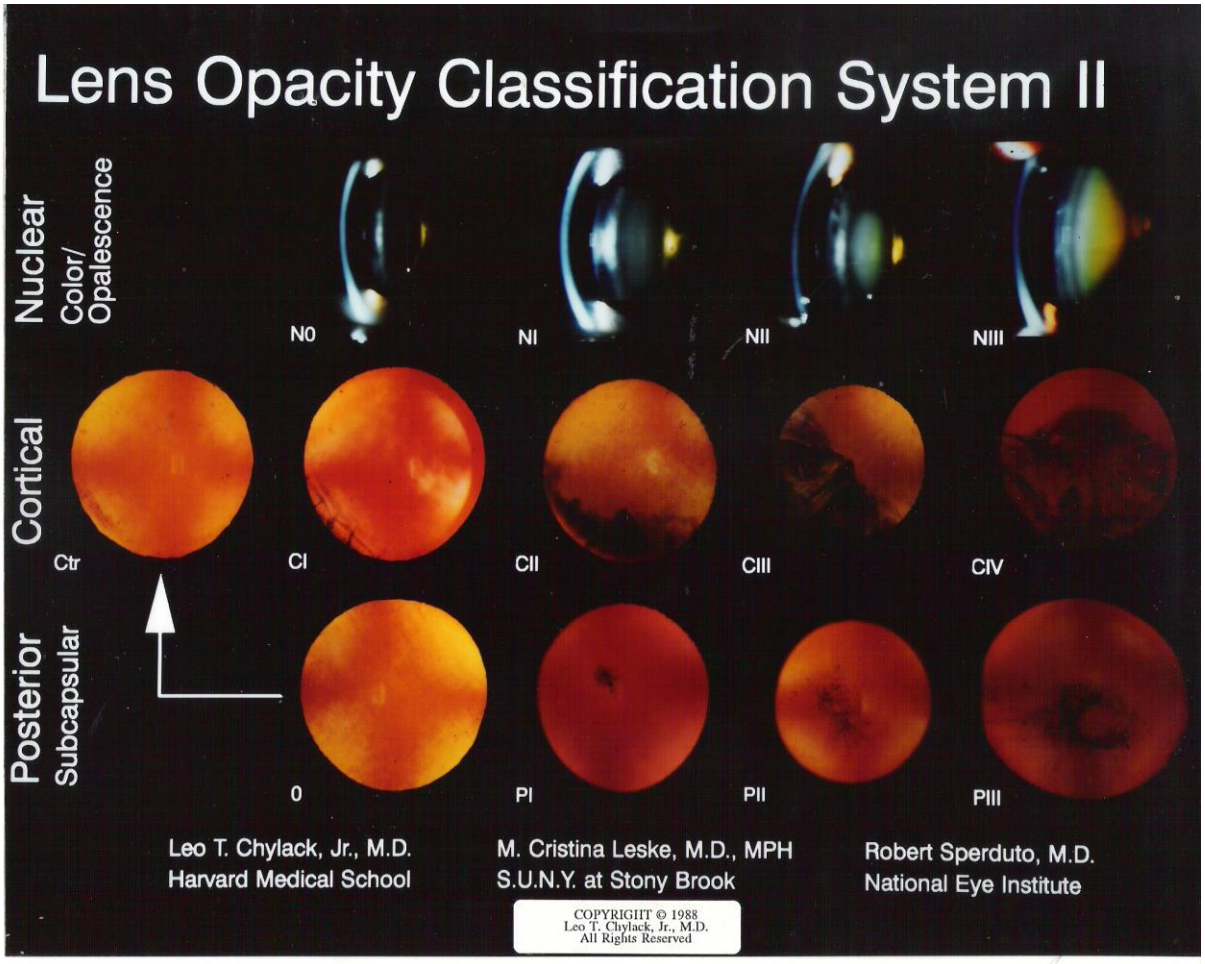


Figure 3.6.5: Classification of cataract using Lens Opacification Classification System

Macular Degeneration:

The International Epidemiological Study Group defines Age Related Macular Degeneration (Bird et al. 1995) (ARMD) as a disorder of the macular area, often clinically apparent after 50 years of age, and characterized by:

1. Discrete whitish-yellow spots identified as drusen
2. Increased pigment or hyperpigmentation associated with drusen
3. Sharply demarcated areas of depigmentation or hypopigmentation of the retinal pigment epithelium and associated drusen

In the current study, Macular Degeneration was defined as presence of drusen on the macula region (Figure 3.6.6). This was classified by trained ophthalmologists.

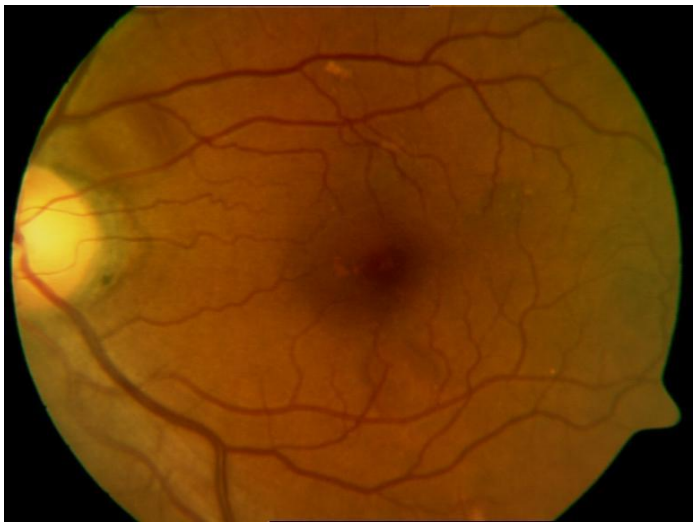


Figure 3.6.6: Fundus Photograph with Macular Degeneration

Visual Impairment and Blindness:

Visual impairment was graded based on WHO criteria. Incident visual impairment was defined as BCVA of ≥ 6/18 at baseline in the better-seeing eye and BCVA of <6/18 and ≥3/60 in the better-seeing eye at follow-up. Incident blindness was defined as visual acuity of less than 6/120 (3/60) and/or a visual field of less than 10° in the better seeing eye at the 6-year follow-up provided that eye had a visual acuity better than or equal to 6/ 120 (3/60) and visual field greater than 10° at baseline (Vijaya et al. 2014). The causes for visual impairment and blindness are also analyzed.

Refractive Error:

Subjects with spherical equivalent refractive error (Sphere correction + half of cylindrical correction) between -0.50 DS and +0.50 DS are defined as emmetropia. Less than -0.50 DS are defined as myopia and more than +0.50 DS are defined as hyperopia. Any increase in refractive error from baseline of more than 0.50 DS towards myopia is defined as myopic shift and towards hyperopia was defined as hyperopic shift.

Eye Selection:

The phakic right eye was included for analysis. In case where the right eye had cataract extraction at baseline, the left eye was included for analysis. The presence of each ocular disease was categorized based on the selected eye.

Other Relevant information:

The personal history of each subject was elicited through a questionnaire which was read to the participants and the answers were filled in by the person administering it. Components of questionnaire were as follows: (1) personal characteristics such as age, sex, cigarette smoking, smokeless tobacco use, alcohol consumption and educational qualification (2) environmental variables such as nature of occupation (3) systemic variables include history of diabetes mellitus and its duration, systemic hypertension and its duration and history of steroid use. Details on the form of tobacco use, duration and quantity of use were ascertained. On the basis of the history of tobacco use, data on the number of cigarettes or beedis smoked per day were elicited for current smokers. We classified people with at least primary education as literates and with no formal education as illiterates. We categorized people with predominantly indoor occupation as indoor workers and predominantly outdoor job as outdoor workers.

Diabetes mellitus and systemic hypertension was detected based on current use of anti-diabetic or systemic anti-hypertensive medication and previous history of the condition. Body mass index (BMI) was defined as weight in kilograms divided by the square of height in meters (kg/m2). BMI categories were grouped as underweight (<18.5 kg/m^2), normal (18.5 – 25 kg/m^2), overweight (>25 kg/m^2) obese (≥ 30.0 kg/m^2).

Each subject's clinical examination data, questionnaire data and lifetime ocular UV exposure data was synchronized and compared using statistical analysis.

3.7 Statistical Analysis:

All the collected data were entered into a central database and were rechecked for data entry errors. Statistical analysis was performed using SPSS Version 15(SPSS In, Chicago, IL). Subjects were classified in to four groups based on baseline age – 40 to 49 years, 50 to 59 years, 60 to 69 years and 70 years and above. Statistical significance was set at the $p < 0.05$ level. Odds ratio were presented with 95% confidence interval (CI).

Flow of analysis:

1. Tests for normality were performed.
2. Descriptive analysis was performed for the total population
3. Prevalence and incidence of each condition was analyzed among rural and urban population.
4. Comparison of proportional difference among gender, age group and population was done using Chi square test
5. Risk factor for each condition adjusting for confounding factors was done using multivariate logistic regression.
6. Lifetime ocular UV radiation exposure and its association with each clinical condition was analyzed.

Chapter 4

ORGANISATION OF THESIS

4 Organization of thesis

The thesis is structured such a way that the introduction, review of literature and the methods in common are provided in the chapters 1, 2, 3 and 4. The results of the studies are described along with the discussion of the results as shown in the following flow chart.

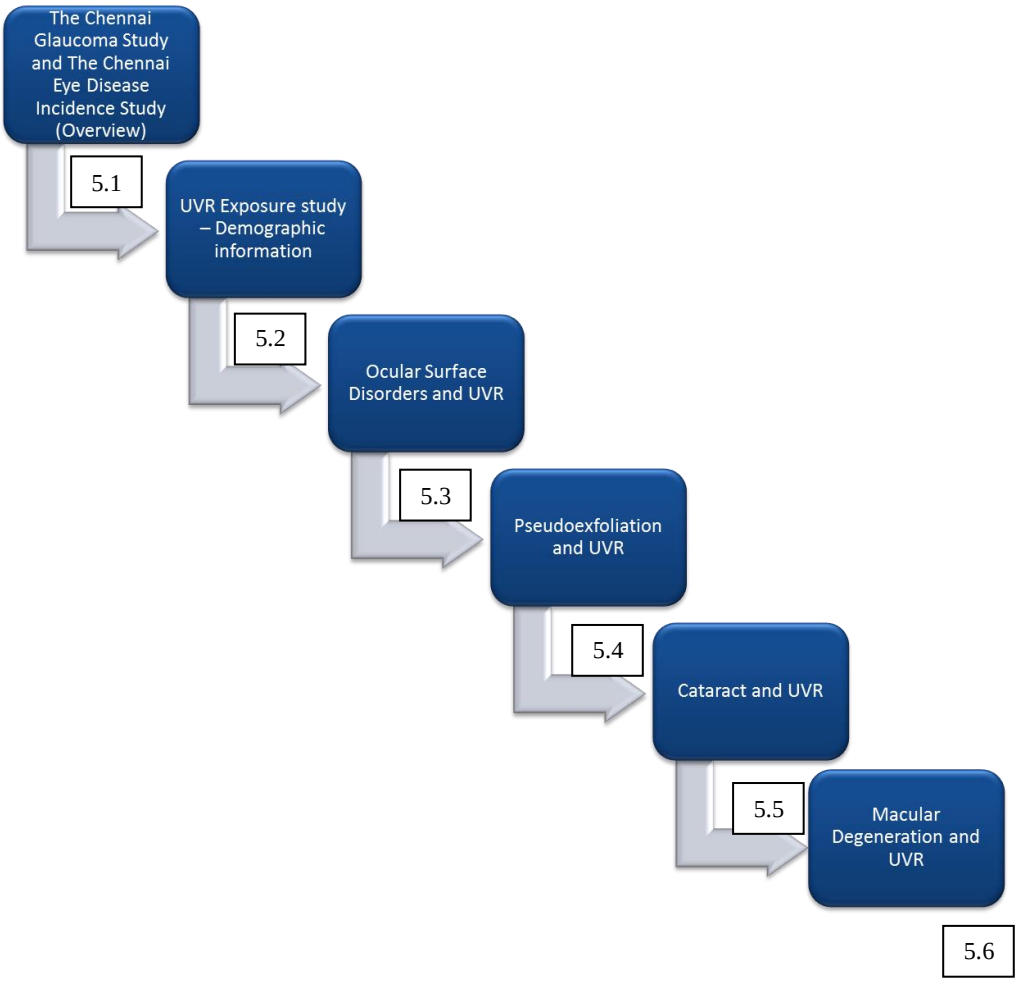


Figure 4.1: Flow chart on the organization of thesis

Chapter 5

RESULTS AND DISCUSSION

5.1 Comparison of participants and non-participants in CEDIS:

In the Chennai Glaucoma Study the total numbers of subjects were 7774. Re-enumeration was possible for 6022 (rural: urban 3047:2975). Out of this 1752 (rural: urban 877:875) subjects could not be contacted in spite of three house visits and 590 people were deceased. Those eligible for the study were 5432 and out of this 4421 (rural: urban 2510:1911) subjects were examined at the base hospital. The reasons for non-participation are given in figure 5.1.1. It showed that in the urban cohort there was a significantly higher proportion of migration which was responsible for a reduced response rate in the study. The response rate for this study was 81.3%. Comparison of baseline characteristics of participants and non-participants in the Chennai Eye Disease Incidence Study (CEDIS) is provided in table 5.1.1. It shows that the proportion of the non-participants were likely to be older, diabetic and hypertensive when compared to participants in urban population. The age and gender wise comparison of the study population is also provided in table 5.1.2.

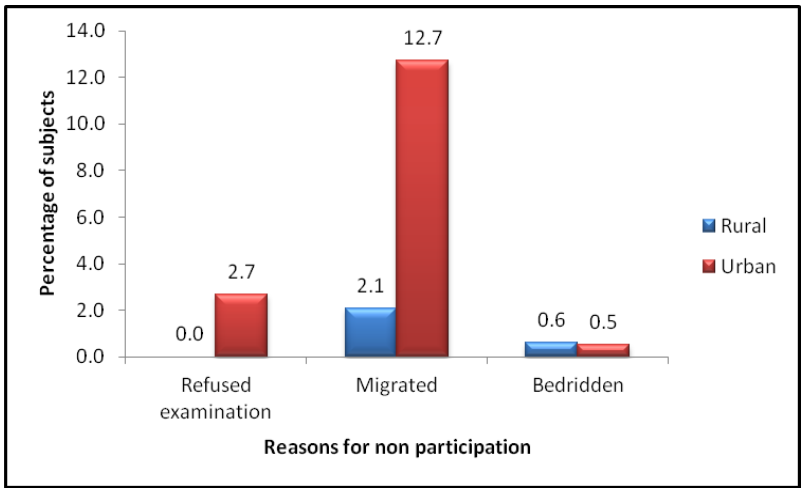


Figure 5.1.1: Reasons for non-participation among eligible subjects after re-enumeration

Table 5.1.1: Comparison of Baseline Characteristics of Participants and Non-participants in the Chennai Eye Disease Incidence Study (CEDIS)

Variables	Participants (n=4421)	Non-Participants (n=3353)	P value
Age (years)*	52.8 (9.7)	56.4 (11.3)	<0.001
Male: Female	1972:2449	1500:1853	0.46
Rural: Urban	2510:1911	1414:1939	<0.001
IOP (mmHg)*	15.2 (4.3)	15.5 (4.4)	0.001
CCT (Microns)*	510.4 (34.9)	511.4 (37.1)	0.19
VCDR*	0.42 (0.2)	0.44 (0.2)	<0.001
Cataract Surgery	359 (8.1)	371 (11.1)	<0.001
Axial length* (mm)	22.6 (0.9)	22.6 (1.0)	0.95
Hypertension (No: Yes)	3831:590	2748:605	<0.001
Diabetes mellitus (No: Yes)	3909:512	2829:524	<0.001

Chi-square test is used for comparison.

*Independent t-test is used for comparison.

Table 5.1.2: Age and Gender wise comparison

Age Group (In years)	Participants (n = 4421)		Non Participants (n=3353)	
	Male	Female	Male	Female
40 – 49	728	1179	465	632
50 – 59	593	674	345	493
60 – 69	447	479	415	458
> 70	204	117	275	270
Total	1972	2449	1500	1853

Table 5.1.3 shows that with increasing age the percentage of cataract surgery increases. Thus the samples drawn for the current study had few cases satisfying inclusion criteria in higher age group.

Table 5.1.3: Lenticular status of the entire study population at baseline (CGS):

Age Group	Phakic (%)	Operated (%)
40 – 49	98.80	1.20
50 – 59	95.05	4.95
60 – 69	83.23	16.77
70 – 79	67.06	32.94
Above 80	60.58	39.42

5.2 UVR exposure study

5.2.1 Geographical location and UV exposure levels

The solar UV-B irradiance at any location depends on the solar zenith angle, column ozone content, column aerosol content, cloud cover and the altitude of the observation site. Erythemal UV dose (EUVD) was developed by TEMIS UV team and was obtained from the website www.temis.nl. Daily EUVD (kJ/m^2) was estimated from the integration of erythemal UV index, as derived from satellite observations, from sunrise to sunset, with a time step of 10 minutes after taking the cloud cover information based on the International Satellite Cloud Climatology Project (ISCCP) database into account. The validation of the EUVD is, however, preliminary. The EUVD is computed at latitude/longitude grid with cells measuring 0.5 by 0.5 degrees, which amounts to about 50 x 50 km at the equator.

For comparison we extracted UV dose levels over a period of one year from April 2008 to March 2009 for different parts of India. The following Indian cities have been selected and are divided as South India, North India and Central India based on their Latitude and Longitude: South India: Chennai (13.13^o N, 80.30^o E), Hyderabad (17.37^o N, 78.48^o E), Bangalore (12.98^{o}N,77.67^o E), Thiruvananthapuram (8.68^o N, 77^o E), Central India: Mumbai (18.91^o N, 72.83^o E), Ranchi (13.13^o N, 80.30^o E), Calcutta (13.13^o N, 80.30^o E),North India: Chandigarh (23.32^o N, 85.45^o E),Shimla (31.03^o N, 77.15^o E), Delhi (28.63^o N, 77.28^o E), and Lucknow (26.83^o N, 81^o E). We have compared the UV doses in these locations and provided in table 5.2.1.1 and figure 5.2.1.1

Table 5.2.1.1 The distribution of UV dose levels at North, Central and South Indian cities

Locations	Annual UV Dose Level (J/cm^2)			
	Cities	Mean (SD)	Minimum	Maximum
North	Chandigarh	5.93 (0.85)	4.28	6.93
	Shimla	4.29 (2.05)	1.45	7.26
	Delhi	4.44 (1.98)	1.75	7.17
	Lucknow	4.57 (1.87)	1.9	7.06
Central	Mumbai	5.5 (1.46)	2.89	7.11
	Ranchi	5.95 (0.58)	4.87	6.64
	Calcutta	5.00 (1.59)	2.47	6.95
South	Hyderabad	5.89 (0.63)	4.69	6.68
	Bangalore	5.91 (0.74)	4.52	6.82
	Chennai	5.77 (0.89)	4.12	6.67
	Trivandrum	5.97 (0.6)	4.87	6.67

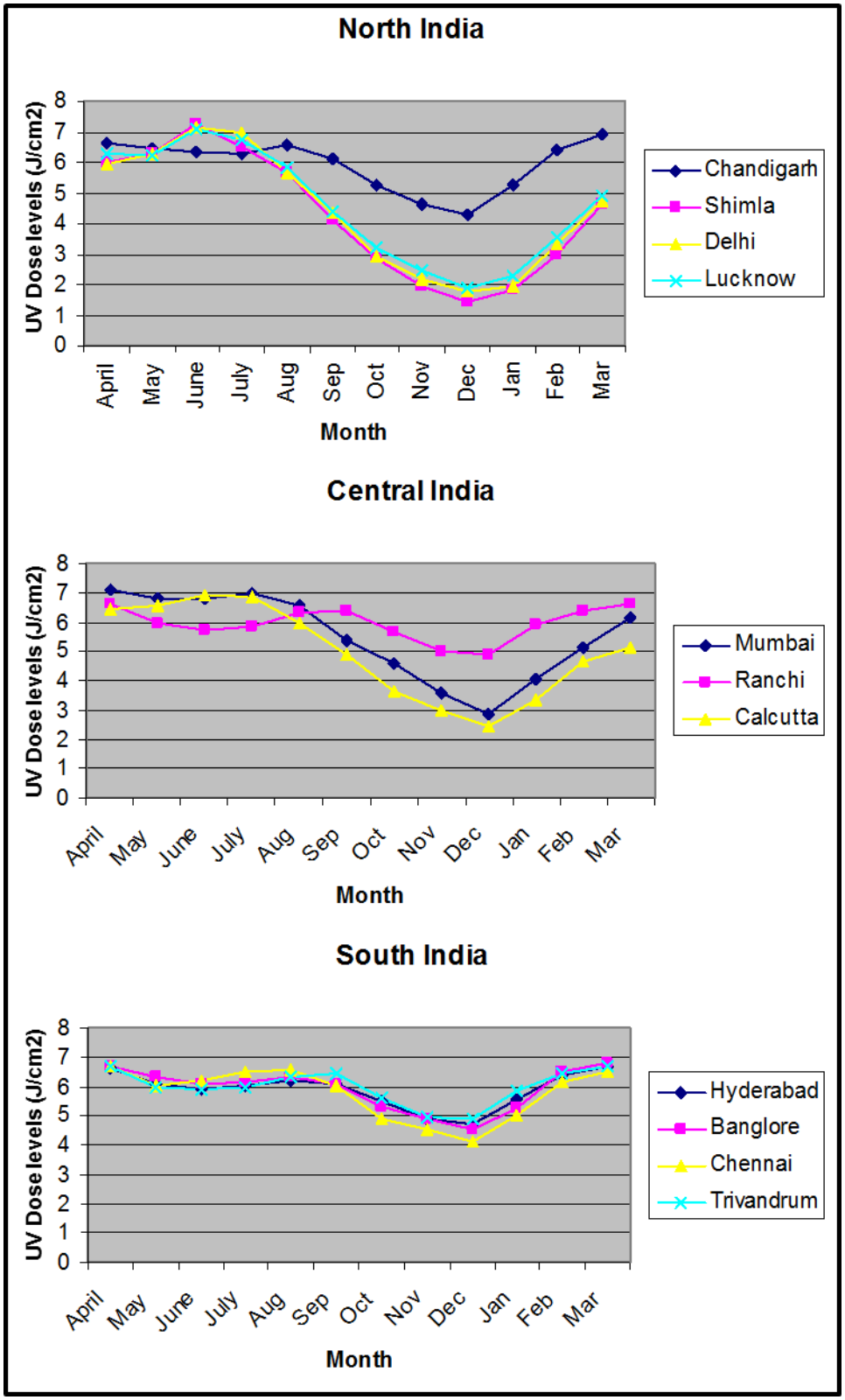


Figure 5.2.1.1 The annual dose of UV levels at North, Central and South Indian cities in different months of an year

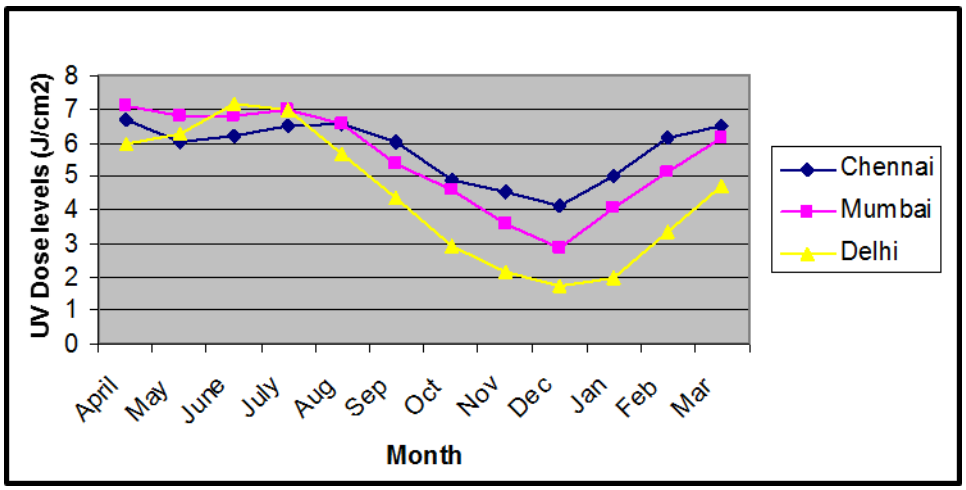


Figure 5.2.1.2 Comparison of annual UV dose levels among North, Central and South Indian cities across a year

5.2.2 Demographic information:

a. Demographics description:

Of the 4421 subjects who participated in the CEDIS, 4101 subjects (2028 Rural and 1651 urban) were eligible for UVR exposure study satisfying the inclusion and exclusion criteria. In the current study we included 2091 subjects (1080 rural subjects and 1011 urban subjects). Post hoc power analysis revealed 96.8% power in estimating the difference of UV dose levels between rural and urban population. The detailed description of the study population is given in table 5.2.2.1 and the distribution of age groups and gender is provided in table 5.2.2.2

Table 5.2.2.1: Demographic information about the UVR exposure study subjects

Parameter studied	**Number of subject, n (%)**
Age (years)* (Mean ±SD)	54.8 ± 10.0
Male: Female (%)	894 (42.8): 1197 (57.2)
Rural: Urban (%)	1080 (51.6): 1011 (48.4)
Smoking (%) No: Yes	1704 (81.5): 387(18.5)
Smokeless tobacco use (%) No: Yes	1754 (83.9): 337(16.1)
Diabetes Mellitus (%) No: Yes	1828 (87.4): 263 (12.6)
Hypertension (%) No: Yes	1255 (60.0): 836 (40.0)
Occupation Outdoor (%): Indoor (%)	 1297 (62): 794 (38)
Literacy Illiterate (%): Literate (%)	 606 (29): 1485(71.0)

Table 5.2.2.2: Distribution of males and females in different age groups among rural and urban population:

Age Group (in years)	Rural (n=1080)		Urban (n=1011)		Total (n=2091)	
	Males n (%)	Females n (%)	Males n (%)	Females n (%)	Males n (%)	Females n (%)
40-49	127 (11.8)	275 (25.5)	97 (9.6)	216 (21.4)	224 (10.7)	491 (23.5)
50-59	159 (14.7)	223 (20.6)	127 (12.6)	192 (19)	286 (13.7)	415 (19.8)
60-69	111 (10.3)	94 (8.7)	143 (14.1)	124 (12.3)	254 (12.1)	218 (10.4)
>70	54 (5)	37 (3.4)	76 (7.5)	36 (3.6)	130 (6.2)	73 (3.5)
Total	451 (41.8)	629 (58.2)	443 (43.8)	568 (56.2)	894 (42.8)	1197 (57.2)

b. Place of residence and migrations:

In the UVR exposure study the participants were asked on the migrations from their birth. The details of number of migrations by each individual are plotted in the bar graph (Figure 5.2.2.1). The majority of the subjects had less than 1 migration in their lifetime (89.4%). About 59.6% of the rural participants did not migrate from their birth place.

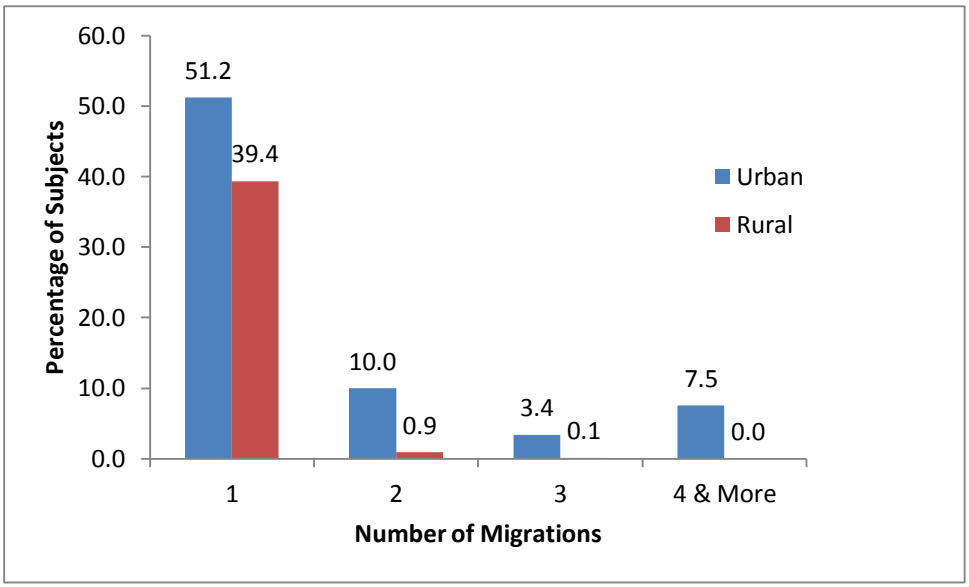


Figure 5.2.2.1: The details of number of migrations by study subjects

c. Distribution of the total lifetime ocular UV exposure of the study subjects:

We have calculated the lifetime ocular UV exposure per individuals (by fitting in the Melbourne Visual impairment Model). The estimated lifetime exposure did not follow a normal distribution. The histogram of the lifetime ocular UV exposure is shown in figure 5.2.2.2a and the histogram for rural and urban population is shown in figure 5.2.2.2b. The annual dosage corrected for the participant's age is shown in figure 5.2.2.c. This shows that even after accounting for age the difference in UV exposure still exists among rural and urban population.

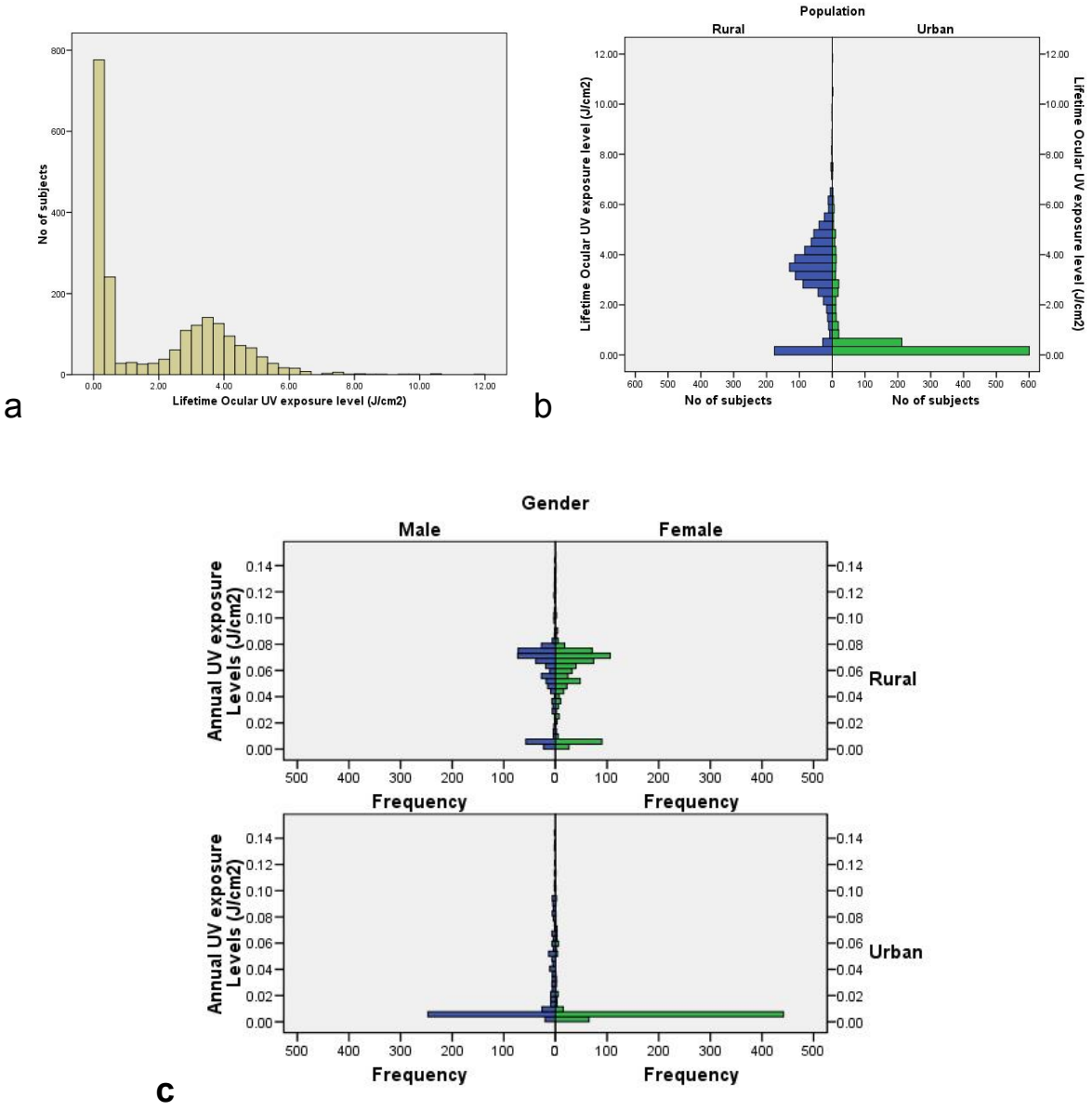


Figure 5.2.2.2 Histogram of the lifetime ocular UV exposure in the study subjects a. With total population b. with rural and urban population c. Annual UV exposure levels (Corrected for their age) among rural and urban, males and females.

d. Spectacle usage:

Since spectacle use can protect against UV radiation, spectacle usage among rural and urban participants was collected using the questionnaire. Among the participants 53.1% of rural and 81.6% of urban subjects were using spectacles. The detailed information on spectacle use is provided in the table 5.2.2.3.

Table 5.2.2.3 Tabulation on the spectacle usage

Variables	Rural (n=573, 53.1%) n (%)	Urban (n=825, 81.6%) n (%)
Use of spectacles		
Regular	103(18.0)	336 (40.7)
Seldom	452 (78.9)	479 (58.1)
Never	18 (3.1)	10 (1.2)
While Outdoor		
Regular	84 (14.7)	332 (40.2)
Seldom	34 (5.9)	67 (8.1)
Never	455 (79.4)	426 (51.6)
Sun glasses / Photochromatics	0	87 (10.5)
Age - Spectacles first worn		
Less than 15 years	0	14 (1.7)
16 to 25 years	1 (0.2)	31 (3.8)
26 to 35 years	6 (1.0)	59 (7.2)
More than 35 years	566 (98.8)	721 (87.4)

e. Comparison of lifetime ocular UV exposure levels among males and females with respect to their place of residence and age:

The lifetime ocular UV exposure levels among the rural and urban subjects were compared. The difference among males and females are also plotted in figure 5.2.2.3.

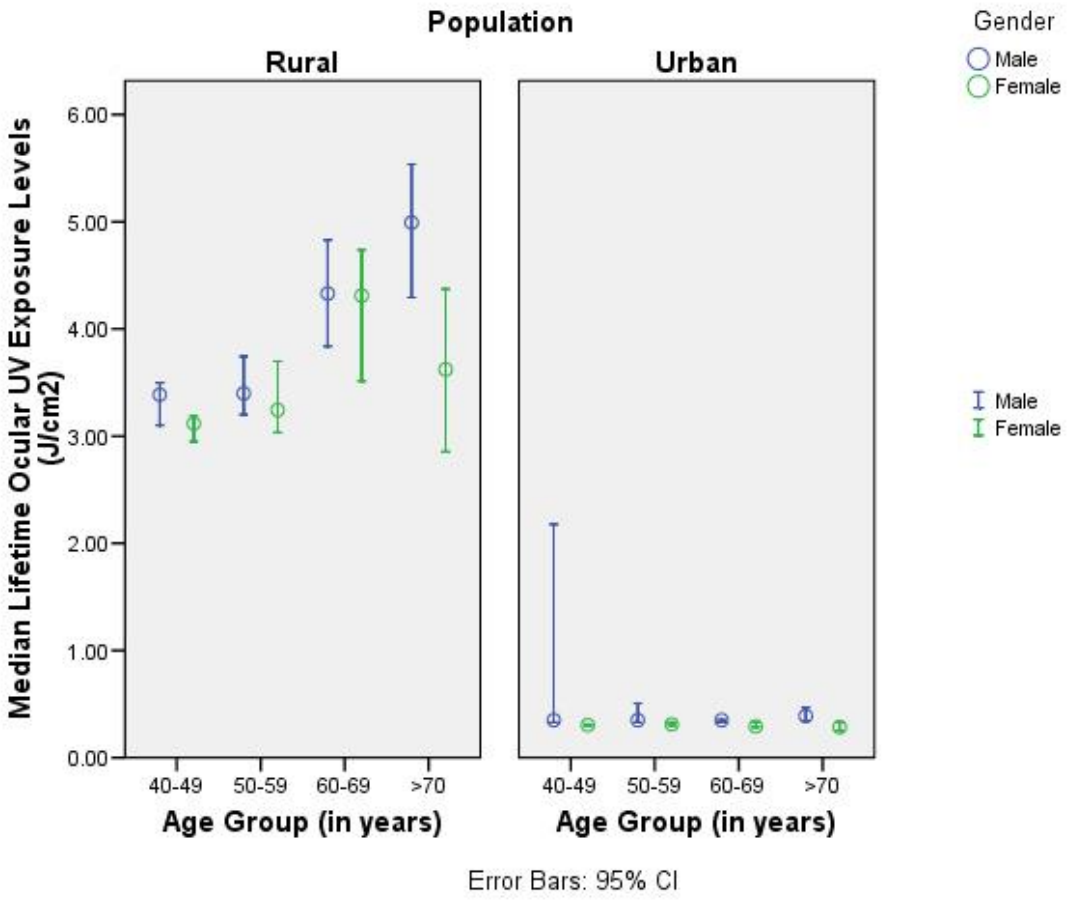


Figure 5.2.2.3. Plot on the comparison of lifetime ocular UV exposure levels among male and female with respect to their place of residence and age

The median lifetime ocular UV exposure was found to be (1.00, IQR: 3.28). There was a significant difference noted among the rural (3.35, IQR: 1.98) and the urban population (0.33, IQR: 0.11) (p value, <0.001).

There was a significant difference in median lifetime ocular UV exposure among males and females, 3.56, IQR (2.24) and 3.21 (IQR 1.88) respectively (p value, <0.001) in rural and in urban among male and female, 0.35 IQR (1.61) and IQR 0.31 (0.08) respectively (p value <0.001).

The UV levels were categorised into five equal divisions (Quintiles) from lowest to highest. The quintiles were 1st quintile (<0.29), 2nd (0.292 to 0.350), 3rd (0.350 to 2.758), 4th (2.758 to 3.844), 5th (>3.884). The number of subjects in each quintile among the rural and urban population in males and females are listed in table 5.2.2.4.

Table 5.2.2.4. Tabulation of proportion of subjects in each quintile of UV exposure level

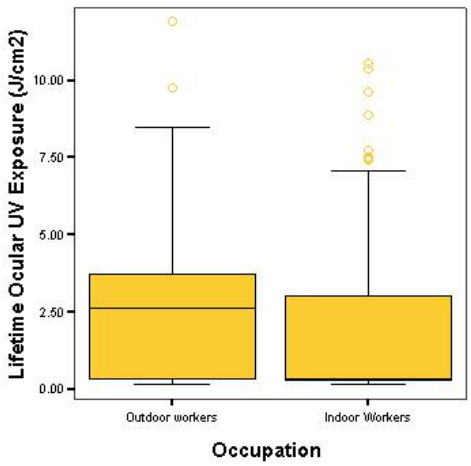
UV Exposure Levels	Rural (n=1080)		Urban (n=1011)	
	Males n (%)	Females n (%)	Males n (%)	Females n (%)
1st Quintile	59 (13.1)	82 (13.0)	71 (16.0)	191 (33.6)
2nd Quintile	17 (3.8)	27 (4.3)	158 (35.7)	286 (50.4)
3rd Quintile	61 (13.5)	102 (16.2)	134 (30.2)	67 (11.8)
4th Quintile	134 (29.7)	238 (37.8)	33 (7.4)	12 (2.1)
5th Quintile	180 (39.9)	180 (28.6)	47 (10.6)	12 (2.1)

f. Association of occupation and UV exposure:

The occupation was categorised as predominantly outdoor and indoor. Jobs with more than 50% of the time spent outdoor were grouped as outdoor work (eg: Farmers) and others were grouped as indoor work (eg: Professsionals). The number of outdoor and indoor workers is shown in table 5.2.2.5. The median lifetime ocular UV exposure levels are shown in figure 5.2.2.4, outdoor workers (2.61, IQR 3.37) and indoor workers (0.33, IQR 2.72), p value <0.0001.

Table 5.2.2.5: Distribution of outdoor and indoor workers in rural and urban residence

Population	Outdoor workers n(%)	Indoor workers n(%)
Rural	802 (74.3)	278 (25.7)
(Male: Female)	382 (35.3) : 420 (38.8)	69 (6.4):209(19.3)
Urban	495 (48.9)	516 (51.0)
(Male: Female)	365 (36.1):130 (12.9)	78 (7.7):438 (43.3)



Chi-square p<0.001

Figure 5.2.2.4: Median lifetime ocular UV exposure levels among outdoor and indoor workers

There was a significant difference in median lifetime ocular UV exposure among outdoor workers (2.61, IQR: 3.37) and indoor workers (0.33, IQR: 2.72) (p value, <0.001).

5.2.3 Proportion of Ocular diseases:

The prevalence of eye disease in the subjects who participated in the current study is given in table 5.2.3.1. The study included 2037 (97.4%) right eyes and 54 (2.6%) left eyes for analysis. There were 285 eyes which had cataract extraction before the follow-up examination. These cases where considered as cataract progressed cases. Totally 1806 phakic eyes were studied. The risk of the disease (Odds Ratio) with the exposure levels to UV is presented graphically, with 1st quintile as reference in figure 5.2.3.1. The prevalence of the disease with UV exposure levels are shown in figure 5.2.3.2.

Table 5.2.3.1: Tabulation of number of subjects with the disease at baseline and follow up (n=2091)

Variables	Number of subjects (%)	
	Baseline at CGS	Follow-up at CEDIS
Pterygium	140 (6.7)	175 (8.4)
Pinguecula	225 (10.8)	245 (11.7)
Spheroidal Degeneration	140 (6.7)	242 (11.6)
Pseudoexfoliation	57 (2.7)	83 (4.0)
Macular Degeneration	87 (4.2)	173 (8.3)
Nuclear Cataract	558 (26.7)	651 (31.1)
Cortical Cataract	505 (24.2)	604 (28.9)
Posterior Sub-capsular Cataract	407 (19.5)	266 (12.7)
Lens status		
No cataract	1286 (61.5)	850 (40.7)
Presence of pure form of cataract	360 (17.2)	524 (25.1)
Presence of Mixed form of cataract	445 (21.3)	432 (20.7)
Pseudophakia	-	273 (13.1)
Aphakia	-	12 (0.5)

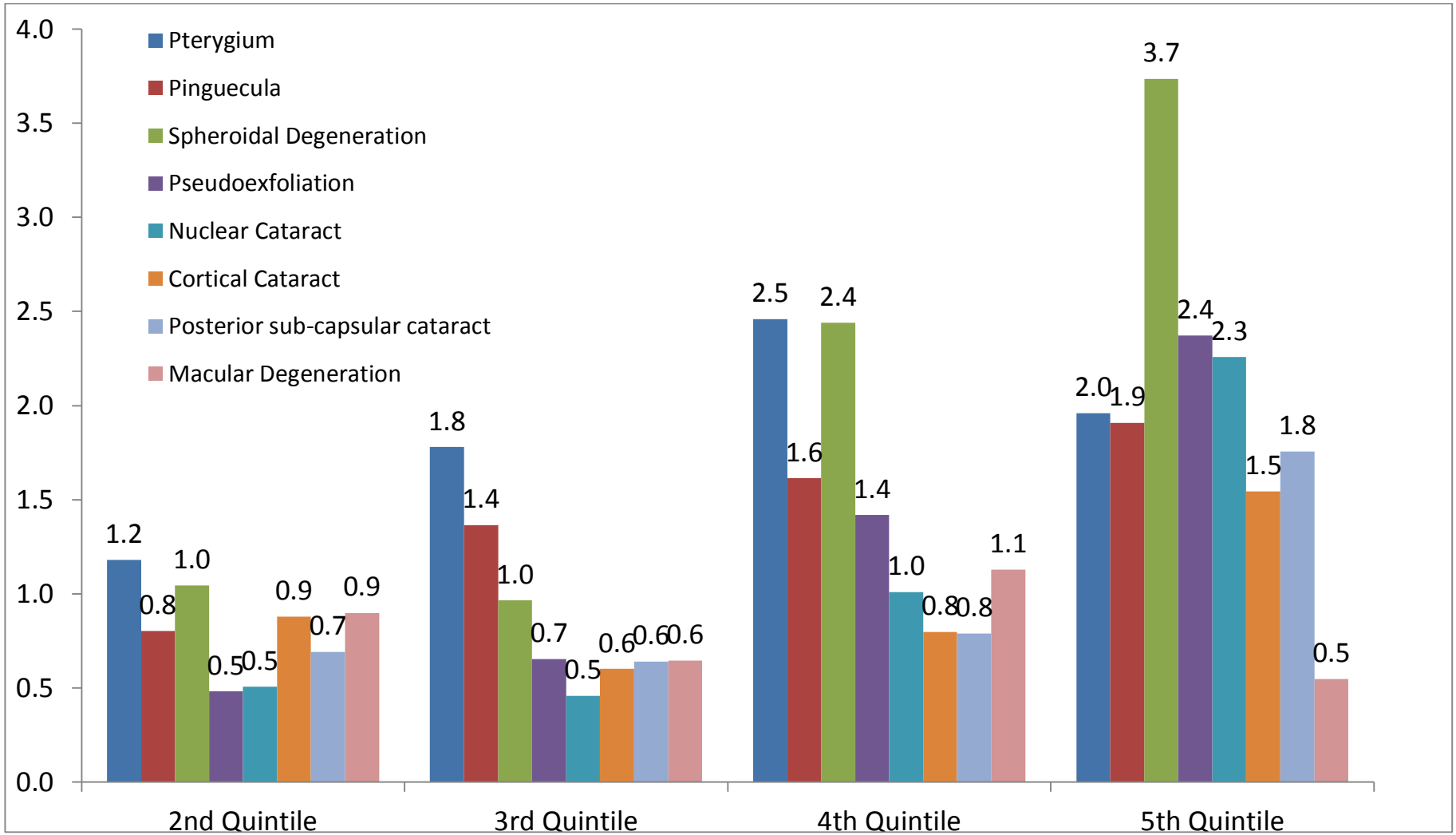


Figure 5.2.3.1: The risk for the disease per quintiles of UV exposure levels

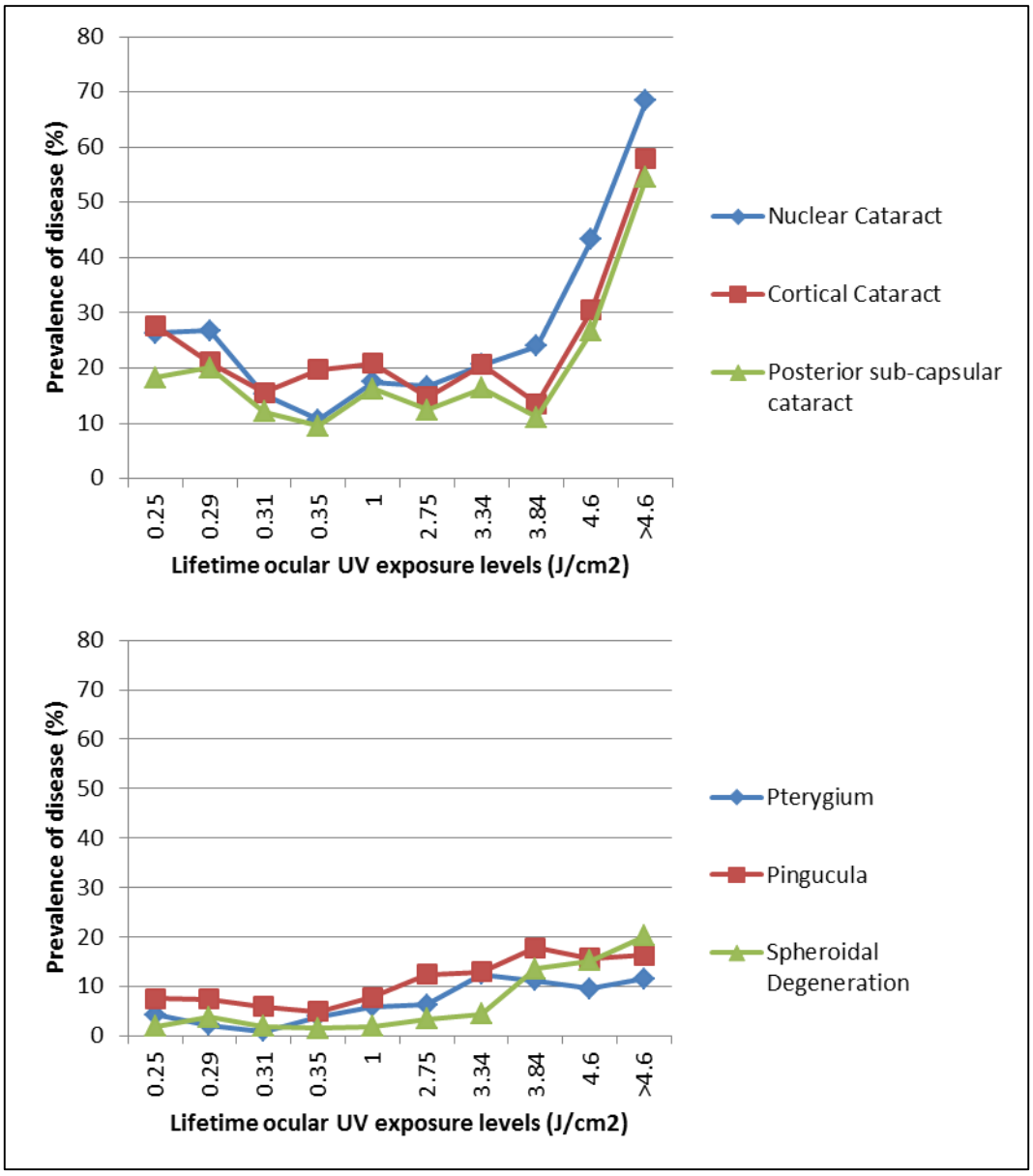


Figure 5.2.3.2: The prevalence of the disease with lifetime ocular UV exposure levels

5.2.4 Discussion

To the best of our knowledge this is the first study describing the difference in lifetime ocular UV exposure in the rural and urban South Indian population. The current study has used the tropospheric emission monitoring system to get the details of UV exposure and averaged it to achieve the annual UV dose for each geographic location (www.temis.nl). Use of internet based system is described here which can be used in epidemiological studies to estimate lifetime personal UV exposure levels.

The Chennai Glaucoma Study and The Chennai Eye Disease Incidence Study was conducted to estimate the prevalence of Glaucoma and incidence of eye disease in south Indian population. The response rate was found to be 81.3% from the eligible subjects. This is comparable to other population based studies. The major reason for non-response by study participant's for the follow-up study was because of migration to distant locations/ Migration without any contact information. The study subjects migrated in and around Chennai were invited for evaluations and participated in the examination.

When we analyzed the difference among participants and non-participants in the study, we found non participants were older and thus bringing them to base hospital was a tougher task. We did not find any gender variation in participation. We found that rural subjects participated more than the urban subjects. This could be because of lack of eye care services in rural areas. We found that non-participants are more likely to be diabetic and hypertensive, perhaps the co-morbidity

makes them avail services from their personal physician and hence they were less willing to participate. There is also a possibility that because of the co-morbidity they could not travel to the base hospital.

Variations in the UV exposure levels with geographical locations are showed in many studies(Taylor 1989; Hiller et al. 1977; Lucas et al. 2015; Wang et al. 2014). We also noted a significant difference in the UV exposure levels among different cities in India. The UV Dose of Indian cities was almost equal when we analyzed its mean value. There was a uniform trend in the spread of UV data in Central and South India. In North India there was a different trend noted with Chandigarh. This could be because of lesser cloud cover over this area. When we analyzed the cities such as Chennai, Mumbai and Delhi, there was a wide variation in the UV doses. In Delhi the UV dose had wide variation as during the month of December i.e. in winter it goes down to the lowest. This variation is not noted in Chennai. This could be because of its location closer to equator.

The current study determined the UV exposure levels with the details of migration by each individual. This will account for any geographical variation and exposure in those specific regions. The migration was less among the rural population. They were more located in the same region of birth place (Fig. 5.2.2.1). Majority of the subjects in the current study had less than one migration in their lifetime.

The proportions of females were higher compared to males in the current study. This is similar to the base study the CGS and CEDIS. Only 53.1 % of rural subjects were using spectacles whereas it was

81.6% among urban subjects. Only 1.2% of rural subjects had a history of using spectacles at younger age (Less than 35 years) whereas 12.7% of urban subjects wore spectacles before 35 years of age. This could be because of low prevalence of refractive error among rural subjects (Raju et al. 2004). There is also a possibility of poor eye care seeking behaviour among rural subjects due to lack of proper health centres in remote regions. Among those who were wearing spectacles, only 18% of rural and 40.7% among urban were using it regularly. This is due to lack of awareness about spectacle usage among rural subjects (Raju et al. 2004).

We found a significant difference of median lifetime ocular UV exposure levels among the rural (3.35, IQR: 1.98) and urban population (0.33, IQR: 0.11) (p value, <0.001) and also among males and females, 3.56, IQR (2.24) and 3.21 (IQR 1.88) respectively (p value, <0.001) of rural and male and female, 0.35 IQR (1.61) and IQR 0.31 (0.08) of urban respectively (p value <0.001). We also found that the proportion of subjects in higher quintiles were higher among rural when compared to urban population. Our study showed that urban females are exposed to lower level of UV exposure when compared with rural females. This difference could be explained based on the nature of work of the individuals. Rural women are involved in agricultural work and are exposed to high levels of UV exposure whereas most of the urban females were home makers or indoor workers.

The occupational status as outdoor and indoor workers clearly maps the UV exposure levels in the current study. It is found that the outdoor

workers are in the higher levels of UV exposure levels both in rural and urban regions. (Rosenthal et al. 1988)

The risk for the diseases for pinguecula, pterygium and spheroidal degeneration increased from 4th quintile and for other disease such as cataracts (Nuclear, Cortical and Posterior sub-capsular cataract), Pseudoexfoliation increased from 5th quintile of UV exposure levels. Macular degeneration did not show an association.

5.3 Ocular Surface disorders

The ocular surface disorders such as pterygium, pinguecula and spheroidal degenerations are discussed in this thesis. The presence of these surface disorders is documented at the baseline and the follow-up visits by the clinicians. The prevalence, incidence association with age and gender, risk factors and associations with lifetime ocular UV exposure are discussed in this section.

5.3.1 Prevalence and incidence of ocular surface disorders

The prevalence of ocular surface disorders among male and female in rural and urban population is listed in table (5.3.1.1). The prevalence and the incidence of ocular surface disorders among rural and urban population with age group are shown in the figure (5.3.1.1). The age and gender adjusted prevalence are calculated and tabulated in table (5.3.1.2).

Table 5.3.1.1: The prevalence of ocular surface disorders among males and females in rural and urban population

Ocular Surface disorder	Age Group (In years)	Rural		Urban		Total	
		Males (%)	Females (%)	Males (%)	Females (%)	Males (%)	Females (%)
Pterygium	40-49	11.0	10.2	2.1	1.4	7.1	6.3
	50-59	6.9	13.0	0.8	1.0	4.2	7.5
	60-69	9.9	16.0	5.6	3.2	7.5	8.7
	>70	9.3	8.1	5.3	0.0	6.9	4.1
	Total	9.1	11.9	3.4	1.6	6.3	7.0
Pinguecula	40-49	10.2	19.6	7.2	4.6	8.9	13.0
	50-59	19.5	13.0	7.9	5.7	14.3	9.6
	60-69	10.8	16.0	7.0	6.5	8.7	10.6
	>70	3.7	13.5	9.2	2.8	6.9	8.2
	Total	12.9	16.4	7.7	5.3	10.3	11.1
Spheroidal Degeneration	40-49	8.7	4.7	3.1	0.0	6.3	2.6
	50-59	11.9	9.9	0.0	1.0	6.6	5.8
	60-69	22.5	13.8	1.4	1.6	10.6	6.9
	>70	25.9	16.2	9.2	2.8	16.2	9.6
	Total	15.3	8.6	2.7	0.9	9.1	4.9

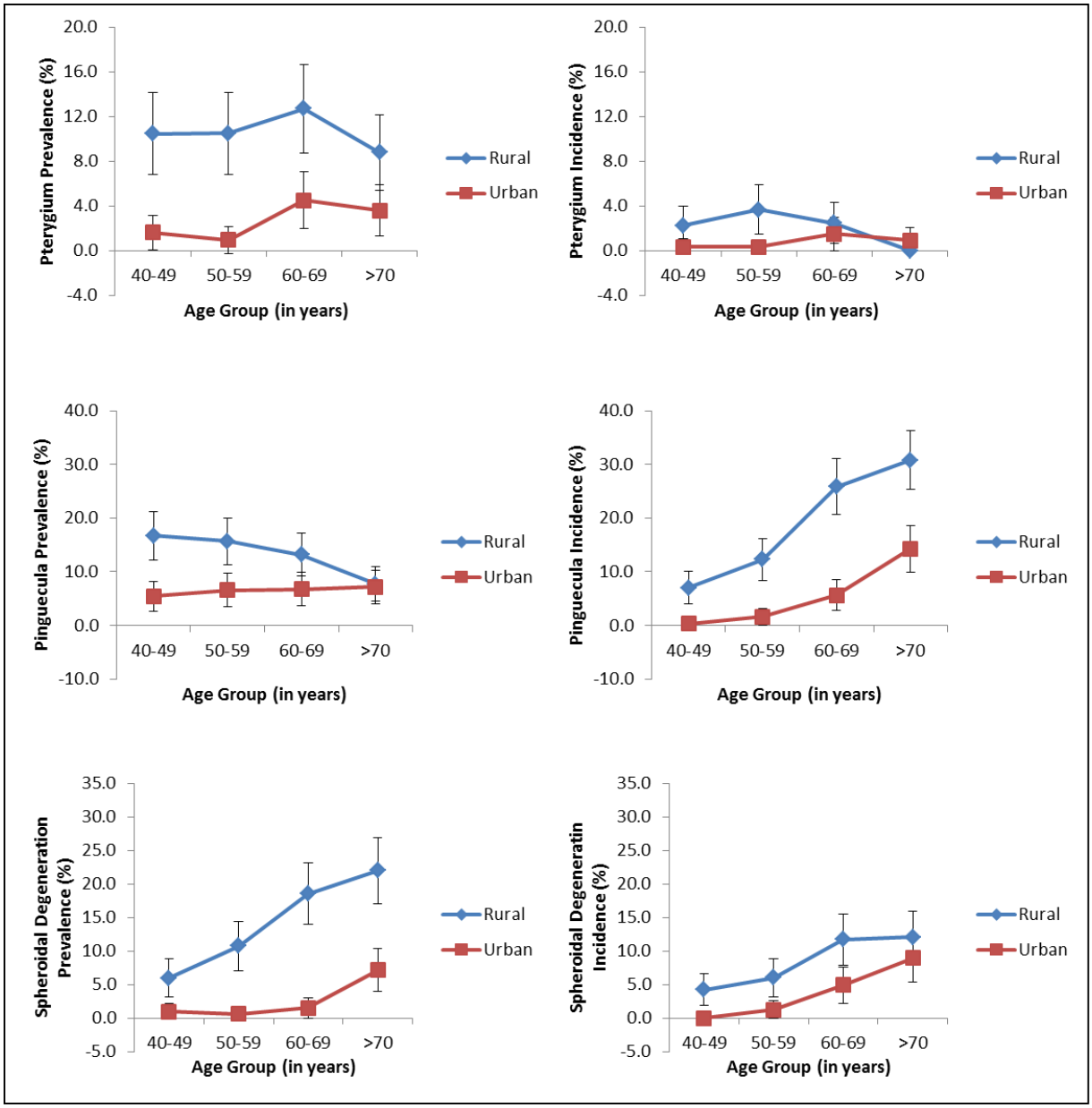


Figure 5.3.1.1: The prevalence and the incidence of ocular surface disorders among rural and urban population with age group

Table 5.3.1.2. The age and gender adjusted prevalence and incidence of ocular surface disorders in rural and urban south Indian population

	Prevalence			Incidence		
Population	**Pterygium (%) (95% CI)**	**Pinguecula (%) (95% CI)**	**Spheroidal Degeneration (%) (95% CI)**	**Pterygium (%) (95% CI)**	**Pinguecula (%) (95% CI)**	**Spheroidal Degeneration (%) (95% CI)**
Rural	10.69 (10.67 - 10.71)	14.22 (14.2 - 14.24)	11.93 (11.92 - 11.95)	2.31 (2.3 - 2.32)	15.4 (15.38 - 15.42)	7.33 (7.31 - 7.34)
Urban	2.07 (2.06 - 2.08)	6.32 (6.31 - 6.34)	1.74 (1.73 - 1.75)	0.63 (0.63 - 0.64)	3.36 (3.35 - 3.37)	2.41 (2.4 - 2.42)
Total	6.59 (6.58 - 6.6)	10.6 (10.59 - 10.61)	6.76 (6.75 - 6.77)	1.56 (1.56 - 1.57)	9.26 (9.25 - 9.28)	4.91 (4.91 - 4.92)

5.3.2 Risk factor assessment:

The risk factors for the ocular surface disorders at baseline were analyzed using logistic regression (table 5.3.2.1). These factors were adjusted for age, gender and location of residence.

Table 5.3.2.1 Baseline risk factors for the prevalence of ocular surface disorders

Variables	No of Subjects	Pterygium		Pinguecula		Spheroidal degeneration	
		OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
Age Group (in years)							
40-49	715	1.00		1.00		1.00	
50-59	701	0.96 (0.62-1.49)	0.86	0.99 (0.71-1.38)	0.99	1.65 (0.99-2.72)	0.051
60-69	472	1.56 (0.98-2.47)	0.06	0.89 (0.60-1.32)	0.56	2.89 (1.72-4.84)	<0.001
70 and above	203	1.09 (0.56-2.15)	0.79	0.66 (0.37-1.19)	0.17	4.67 (2.60-8.38)	<0.001
Population	1011	1.00		1.00		1.00	
Urban	1080	5.15 (3.28-8.09)	<0.001	2.5 (1.87-3.45)	<0.001	8.88 (5.27-14.98)	<0.001
Rural							
Gender							
Male	894	1.00		1.00		1.00	
Female	1197	1.16 (0.81-1.67)	0.41	1.03 (0.77- 1.37)	0.84	0.59 (0.41-0.86)	0.006
Smoking							
No	1704	1.00		1.00		1.00	
Yes	387	0.54 (0.28– 1.04)	0.07	0.92 (0.56 – 1.52)	0.76	1.51(0.86-2.62)	0.15
Smokeless tobacco use							
No	1754	1.00	0.016	1.00	<0.001	1.00	<0.001
Yes	337	1.64 (1.09-2.46)		1.87 (1.34- 2.62)		2.52 (1.69-3.73)	
Alcohol Use							
No	1697	1.00		1.00		1.00	
Yes	394	1.06 (0.56 – 1.99)	0.85	1.11 (0.67-1.83)	0.68	0.68 (0.39-1.21)	0.19

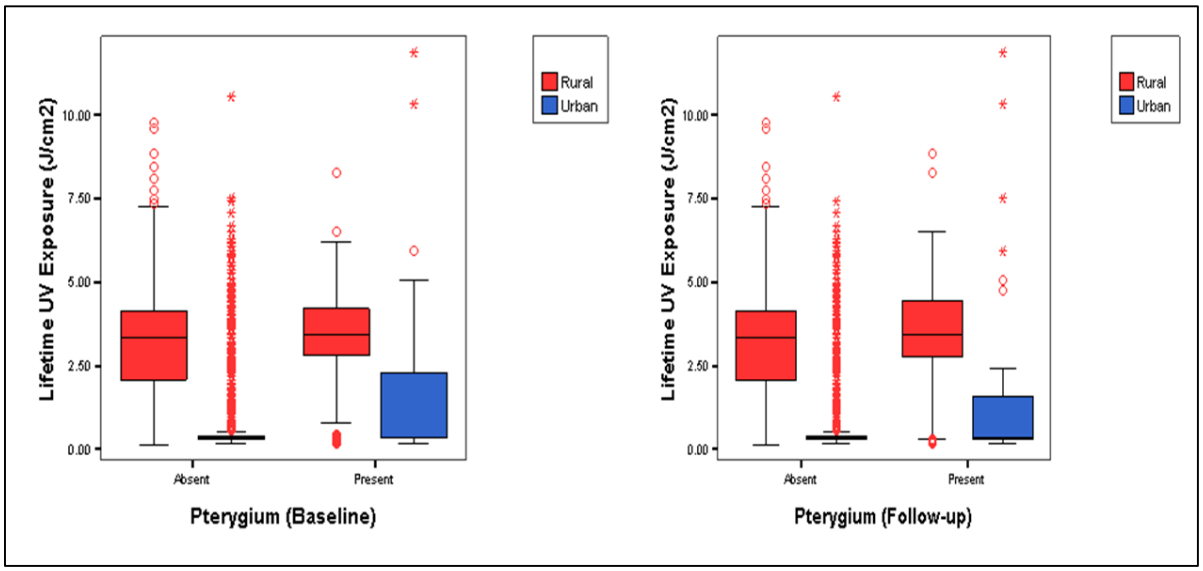
Occupation							
Indoor workers	794	1.00		1.00		1.00	
Outdoor workers	1297	0.78 (0.52-1.16)	0.22	1.07 (0.76-1.49)	0.68	0.88 (0.58-1.33)	0.54
Literacy							
Literate	1485	1.00		1.00		1.00	
Illiterate	606	1.07 (0.71 - 1.59)	0.61	1.56 (1.12 – 2.17)	0.008	1.58 (1.05-2.37)	0.02
Spectacle usage							
Yes	1398	1.00		1.00		1.00	
No	693	1.28 (0.89-1.84)	0.17	1.22 (0.91-1.64)	0.19	2.15 (1.48-3.12)	<0.001
Diabetes Mellitus							
No	1828	1.00		1.00	0.83	1.00	0.003
Yes	263	1.02 (0.54-1.94)	0.94	1.05 (0.64 – 1.71)		0.12 (0.02-0.49)	
Hypertension							
No	1255	1.00		1.00		1.00	
Yes	836	0.98 (0.66-1.47)	0.95	1.13 (0.82-1.54)	0.45	1.46 (0.98-2.17)	0.06
Lifetime ocular UV exposure	2091	1.14 (1.02 – 1.26)	0.016	1.17 (1.07-1.28)	<0.001	1.26 (1.14-1.39)	<0.001
BMI							
Normal	959	1.00		1.00		1.00	
Underweight	339	0.87 (0.5-1.4)	0.58	1.1 (0.7-1.6)	0.69	2.2 (1.5-3.3)	<0.001
Overweight	463	0.58 (0.3-1.1)	0.08	1.0 (0.7-1.5)	0.94	0.45 (0.2-1.0)	0.05
Obese	147	0.15 (0.2-1.1)	0.06	0.9 (0.4-1.8)	0.69	0.28 (0.03-2.1)	0.224
Refractive Error Shift							
No change	693	1.00		1.00		1.00	
Myopic Shift	555	1.21 (0.75-1.92)	0.44	1.21 (0.84-1.72)	0.29	1.55 (0.93-2.59)	0.09
Hyperopic Shift	558	1.05 (0.63-1.73)	0.84	0.94 (0.64-1.38)	0.77	1.27 (0.73-2.24)	0.39

All the variables in multivariate logistic regression were adjusted for age, gender and population. Smoking was adjusted for smokeless tobacco and alcohol use. Education and occupation were adjusted to each other. Refractive error shift was done only for phakic eyes.

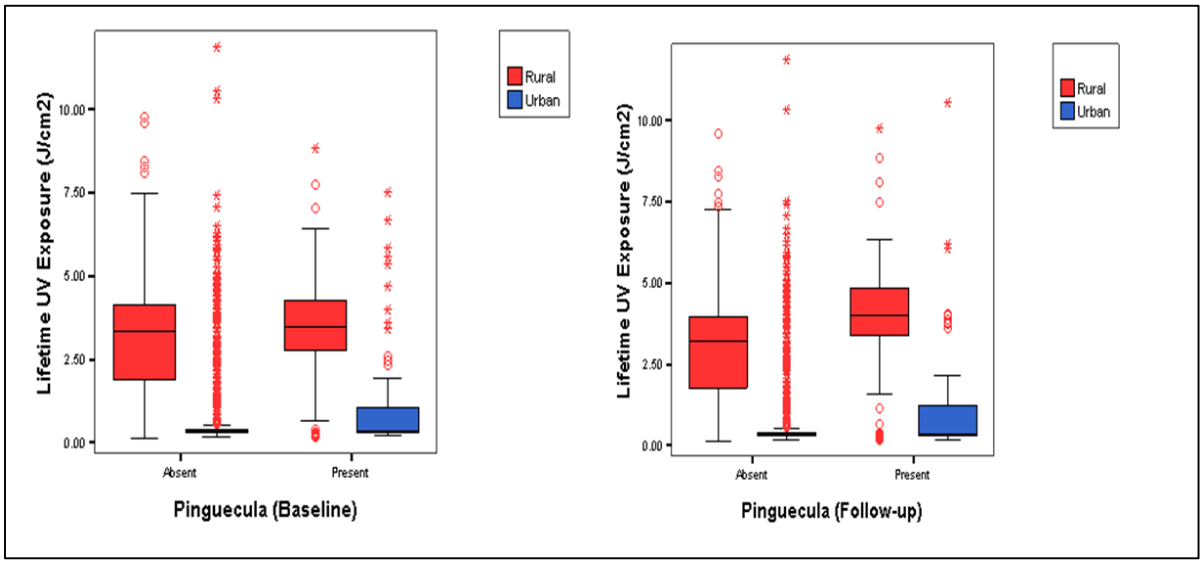
5.3.3 Association with lifetime ocular UV exposure:

The presence of ocular surface disorders was compared with the estimated lifetime ocular UV exposure. This was also categorised based on the population. The figure 5.3.3.1a to 5.3.3.1c summarises the association between the presence of the disease and lifetime ocular UV exposure.

a. Pterygium



b. Pinguecula



c. Spheroidal Degeneration

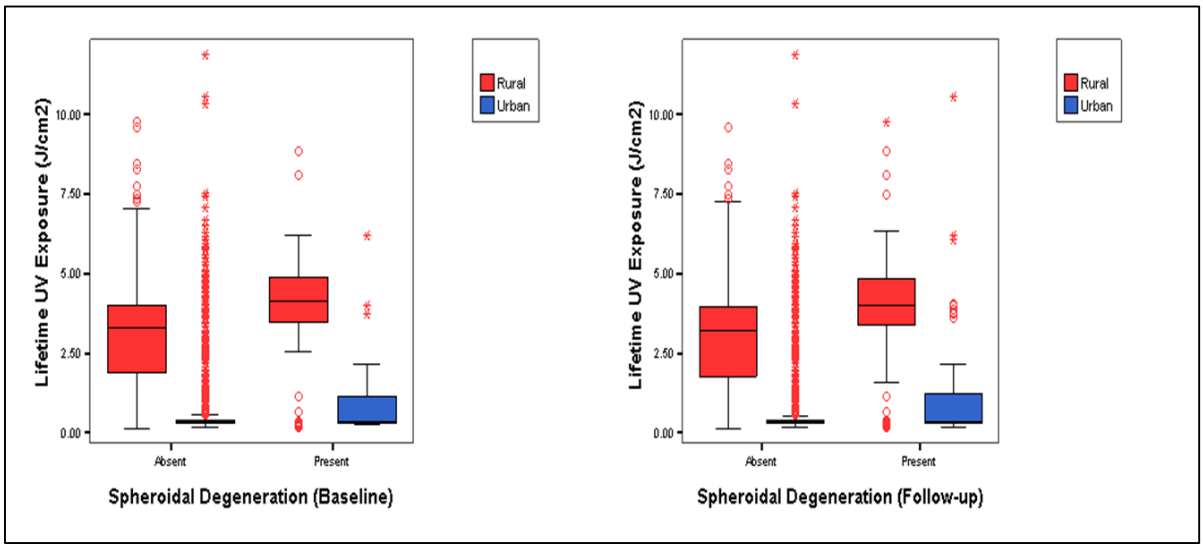


Figure 5.3.3.1: The median lifetime ocular UV exposure levels in subjects with and without ocular surface disorders among rural and urban population at baseline and follow-up

5.3.4 Discussion

The prevalence of pterygium in the current study was 6.7% (95% CI: 5.6 to 7.8), in rural and urban population was 10.7% (95% CI: 8.9 to 12.6) and 2.4% (95% CI: 1.4 to 3.3) respectively. The age and gender adjusted prevalence for pterygium was significantly different in the rural and urban populations. These results are similar to those reported by the Melbourne visual impairment study where rural residents had a higher prevalence of pterygium (6.7%) (McCarty et al. 2000). A similar trend was noted in the incidence of the pterygium in the current study population. This difference could be due to differences in the nature of work between the rural and urban populations. Most of our rural subjects were outdoor workers as they were involved in agricultural work and that could explain the wide differences in prevalence among the rural and urban population. We did not find any differences in prevalence with gender. This was similar to the equivocal evidence reported by other studies between gender and the development of pterygium (Saw & Tan 1999; Nemesure et al. 2008; Pham et al. 2005). Even after accounting for the protective effect of using a hat or turban while calculating lifetime UV exposure, there was a significant difference noted. This could possibly be attributed to the way that the turban is tied, as this does not provide adequate shielding of the ocular surface from the sunrays. The risk factors for pterygium were rural residence, smokeless tobacco use and increased lifetime ocular UV exposure.

The prevalence of pinguecula in the current study was 10.8% (95% CI: 9.4 to 12.1), in rural and urban population was 14.9% (95% CI: 12.8 to 17.0) and 6.3% (95% CI: 4.8 to 7.8) respectively. The prevalence of

pinguecula in our population was lower than reports from other countries (Viso et al. 2011; Panchapakesan et al. 1998). The prevalence in rural central India was noted to be 2.4% which is much lower than reported in the current study (Singh et al. 1997). This difference from other countries could be attributed to the age at presentation of pinguecula in the current study population. As we have included subjects 40 years or older in age we could not measure prevalence in younger age groups. Hussain et al. reported the prevalence of pinguecula to be higher at an earlier age (15–29 years) with decreased prevalence with increasing age (Hussain et al. 2004). We also report a similar trend of decreasing prevalence of pinguecula with increasing age. This difference could be attributed to the pathophysiology of both conditions, since a pinguecula can eventually develop into a pterygium. The pinguecula could act as the triggering factor in the development of pterygium (Detorakis & Spandidos 2009). This could account for the decreased prevalence of pinguecula with age. The risk factors for pinguecula were rural residence, smokeless tobacco use, illiterates and increased lifetime ocular UV exposure.

The prevalence of spheroidal degeneration in the current study was 6.7% (95% CI: 5.6 to 7.8), in rural and urban population was 11.4% (95% CI: 9.5 to 13.3) and 1.7% (95% CI: 0.9 to 2.5) respectively. The age and gender adjusted prevalence for spheroidal degeneration was significantly different in the rural and urban populations. The prevalence of spheroid degeneration is much lower in the urban than the rural population. This is similar to other studies (Bartholomew 1977; Gray et al. 1992). The prevalence of spheroidal degeneration among South African Negroes of the Pondo tribe was 7.0% They also found that it is

more prevalent in men (9.9%) than in women (4.3%) and the prevalence increased with age over 50 for both gender (Bartholomew 1977). The risk factors for spheroidal degeneration were increasing age, rural residence, smokeless tobacco use, illiterates, non-use of spectacles, presence of diabetes mellitus and increased lifetime ocular UV exposure.

To the best of our knowledge the current study reports for the first time the lifetime ocular UV exposure in South India. We have used the well-established Melbourne visual impairment model to calculate UV exposure (McCarty et al. 1996). We found those with a higher lifetime ocular UV exposure to be at 2.5 times greater risk for the development of pterygium, similar to the findings from an epidemiological study conducted in Victoria. McCarty et al. reported that the lifetime ocular sun exposure was an independent risk factor for pterygium (OR: 1.63, 95% CI: 1.18–2.25); the attributable risk of sunlight for pterygium was estimated to be 43.6% (95% CI: 42.7–44.6) (McCarty et al. 2000). In another report Sekelj et al. have shown that the recurrence of pterygium in a UV exposed group was higher at 27% compared to 10% in a UV unexposed group. UV exposure appears to be significantly associated with pterygium formation (Sekelj et al. 2007). Molecular studies have also shown a relationship between UV irradiation and cyclooxygenase-2 expression in the cytoplasm of keratinocytes from the cytoplasm of pterygium specimens (Maxia et al. 2009). We have found association of pinguecula with increased lifetime ocular UV exposure levels. We have noted 1.6 times increased risk with UV exposure levels beyond 4th quintile. The association of spheroidal degenerations with UV exposure is been reported in many studies (Johnson 1981; Bartholomew 1977;

Gray et al. 1992). In spheroidal degenerations, the corneal deposits are thought to be derived from plasma proteins, which diffuse into the normal cornea. These deposits are photochemically degraded by excessive exposure to ultra-violet light (UV). The degraded protein material gets deposited in the superficial stroma (Gray et al. 1992). The loss of keratocytes were noticed in the UVR induced apoptotic corneal stroma of mice eyes(Newkirk et al. 2007). This shows evidence of damage on the ocular surface with long term exposure to UV Radiation.

Spectacles are known to significantly reduce the amount of UV radiation reaching the eye. Non-use of spectacles in the current study subjects had higher risk for the development of spheroidal degeneration and not associated with pterygium and pinguecula. In our baseline study we found an association with the non-use of spectacles with pterygium and pinguecula (Asokan et al. 2012). The Barbados Eye study has also shown that use of spectacles is protective against the development of pterygium (Luthra et al. 2001). Our rural population have a low prevalence of use of refractive correction, possibly due to the difference in the penetration of ophthalmic services or differences in the perceived need for the use of spectacles in both populations (Raju et al. 2004). Awareness about the usage of glasses especially among outdoor workers could help in reducing the occurrence of spheroidal degeneration.

5.4 Pseudoexfoliation:

The presence of pseudoexfoliation in the ocular structures such as cornea, pupillary border and lens surface are documented at the baseline and the follow-up visits by the clinicians. The prevalence, incidence, association with age and gender, risk factors and associations with lifetime ocular UV exposure are discussed in this section.

5.4.1 Prevalence and incidence of pseudoexfoliation

The prevalence of pseudoexfoliation among male and female in rural and urban population is listed in table (5.4.1.1). The prevalence and the incidence of pseudoexfoliation among rural and urban population with age group are shown in the figure (5.4.1.1). The age and gender adjusted prevalence and incidence are calculated and tabulated in table (5.4.1.2).

Table 5.4.1.1: The prevalence of pseudoexfoliation among males and females in rural and urban population

Age Group (in years)	Pseudoexfoliation Prevalence					
	Rural		Urban		Total	
	Males (%)	Females (%)	Males (%)	Females (%)	Males (%)	Females (%)
40-49	0.0	0.4	0.0	0.0	0.0	0.2
50-59	3.1	1.8	1.6	0.5	2.4	1.2
60-69	7.2	5.3	4.9	1.6	5.9	3.2
>70	13.0	2.7	11.8	13.9	12.3	8.2
Total	4.4	1.7	4.1	1.4	4.3	1.6

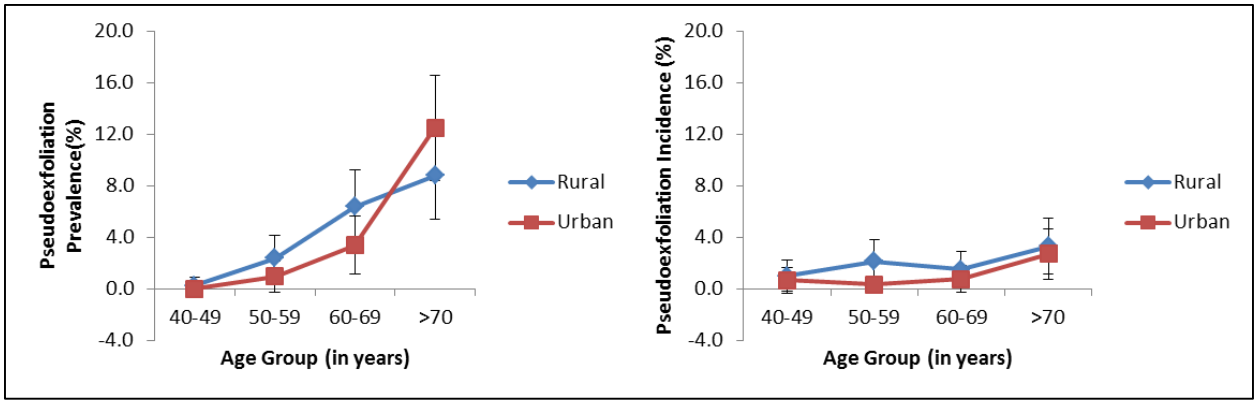


Figure 5.4.1.1: The prevalence and the incidence of pseudoexfoliation among rural and urban population with age group

Table 5.4.1.1: The age and gender adjusted prevalence and incidence of pseudoexfoliation in rural and urban south Indian population

Population	Pseudoexfoliation Prevalence (%) (95% CI)	Pseudoexfoliation Incidence (%) (95% CI)
Rural	2.98 (2.98 - 2.99)	1.68 (1.68 - 1.69)
Urban	2.37 (2.36 - 2.37)	0.82 (0.82 - 0.83)
Total	2.64 (2.64 - 2.65)	1.28 (1.27 - 1.28)

5.4.2 Risk factor assessment:

The risk factors for the pseudoexfoliation was analyzed using logistic regression (table 5.4.2.1). These factors were adjusted for age, gender and location of residence.

Table 5.4.2.1 Baseline risk factors for the prevalence of pseudoexfoliation

Variables	No of Subjects	Pseudoexfoliation	
		OR (95% CI)	p value
Age Group (in years)			
40-49	715	1.00	
50-59	701	11.83 (1.53-91.37)	0.018
60-69	472	32.23 (4.31-241.28)	0.001
70 and above	203	76.24 (10.12-574.25)	<0.001
Population			
Urban	1011	1.00	
Rural	1080	1.42 (0.83-2.45)	0.201
Gender			
Male	894	1.00	0.41
Female	1197	0.57 (0.32-1.01)	
Smoking			
No	1704	1.00	
Yes	387	NA	0.99
Smokeless tobacco use	1754	1.00	
No	337	NA	0.99
Yes			
Alcohol Use			
No	1697	1.00	
Yes	394	NA	0.99

Occupation			
Indoor workers	794	1.00	
Outdoor workers	1297	0.57 (0.32-1.02)	0.06
Literacy			
Literate	1485	1.00	
Illiterate	606	2.98 (1.55 – 5.75)	0.001
Spectacle usage			
Yes	1398	1.00	
No	693	1.56 (0.86-2.82)	0.14
Diabetes Mellitus			
No	1828		
Yes	263	0.99 (0.46-2.14)	0.99
Hypertension			
No	1255	1.00	
Yes	836	0.81 (0.45-1.44)	0.47
Lifetime ocular UV exposure	2091	1.20 (1.05 – 1.37)	0.006
Nuclear Cataract			
No	1533	1.00	
Yes	558	5.46 (2.45-12.17)	<0.001
Cortical Cataract			
No	1586	1.00	
Yes	505	1.12 (0.61-2.06)	0.71
Posterior sub-capsular cataract			
No	1684	1.00	
Yes	407	1.62 (0.83-3.14)	0.15
BMI			
Normal	959	1.00	
Underweight	339	1.41 (0.70-2.83)	0.336
Overweight	463	0.55 (0.23-1.33)	0.189
Obese	147	0.32 (0.04-2.47)	0.274

Refractive Error Shift			
No change	693	1.00	
Myopic Shift	555	1.85 (0.71-4.78)	0.20
Hyperopic Shift	558	1.99 (0.76-5.18)	0.15

All the variables in multivariate logistic regression were adjusted for age, gender and population. Smoking was adjusted for smokeless tobacco and alcohol use. Education and occupation were adjusted to each other. Refractive error shift was done only for phakic eyes.

5.4.3 Association with lifetime ocular UV exposure:

The presence of pseudoexfoliation was compared with the estimated lifetime UV exposure. This was also categorised based on the population. The figure 5.4.3.1 summarises the association between the presence of the disease and lifetime ocular UV exposure at baseline and follow-up.

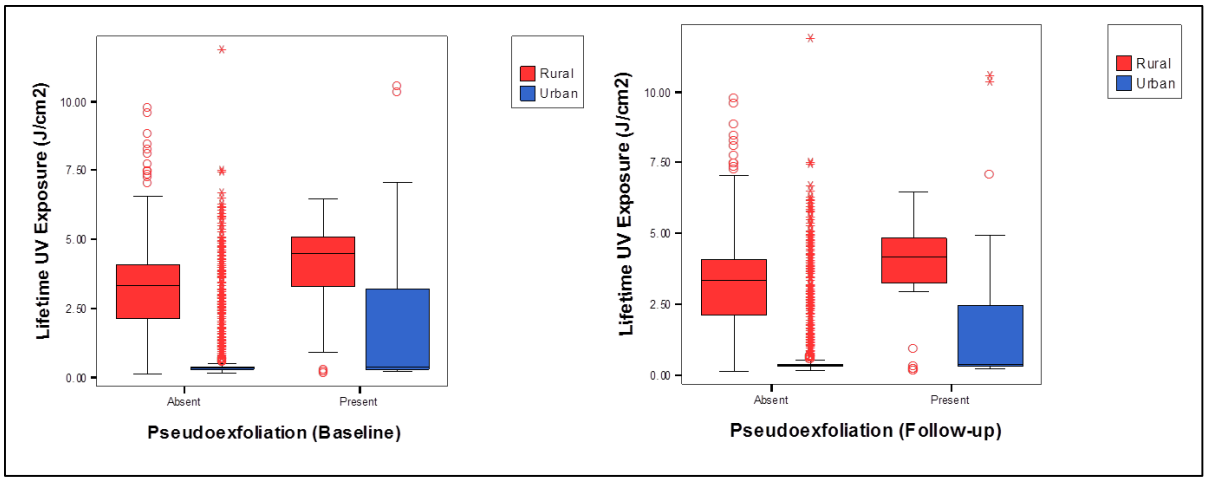


Figure 5.4.3.1: The median lifetime ocular UV exposure levels in subjects with and without pseudoexfoliation among rural and urban population at baseline and follow-up

5.4.4 Discussion:

The prevalence of pseudoexfoliation in the current study was 2.7% (95% CI: 2.0 to 3.4), in the rural and urban population it was 2.9% (95% CI: 1.9 to 3.9) and 2.6% (95% CI: 1.6 to 3.5) respectively. The age and gender adjusted prevalence showed higher rural prevalence than in urban. There are notable variations in the reported prevalence of PEX. The prevalence of PEX is reported in India from four population based studies. (Arvind et al. 2003; Thomas et al. 2005; Krishnadas R, Nirmalan PK 2003; Jonas et al. 2013). The prevalence of PEX in south India was 3.8% (Arvind et al. 2003), 6.0% (Krishnadas R, Nirmalan PK 2003), 3.01% (Thomas et al. 2005) and in central rural India it was only 1.96% (Jonas et al. 2013). The prevalence varied across geographical locations. The reported prevalence in the Finnish population was 8.1 % (above 50 years) (Forsman et al. 2007), 10.7 % in Icelanders in Sweden (Arnarsson et al. 2007), 11.9% in Greece (Anastasopoulos et al. 2011), 7.7% among black South Africans (Rotchford et al. 2003). In Australia the prevalence varied from 0.98% to 4.7% (Mccarty & Taylor 2000; Mitchell et al. 1999; Landers et al. 2012). From Asia the figures were – 3.4% in Myanmar(Abdul-Rahman et al. 2008), 1.1% in Sri Lanka (Rudkin et al. 2008), 3.4% in Japan (Miyazaki et al. 2005) and 5.8% in north China (Foster & Seah 2005).

The risk factors for PEX were increasing age, illiterate, increased lifetime ocular UV exposure and presence of nuclear cataract. Increasing age is reported to be the common risk factors among all the studies.

Nuclear cataract is known to be associated with PEX. Cataract development is possibly linked to the ocular ischemia, hypoxia and

reduced protection against ultraviolet rays due to lower levels of ascorbic acid in the aqueous humor (Naumann et al. 1998). The current study also showed an association with PEX by 5.46 times. There was no association noted with posterior sub-capsular cataract and cortical cataract.

The current study reported the association with lifetime ocular UV exposure levels. Subjects with exposure to UV radiation are 1.2 times at higher risk for the development of PEX. Stein et al have reported the effect of geographic and climatic factors on PEX in a large retrospective study involving beneficiaries in a managed-care network covering almost the entire United States of America (Stein et al. 2011). Stein et al. found that compared to those residing in the middle geographic tier, those living in the northern tier (above 42^0 N) were more likely to have PEX, conversely the prevalence was lower for the people living in the southern tier (below 37^0 N). They concluded that greater sunshine exposure and lower ambient temperatures, in summer and winter, increase the likelihood of pseudoexfoliation. Environment and the geography seem to be important associations for PEX. Pasquale et al in his study with residential history has found that the degree of weighted lifetime average residential latitude away from the equator was associated with an 11% increased odds of exfoliation syndrome (pooled odds ratio = 1.11; 95% CI: 1.05-1.17; $p < .001$) (Pasquale et al. 2014). This is similar to our results where we found away from the equator the odds increased. This geographical variation can probably partly explain the lower prevalence of PEX from central India in comparison to reports from southern India.

5.5 Cataract:

The presence of cataract was seen in dilated condition and categorised as nuclear cataract, cortical cataract and posterior sub-capsular cataract based on LOCS II at baseline and follow-up. The prevalence, incidence and progression association with age and gender, risk factors and associations with lifetime ocular UV exposure are discussed in this section.

5.5.1 Prevalence and incidence of types of cataract

The prevalence of nuclear, cortical and posterior sub-capsular cataract among males and females in the rural and urban population is listed in table (5.5.1.1). The prevalence and the incidence of all the types of cataract among rural and urban population with age group are shown in the figure (5.5.1.1). The age and gender adjusted prevalence are calculated and tabulated in table (5.5.1.2).

Table 5.5.1.1: The prevalence of types of cataract among males and females in rural and urban population

Cataract Types	Age Group (in years)	Rural		Urban		Total	
		Males (%)	Females (%)	Males (%)	Females (%)	Males (%)	Females (%)
Nuclear Cataract	40-49	5.5	11.6	7.2	4.2	6.3	8.4
	50-59	26.4	32.7	8.7	9.4	18.5	21.9
	60-69	53.2	81.9	21.7	33.1	35.4	54.1
	>70	90.7	91.9	56.6	69.4	70.8	80.8
	Total	**34.8**	**34.3**	**20.8**	**16.4**	**27.9**	**25.8**
Cortical Cataract	40-49	3.1	10.2	8.2	5.6	5.4	8.1
	50-59	17.0	29.6	10.2	14.6	14.0	22.7
	60-69	53.2	67.0	27.3	33.9	38.6	48.2
	>70	68.5	56.8	50.0	55.6	57.7	56.2
	Total	**28.2**	**28.3**	**22.1**	**18.0**	**25.2**	**23.4**
Posterior Sub-capsular Cataract	40-49	5.5	6.5	5.2	4.2	5.4	5.5
	50-59	13.8	22.0	4.7	7.8	9.8	15.4
	60-69	43.2	61.7	19.6	23.4	29.9	39.9
	>70	70.4	75.7	38.2	50.0	51.5	63.0
	Total	**25.5**	**24.3**	**15.3**	**12.5**	**20.5**	**18.7**

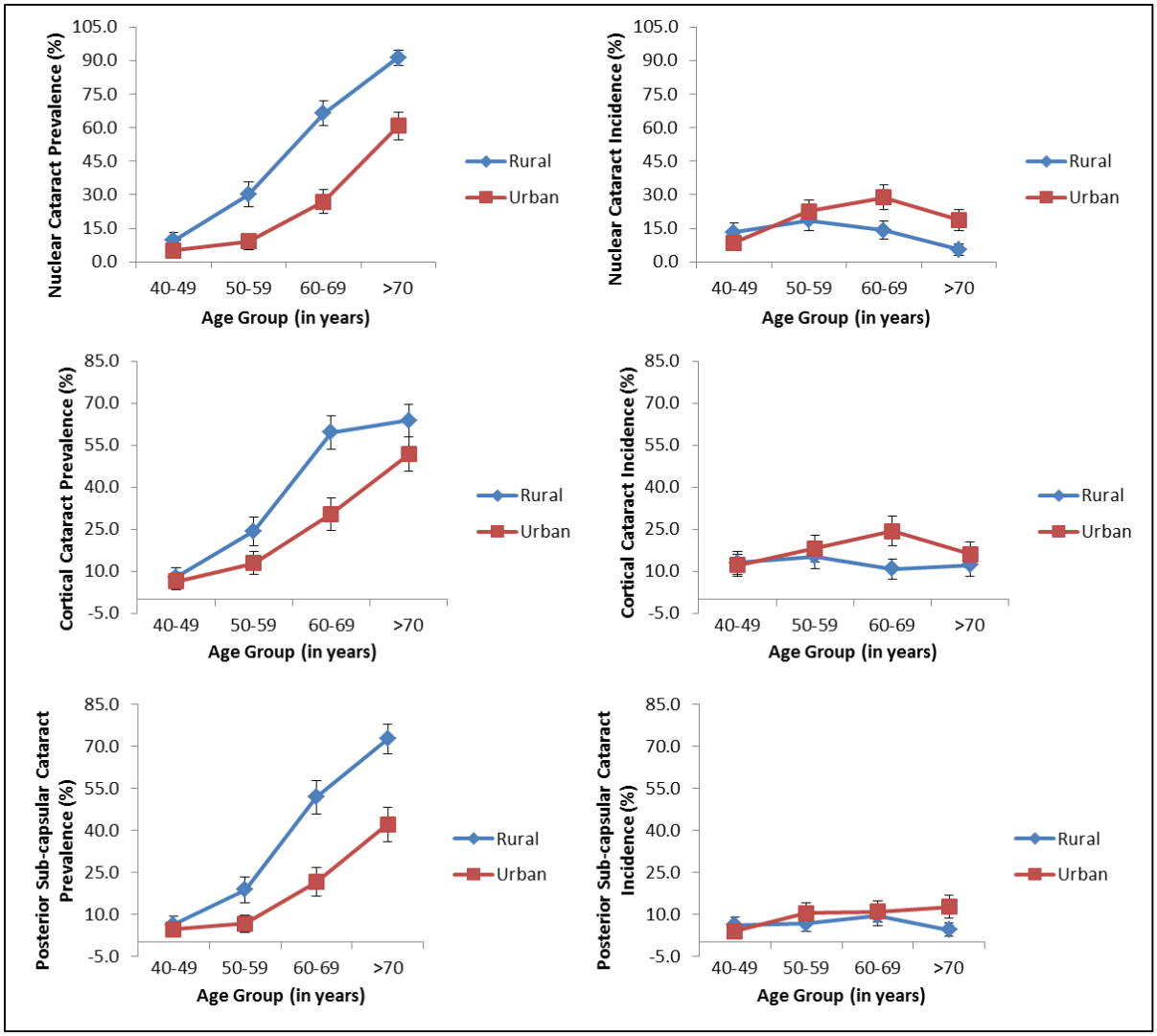


Figure 5.5.1.1: The prevalence and the incidence of all types of cataract among rural and urban population with age group

Table 5.5.1.2 The age and gender adjusted prevalence and incidence of all types of cataract in rural and urban south Indian population

	Prevalence			Incidence		
Population	**Nuclear Cataract (%) (95% CI)**	**Cortical Cataract (%) (95% CI)**	**Posterior Sub-capsular Cataract (%) (95% CI)**	**Nuclear Cataract (%) (95% CI)**	**Cortical Cataract (%) (95% CI)**	**Posterior Sub-capsular Cataract (%) (95% CI)**
Rural	36.7 (36.67 - 36.72)	29.11 (29.09 - 29.14)	27.10 (27.07 - 27.12)	13.65 (13.63 - 13.67)	12.74 (12.72 - 12.75)	6.36 (6.35 - 6.38)
Urban	17.19 (17.17 - 17.21)	18.04 (18.02 - 18.07)	12.72 (12.7 - 12.73)	17.2 (17.18 - 17.22)	16.18 (16.16 - 16.2)	7.64 (7.63 - 7.66)
Total	26.37 (26.35 - 26.39)	23.05 (23.03 - 23.07)	19.34 (19.32 - 19.35)	15.86 (15.85 - 15.88)	14.77 (14.75 - 14.78)	7.09 (7.08 - 7.1)

5.5.2 Risk factor assessment:

The risk factors for the types of cataract at baseline were analyzed using logistic regression (table 5.5.2.1). These factors were adjusted for age, gender and location of residence.

Table 5.5.2.1 Baseline risk factors for the prevalence of all types of cataract

Variables	No of Subjects	Nuclear Cataract		Cortical Cataract		Posterior Sub-capsular Cataract	
		OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
Age Group (in years)							
40-49	715	1.00		1.00		1.00	
50-59	701	3.6 (2.5-4.9)	<0.001	3.2 (2.3-4.6)	<0.001	2.8 (1.9-4.2)	<0.001
60-69	472	15.8 (11.0-22.8)	<0.001	12.5 (8.8-17.8)	<0.001	12.9 (8.7-19.2)	<0.001
70 and above	203	72.8 (45.3-116.9)	<0.001	23.5 (15.4-35.7)	<0.001	34.6 (21.8-54.8)	<0.001
Population							
Urban	1011	1.00		1.00		1.00	
Rural	1080	4.5 (3.5-5.8)	<0.001	2.2 (1.8-2.9)	<0.001	3.2 (2.5-4.2)	<0.001
Gender							
Male	894	1.00		1.00		1.00	
Female	1197	1.7 (1.3-2.1)	<0.001	1.5 (1.2- 1.9)	0.001	1.5 (1.2-1.9)	0.001
Smoking							
No	1704	1.00		1.00		1.00	
Yes	387	1.3 (0.9– 1.9)	0.20	0.9 (0.7 – 1.5)	0.93	1.2 (0.73-1.87)	0.39
Smokeless tobacco use							
No	1754	1.00	<0.001	1.00	0.115	1.00	0.006
Yes	337	1.9 (1.5-2.6)		1.3 (0.9- 1.7)		1.5 (1.1-2.1)	

Alcohol Use							
No	1697	1.00		1.00		1.00	
Yes	394	1.1 (0.7 – 1.6	0.75	0.7 (0.5-1.1)	0.09	0.7 (0.5-1.2)	0.31
Occupation							
Indoor workers	794	1.00		1.00		1.00	
Outdoor workers	1297	0.6 (0.5-0.8)	<0.001	0.8 (0.6-1.0)	0.105	0.7 (0.5-0.9)	0.010
Literacy							
Literate	1485	1.00		1.00		1.00	
Illiterate	606	2.7 (2.0-3.6)	<0.001	1.3 (0.9 – 1.7)	0.065	2.1 (1.5-2.8)	<0.001
Spectacle usage							
Yes	1398	1.00		1.00		1.00	
No	693	2.6 (1.8-3.1)	<0.001	1.1 (0.8-1.4)	0.66	1.6 (1.2-2.1)	<0.001
Diabetes Mellitus							
No	1828	1.00		1.00		1.00	
Yes	263	0.6 (0.5-0.9)	0.02	0.9 (0.7 – 1.3)	0.76	0.6 (0.4-0.9)	0.015
Hypertension							
No	1255	1.00		1.00		1.00	
Yes	836	1.0 (0.8-1.3)	0.75	0.9 (0.7-1.2)	0.54	1.2 (0.9-1.6)	0.16
Lifetime ocular UV exposure	2091	1.3 (1.2 – 1.4)	<0.001	1.1 (1.0-1.2)	<0.001	1.2 (1.2-1.3)	<0.001
BMI							
Normal	959	1.00		1.00		1.00	
Underweight	339	2.1 (1.5-2.9)	<0.001	1.2 (0.8-1.6)	0.31	1.5 (1.1-2.1)	0.02
Overweight	463	0.4 (0.3-0.6)	<0.001	0.9 (0.7-1.3)	0.93	0.9 (0.6-1.3)	0.64
Obese	147	0.5 (0.3-0.9)	0.03	0.8 (0.5-1.4)	0.57	0.9 (0.5-1.6)	0.75
Refractive Error Shift							
No change	693	1.00		1.00		1.00	
Myopic Shift	555	3.3 (2.3-4.6)	<0.001	1.6 (1.2-2.1)	0.003	2.1 (1.4-3.1)	<0.001
Hyperopic Shift	558	1.7 (1.2-2.5)	0.007	1.2 (0.9-1.7)	0.218	1.9 (1.3-3.0)	0.001

All the variables in multivariate logistic regression were adjusted for age, gender and population. Smoking was adjusted for smokeless tobacco and alcohol use. Education and occupation were adjusted to each other. Refractive error shift was done only for phakic eyes.

5.5.3 Risk factor assessment for cataract progression:

Out of 2091 subjects, 273 (13.1%) and 12 (0.6%) had cataract surgery done with and without IOL implantation respectively. Those who had cataract surgery at follow-up were considered to have progressed for analysis. There were 500 subjects (23.9%), 918 (43.9%) and 540 (25.8%) with progression of nuclear, cortical and posterior sub-capsular cataract respectively. The risk factors at baseline for progression of all types of cataract were analyzed using logistic regression (table 5.5.3.1). These factors were adjusted for age, gender and location of residence.

Table 5.5.3.1 Baseline risk factors for the progression of all types of cataract

Variables	No of Subjects	Nuclear Cataract		Cortical Cataract		Posterior Sub-capsular Cataract	
		OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
Age Group (in years)							
40-49	715	1.00		1.00		1.00	
50-59	701	2.7 (1.9-3.6)	<0.001	2.2 (1.7-2.7)	<0.001	2.3 (1.7-3.1)	<0.001
60-69	472	7.4 (5.4-10.3)	<0.001	5.1 (3.9-6.6)	<0.001	7.1 (5.1-9.6)	<0.001
70 and above	203	13.6 (9.2-20.1)	<0.001	8.1 (5.7-11.6)	<0.001	12.4 (8.5-18.1)	<0.001
Population							
Urban	1011	1.00		1.00		1.00	
Rural	1080	1.6 (1.3-1.9)	<0.001	1.2 (1.0-1.5)	0.023	1.9 (1.5-2.3)	<0.001
Gender							
Male	894	1.00		1.00		1.00	
Female	1197	1.5 (1.2-1.8)	<0.001	1.6 (1.3- 1.9)	0.001	1.4 (1.1-1.7)	0.007
Smoking							
No	1704	1.00		1.00		1.00	
Yes	387	0.8 (0.6– 1.3)	0.44	1.2 (0.8 – 1.7)	0.21	0.9 (0.6-1.3)	0.71

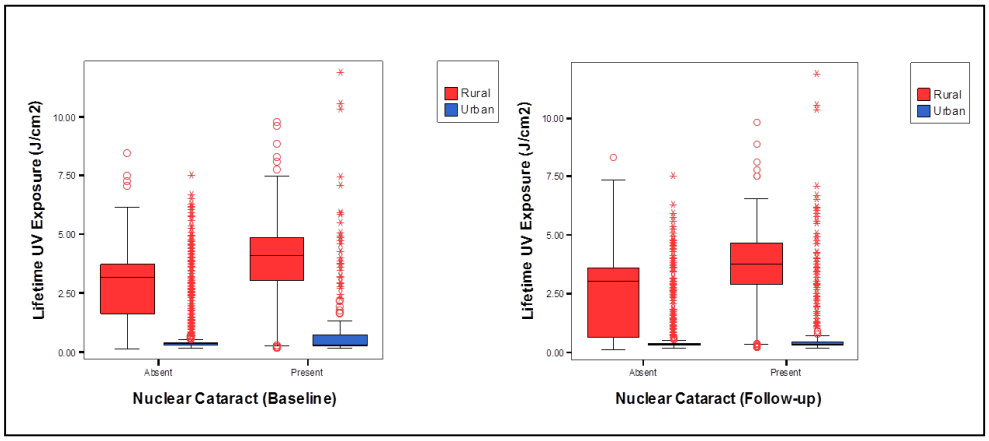
Smokeless tobacco use							
No	1754	1.00		1.00		1.00	
Yes	337	1.4 (1.1-1.8)	0.02	1.2 (0.9- 1.5)	0.22	1.6 (1.2-2.1)	0.001
Alcohol Use							
No	1697	1.00		1.00		1.00	
Yes	394	0.8 (0.5 – 1.2)	0.23	1.1 (0.7-1.5)	0.56	0.7 (0.5-1.1)	0.19
Occupation							
Indoor workers	794	1.00		1.00		1.00	
Outdoor workers	1297	0.8 (0.6-0.9)	0.05	1.0 (0.7-1.2)	0.904	0.7 (0.6-1.0)	0.03
Literacy							
Literate	1485	1.00		1.00		1.00	
Illiterate	606	1.4 (1.0-1.8)	0.03	1.4 (1.1 – 1.8)	0.004	1.5 (1.1-1.9)	0.004
Spectacle usage							
Yes	1398	1.00		1.00		1.00	
No	693	0.9 (0.7-1.1)	0.34	0.8 (0.7-1.0)	0.13	0.8(0.6-1.0)	0.08
Diabetes Mellitus							
No	1828	1.00		1.00		1.00	
Yes	263	1.2 (0.8-1.6)	0.35	1.0 (0.8 – 1.4)	0.73	0.9 (0.7-1.3)	0.76
Hypertension							
No	1255	1.00		1.00		1.00	
Yes	836	1.3 (1.0-1.6)	0.03	1.2 (1.0-1.5)	0.05	1.4 (1.1-1.7)	0.005
Lifetime ocular UV exposure	2091	1.2 (1.1 – 1.2)	<0.001	1.1 (1.0-1.2)	0.007	1.1 (1.1-1.2)	<0.001
BMI							
Normal	959	1.00		1.00		1.00	
Underweight	339	1.1 (0.8-1.6)	0.41	0.9 (0.7-1.2)	0.42	1.2 (0.8-1.6)	0.36
Overweight	463	0.8 (0.6-1.1)	0.12	1.0 (0.8-1.2)	0.81	0.9 (0.7-1.2)	0.59
Obese	147	0.9 (0.5-1.4)	0.54	1.0 (0.6-1.4)	0.71	1.0 (0.6-1.5)	0.86
Refractive Error Shift							
No change	693	1.00		1.00		1.00	
Myopic Shift	555	2.5 (1.7-3.6)	<0.001	1.1 (0.9-1.4)	0.43	1.7 (1.2-2.3)	0.001
Hyperopic Shift	558	1.3 (0.9-1.9)	0.14	1.0 (0.8-1.3)	0.86	1.2 (0.8-1.7)	0.34

All the variables in multivariate logistic regression were adjusted for age, gender and population. Smoking was adjusted for smokeless tobacco and alcohol use. Education and occupation were adjusted to each other. Refractive error shift was done only for phakic eyes.

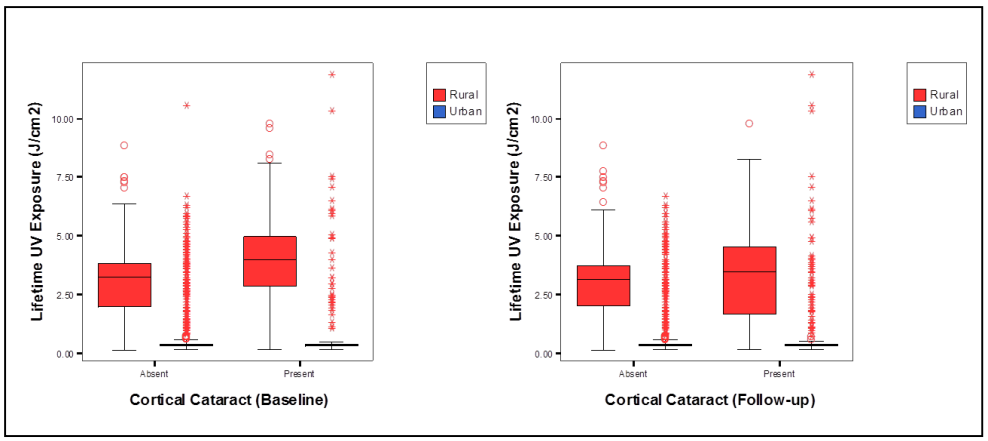
5.5.4 Association with lifetime ocular UV exposure:

The presence of all types of cataract was compared with the estimated lifetime ocular UV exposure. This was also categorised based on the population. The figure 5.5.4.1a to 5.5.4.1c summarises the association between the presence of the disease and lifetime ocular UV exposure. The association with progression of cataract and UV exposure levels are plotted in figure 5.5.4.2. We also plotted the difference in progression of cataract types with the five levels of lifetime ocular UV exposure levels. These quintiles were categorised based on the equal cut off of UV exposure levels in the study population.

a. Nuclear Cataract



b. Cortical Cataract



c. Posterior Sub-capsular Cataract

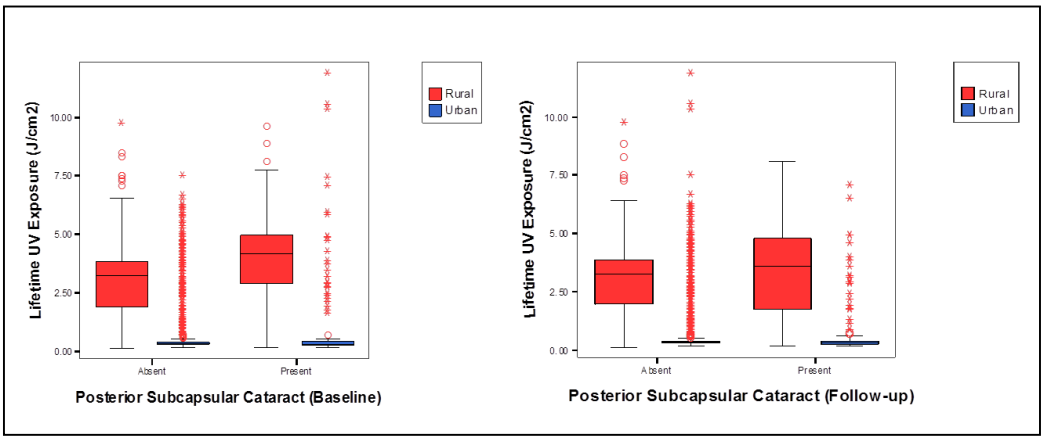


Figure 5.5.4.1: The median lifetime ocular UV exposure levels in subjects with and without any type of cataract among rural and urban population at baseline and follow-up

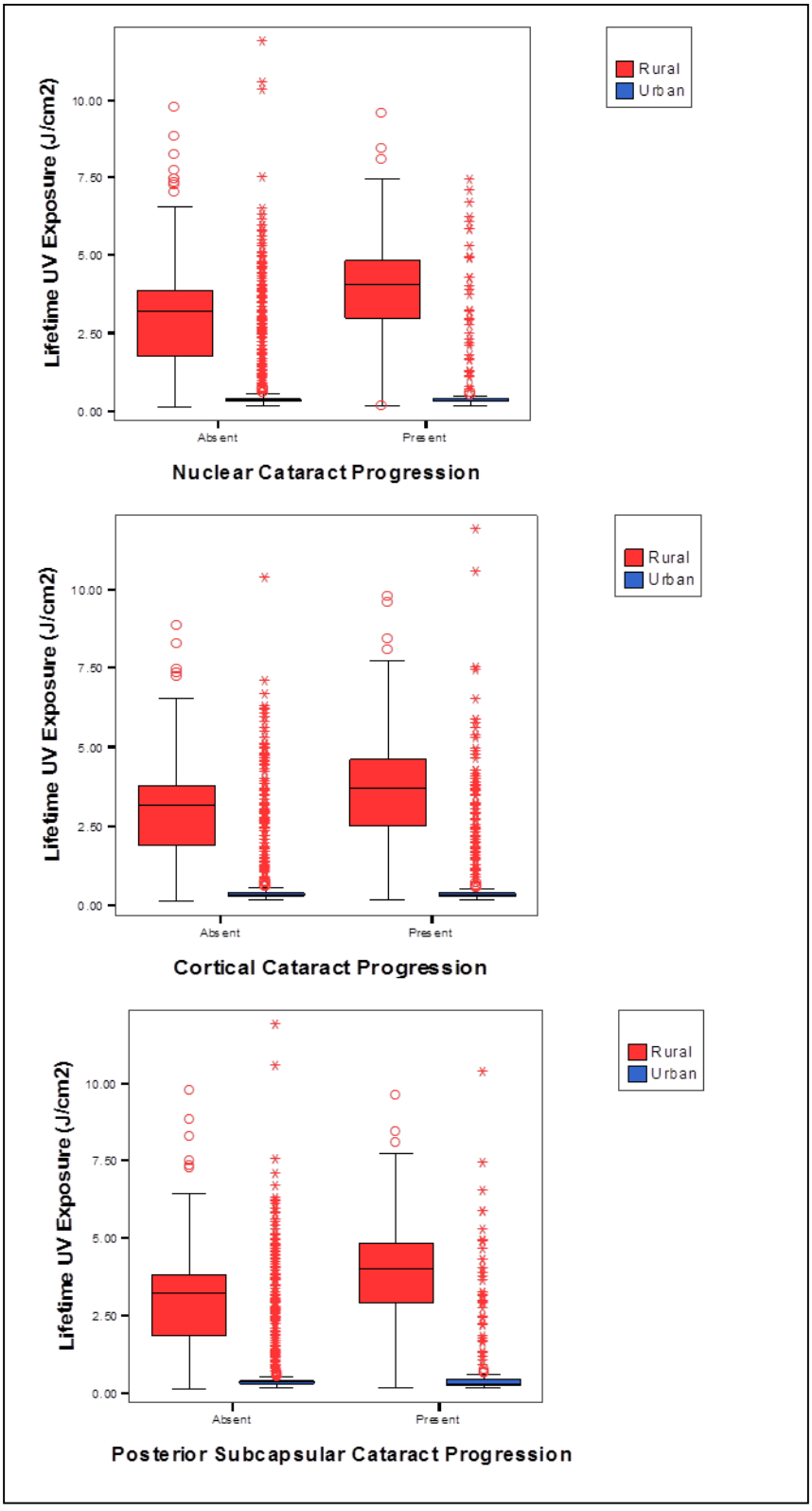


Figure 5.5.4.2: The median lifetime ocular UV exposure levels in subjects with and without progression of any type of cataract among rural and urban population at baseline and follow-up

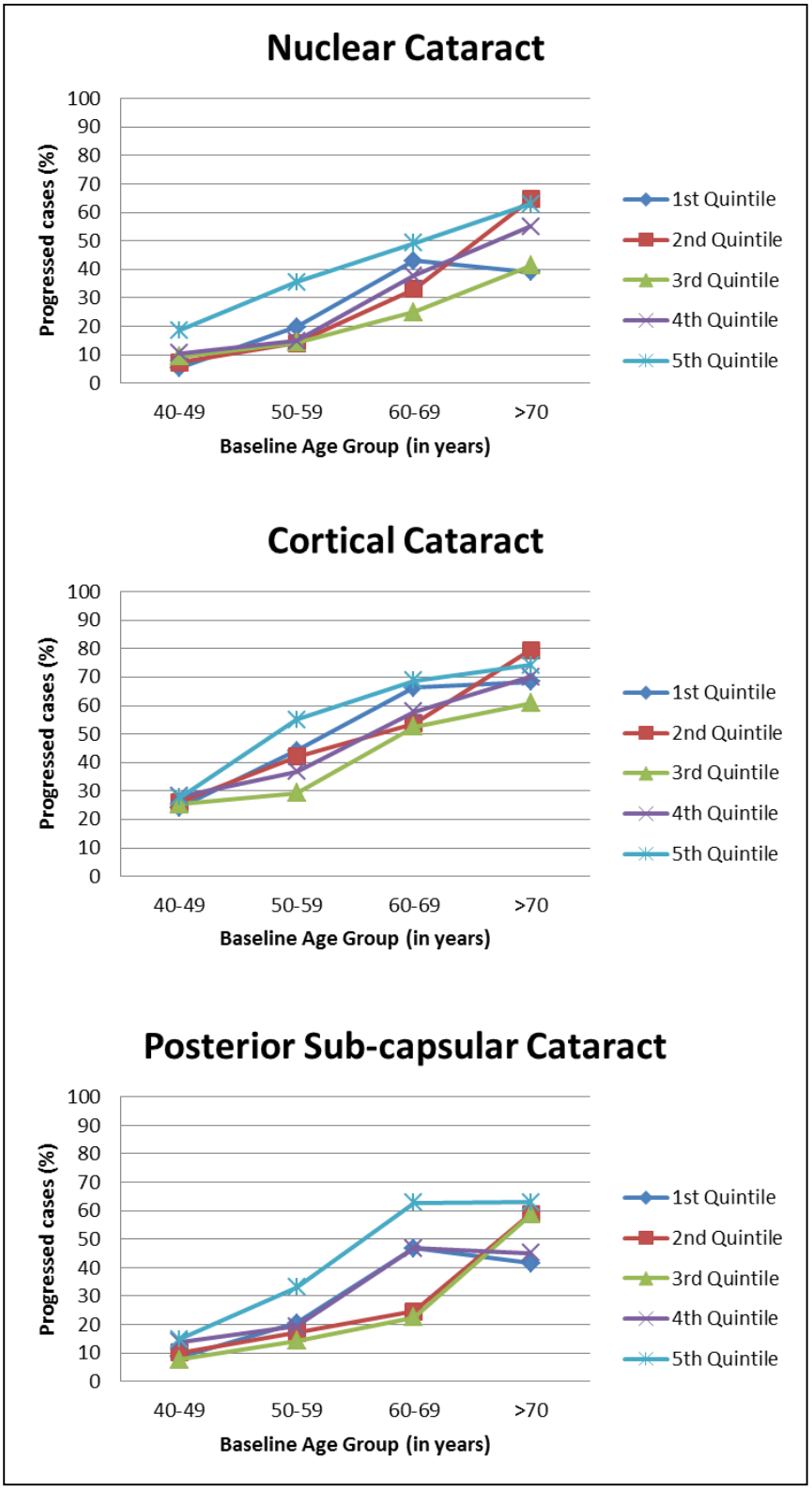


Figure 5.5.4.3: The distribution of percentage of progressed cases of each type of cataract among different quintiles of lifetime ocular UV exposure

5.5.5 Discussion

The prevalence of cataract in the current study was 26.7% (95% CI: 24.8 to 28.6) for nuclear cataract, 24.2% (95% CI: 22.3 to 25.9) for cortical cataract and 19.5% (95% CI: 17.8 to 21.2) for posterior sub-capsular cataract. The age and gender adjusted prevalence for all types of cataract was significantly different in the rural and urban populations. Similar trend is noted in the incidence of the cataract in the current study population. This difference could be due to differences in the nature of work between the rural and urban populations. Similar results of prevalence and incidence were reported in other studies. (Klein et al. 2008; Vashist et al. 2011; Cathy A. McCarty et al. 1999; Italian-American Cataract Study Group 1991; Storey et al. 2013; Panday et al. 2015). The prevalence of cataract in Indian population above 60 years of age was found to be 58% in north India (95% CI, 56–60) and 53% (95% CI, 51–55) in south India. Nuclear cataract was identified as the most common type: 48% (95% CI, 46–50) in north India and 38% (95% CI, 37–40) in south India. We also found the nuclear cataract to be more prevalent than other types.

Klein et al reported the incidence to be incidence of nuclear cataract in right eyes 12%, cortical cataract 8%, and posterior sub-capsular cataract 3% (Klein et al. 2008) whereas the visually significant cataract among south Indian population reported from the Chennai Eye Disease incidence study was 6.36% (95% CI: 5.40-7.32) (Panday et al. 2015). The Barbados Eye Study found a nuclear progression rate of 3.6% over 4 years (Leske et al. 2000), Salisbury Eye Evaluation study was 22.9% over 2 years (Storey et al. 2013). The Barbados Eye Study and Salisbury Eye Evaluation study found cortical incidence rates of 22.2%

and 6.9% and cortical progression rates of 12.5% and 38.4% respectively. In our study the incidence of nuclear cataract was 15.8%, cortical cataract 14.8%, and posterior sub-capsular cataract 7.1% and the progression of nuclear cataract was 23.9%, cortical cataract 43.9%, and posterior sub-capsular cataract 25.8% over six years duration.

The current study reported increasing age, female subjects, rural residence and higher lifetime ocular UV exposure to be at risk for development and progression of any type of cataract. Other than these factors, smokeless tobacco users, illiterates, non-use of spectacles, low BMI (lean) were at higher risk for nuclear cataract and posterior sub-capsular cataract development and not with cortical cataract. Low BMI and non-use of spectacles did not show an association with progression of any type of cataract. Subjects with hypertension were at higher risk for progression of all the types of cataract.

The Beaver Dam eye study and Melbourne visual impairment study also reported that women were at higher risk for the development of cataract(K J Cruickshanks et al. 1992; C A McCarty et al. 1999). This could be because of difference in exposures between gender and hormonal influence. The details of nutritional status and hormonal dysfunctions were not currently studied. Exposure to indoor smoke has also been proved to be associated with the development of cataract due to accumulation of toxins on the lens substance (Pokhrel et al. 2005) and is a common practice in India, this is a potential confounder for our results.

Smokeless tobacco users had greater risk of progression of nuclear and posterior sub capsular cataract. We had previously reported the effect of tobacco use and its association with cataract in a rural south Indian population (Raju et al. 2006). The study reported that tobacco use was significantly associated with cataract formation; however, smokeless tobacco use was more strongly associated with cataract. Several studies have shown the association of nuclear and cortical cataract with smoking. Other population based studies from south India have reported an association between cigarette smoking and cataract(Krishnaiah et al. 2005). The Andhra Pradesh Eye Disease Study was carried out in an urban setting and did not find a relationship between smoking and cataract. The Aravind Comprehensive Eye Study reported information only for the cigarette-smoking population (Nirmalan PK et al, 2004).

There was a weak negative association between diabetes and nuclear and posterior sub-capsular cataract development. Subjects with hypertension were at higher risk for progression of nuclear, cortical and posterior sub-capsular cataract. This weak association could be because of the definition of the condition. We identified cases based on self-reporting or a history of treatment for the condition. The actual value for the blood pressure or sugar estimation was not collected. Definitions based on these parameters have limitations of recall bias and is influenced by health seeking behavior and may not accurately identify all affected individuals.

Illiterates were found to be at higher risk for the progression of all the type of cataract, this could be related to the fact that they were more likely to be involved in outdoor activity and thus have greater UV

exposure risk. Literacy can also influence health awareness and health seeking behavior which could influence cataract progression. Illiteracy is associated with lower socio-economic status; those with lower SES are more likely to be exposed to indoor smoke.

The lean body mass index was found to be significantly associated with the progression of nuclear and posterior sub-capsular cataract. Other studies have also shown lean body mass to be a risk factor for nuclear and posterior sub- capsular cataract(Nirmalan et al. 2003). Higher body mass index was found to be a protective factor against cataract formation. This relationship could not be proven statistically as we had few persons (7.7%) in the higher BMI group. The age could also be a confounding factor here. Only 1.6% of subjects were in the higher BMI level in higher age group. This could be because of decreased life span in obese subjects rather than an actual protective behavior (Flegal KM et al, 2007). In addition it is unlikely that they were involved in physically demanding outdoor activities and therefore had lower UV exposure.

In this study the higher lifetime UV exposure was found to confer 1.3 times greater risk for the development of nuclear cataract, 1.1 times for cortical cataract and 1.2 times for posterior sub-capsular cataract at the baseline. Valero MP et al showed that exposure to sunlight from 25 to 45 years of age to be associated with increased risk of nuclear cataract in later life (Pastor-Valero et al. 2007).

In our study the lifetime ocular UV exposure was associated with 1.2 times fold increased risk for posterior sub-capsular cataract. This could be because of the increased prevalence of posterior sub-capsular

cataract in the current population which also had higher progression rates. The Chesapeake Bay study and the Beaver Dam study did not show any association with the posterior sub-capsular cataract and the lifetime ocular ultraviolet radiation. This could be because of the lower prevalence of the posterior sub-capsular cataract in their study group; only 2% of cases had posterior sub-capsular cataract in The Chesapeake Bay study and 6% of cases in Beaver Dam study (Taylor 1989; K. J. Cruickshanks et al. 1992). Bochow et al have shown an association between posterior sub-capsular cataract and the UV exposure even after adjusting for other type of cataract (Bochow et al, 1989).

When progression was analyzed it too did not show any relation with the lifetime ocular UV exposure. This can be explained by the slower rate of progression in the study group when compared to other types of cataract. Even after adjusting for the confounding factors there was no association with the lifetime ocular UV exposure and the progression of cataract. Other studies have shown an increase risk of UV exposure to be associated with the prevalence of cortical cataract (C A McCarty et al. 1999; K. J. Cruickshanks et al. 1992). We also noted that the progression is more pronounced with higher quintiles of UV exposure levels in all types of cataract.

Studies have shown the protective nature of vitamin C intake with the prevalence of cortical cataract. In the current study we did not assess nutritional aspects.

Non spectacle users were found to be at risk for development of nuclear cataract (OR: 2.6, 95 % CI, 1.8, 3.1, p <0.001). There was no association with other types of cataract. Spectacle use is known to reduce UV transmission to the ocular tissues and could explain this finding. Spectacle use is again associated with literacy (Raju et al. 2004) which had an influence on progression as described above. However use of sunglasses was not found to be associated with the progression of any type of cataract. This could be explained because using sun glasses could be an after effect of the progression of cataract and therefore would not show any positive association with the progression of cataract. Segre et al have reported that use of sun glasses actually increase the ocular UV exposure by causing pupil dilation (Segrè et al. 1981). Rosenthal et al have concluded that the sun glasses reduce the light reaching the eye provided it has wider shape and size with effective side shield (Rosenthal et al. 1986).

Table 5.5.6.1: Comparison of association of cataract and UV exposure in other studies

Study	Location	Study Design	Variable	Risk Evaluation
Current study	South India	Cohort	Lifetime ocular UV exposure	OR: 1.3, 1.2 - 1.4 (Nuclear) OR: 1.1, 1.0 - 1.2 (Cortical) OR: 1.2, 1.2 – 1.3 (PSC)
Leske MC et al, 1991	Massachusetts, USA	Case control	Occupational sun exposure	OR: 1.28, 0.72 - 2.26 (PSC)
Mc Carty CA et al, 1999	Victoria, Australia	Cross Sectional	Average annual ocular UV B exposure	OR: 1.44, 1.21-1.73 (Cortical), OR: 1.15, 0.90 - 1.46 (PSC)
Mohan M et al, 1989	North India	Hospital based case control	Increase in cloud cover	OR: 0.78, 0.68 - 0.90 (all types)
Taylor HR et al, 1988	Maryland, USA	Cross Sectional	Average annual ocular UV B exposure	OR: 3.30, 0.90 - 9.97 (Cortical)
West SK et al, 1993	Maryland, USA	Cohort	Average annual ocular UV B exposure	OR: 1.57, 1.04 - 2.38 (Cortical)
Wong TY et al, 1983	Hong Kong	Cross Sectional	Sun exposure score	OR: 2.10, 0.60 - 7.90 (Any type)
Cruickshanks KJ et al, 1992	Wisconsin, USA	Cross Sectional	Average annual ambient UV B exposure	OR: 0.93, 0.69 - 1.25 (Cortical: Female), OR: 1.13, 0.73 - 1.75 (PSC: Female)
Delcourt C et al, 2000	Sete, France	Cross Sectional	Annual ambient solar radiation	OR: 2.48, 1.24 - 4.99 (Cortical), OR: 1.76, 0.95 - 3.24 (Nuclear)
Collman GW et al, 1988	North Carolina, USA	Case control	Sunlight exposure	OR: 1.53, 0.21 - 7.19 (Cortical), OR: 1.52, 0.28 - 5.44 (PSC)
Valero M et al, 2007	Valencia, Spain	Case control	Years of outdoor exposure	OR:2.22, 0.88, 5.61 (Nuclear)
Bochow W et al, 1989	Maryland, USA	Case control	Average annual ocular UV B exposure	OR: 1.45, 0.41-2.49 (PSC)

5.6 Macular degeneration:

The presence of macular degeneration was documented at baseline and the follow-up visits by the clinicians. The prevalence, incidence, association with age and gender, risk factors and associations with lifetime ocular UV exposure are discussed in this section.

5.6.1 Prevalence and incidence of any macular pathology

The prevalence of macular pathology among male and female in rural and urban population is listed in table (5.6.1.1). The prevalence and the incidence of any macular pathology among rural and urban population with age group are shown in the figure (5.6.1.1)

Table 5.6.1.1: The prevalence of macular degeneration among males and females in rural and urban population

Age Group (in years)	Rural		Urban		Total	
	Males (%)	Females (%)	Males (%)	Females (%)	Males (%)	Females (%)
40-49	4.7	3.3	5.2	4.6	4.9	3.9
50-59	3.1	3.6	7.9	6.3	5.2	4.8
60-69	3.6	0.0	3.5	4.0	3.5	2.3
>70	0.0	0.0	9.2	2.8	5.4	1.4
Total	3.3	2.7	6.1	4.9	4.7	3.8

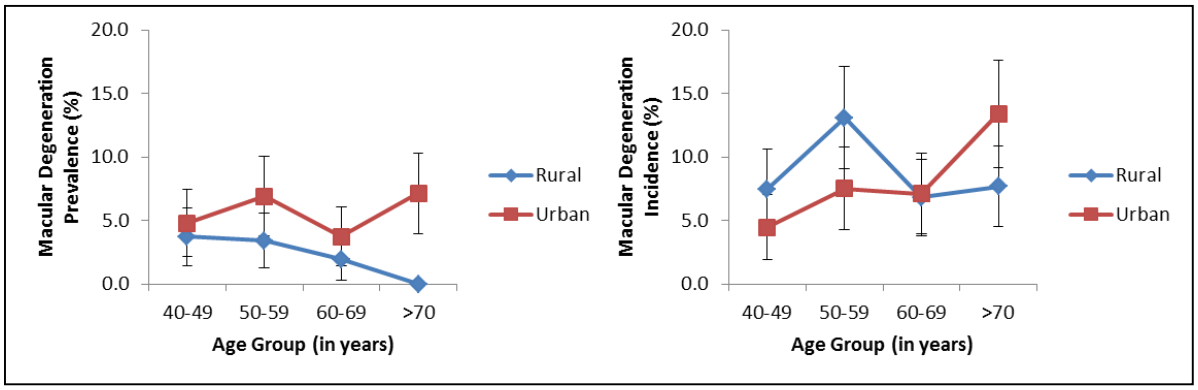


Figure 5.6.1.1: The prevalence and the incidence of macular degeneration among rural and urban population with age group

Table 5.6.1.1: The age and gender adjusted prevalence and incidence of macular degeneration in rural and urban south Indian population

Population	Macular degeneration	
	Prevalence (%) (95% CI)	Incidence (%) (95% CI)
Rural	2.87 (2.86 - 2.88)	8.86 (8.84 - 8.87)
Urban	5.42 (5.41 - 5.43)	6.65 (6.64 - 6.66)
Total	4.16 (4.15 - 4.17)	8.01 (8 - 8.02)

5.6.2 Risk factor assessment:

The risk factors for any macular degeneration were analysed using logistic regression (table 5.6.2.1). These factors were adjusted for age, gender and location of residence.

Table 5.6.2.1 Baseline risk factors for the prevalence of macular degeneration

Variables	No of Subjects	Macular Degeneration	
		OR (95% CI)	p value
Age Group (in years)			
40-49	715	1.00	
50-59	701	1.15 (0.69-1.91)	0.575
60-69	472	0.59 (0.31-1.15)	0.127
70 and above	203	0.79 (0.35-1.77)	0.563
Population			
Urban	1011	1.00	
Rural	1080	0.51 (0.32-0.79)	0.003
Gender			
Male	894	1.00	
Female	1197	0.75 (0.48-1.16)	0.194
Smoking			
No	1704	1.00	
Yes	387	1.09 (0.52– 2.25)	0.814
Smokeless tobacco use			
No	1754	1.00	
Yes	337	0.93 (0.48- 1.81)	0.836
Alcohol Use			
No	1697	1.00	
Yes	394	0.85 (0.40-1.78)	0.659
Occupation			
Indoor workers	794	1.00	
Outdoor workers	1297	0.93 (0.55-1.57)	0.801

Literacy Literate Illiterate	 1485 606	 1.00 1.31 (0.70 – 2.44)	 0.393
Spectacle usage Yes No	 1398 693	 1.00 1.28 (0.79-2.08)	 0.317
Diabetes Mellitus No Yes	 1828 263	 1.00 1.66 (0.95 – 2.92)	 0.075
Hypertension No Yes	 1255 836	 1.00 1.22 (0.76-1.93)	 0.405
Lifetime ocular UV exposure	2091	0.89 (0.76-1.04)	0.145
BMI Normal Underweight Overweight Obese	 959 339 463 147	 1.00 0.61 (0.28-1.36) 0.78 (0.44-1.36) 0.59 (0.22-1.59)	 0.232 0.380 0.303
Refractive Error Shift No change Myopic Shift Hyperopic Shift	 693 555 558	 1.00 1.09 (0.64-1.87) 1.05 (0.53-1.56)	 0.73 0.75

All the variables in multivariate logistic regression were adjusted for age, gender and population. Smoking was adjusted for smokeless tobacco and alcohol use. Education and occupation were adjusted to each other. Refractive error shift was done only for phakic eyes.

5.6. 3 Association with lifetime ocular UV exposure:

The presence of macular degeneration was compared with the estimated lifetime ocular UV exposure. This was also categorised based on the population. The figure 5.3.3.1 summarises the association between the presence of the disease and lifetime ocular UV exposure at baseline and follow-up.

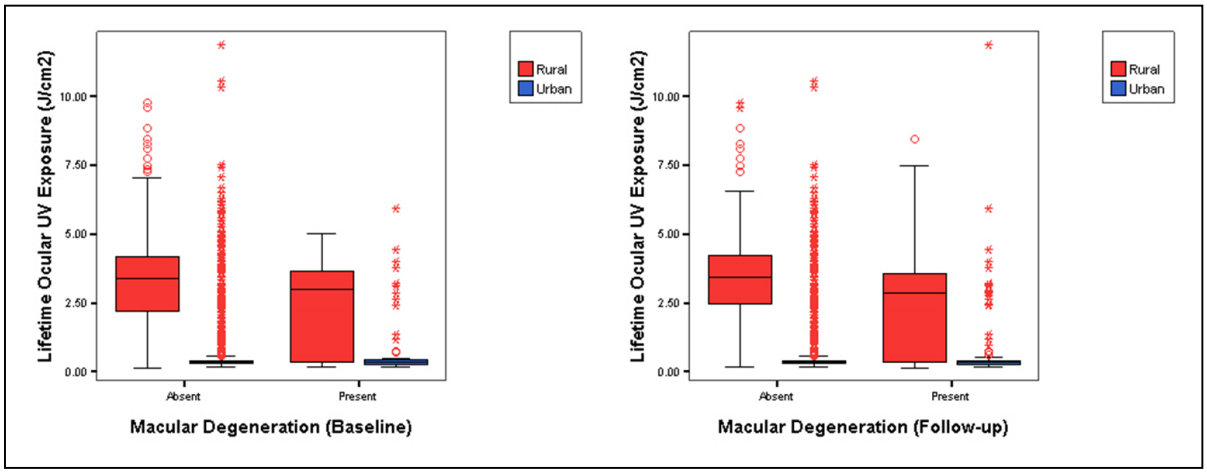


Figure 5.6.3.1: The median lifetime ocular UV exposure levels in subjects with and without macular degeneration among rural and urban population at baseline and follow-up

5.6.4 Discussion

The prevalence of AMD in the current study was 4.2% (95% CI: 3.3 to 5.0). The age and gender adjusted prevalence is significantly different in the rural and urban populations. It was more prevalent in urban (5.4%) than rural (2.9%). Urban residence was the only risk factor associated with the prevalence of AMD. Other studies have shown association with age but we did not find an association. The prevalence increases from 1.6% in 52-64 years to 11% in 65-74 years and 27.9% in more than 74 years(Klein et al. 1992). We suspect that this is because of higher prevalence of cataract which hides the view of macular changes in the current study population. We did not find any association with gender which is similar to other studies (McCarty et al. 2001; Tomany et al. 2004). There are other reports that women tend to be at slightly higher risk of developing macular degeneration (Mitchell et al. 1995). There seems to be a link between the onset of menopause and macular degeneration. Studies have shown in early onset menopause the development of macular degeneration is earlier. We didn't capture this information during the study.

Studies also have shown that ARMD is associated with peripheral cataracts than central cataracts. Central cataracts are protective as they reduce the solar rays reaching macula thus preventing or delaying ARMD. We did not find any association with cataract or refractive error. We did not find any association between refractive error shift and ARMD. Smoking is strongly associated with the presence of ARMD. The damage could be directly through oxidative stress, or indirectly by promotion of atherosclerosis, or by decreasing macular pigment density. ARMD is found to be associated with the duration of smoking and not

amount of smoking. In the current study there was no association noted with ARMD.

BMI and dry ARMD show a J-shaped association i.e. the obese and the leanest individuals are at higher risk of ARMD. In obesity there is high level of oxidative stress and in lean there are dietary deficiencies that could cause ARMD (Schaumberg et al. 2001). In the current study we did not find any association with BMI.

Illiterates and lower socio economic status were independently associated with increased risk of early ARMD. In the current study neither occupation nor educational status was found to be associated with ARMD.

Increase in linoleic acid increases the risk for ARMD. Intake of diet rich in omega 3 fatty acids and fish is inversely associated with the risk of ARMD (intake of linoleic acid is low). Specific types of fats like vegetables, monounsaturated and polyunsaturated fats and linoleic acid increase the risk of ARMD (Seddon et al. 2001). We did not enquire on the details of diet in the current study.

Increase in exposure to sunlight is significantly associated with ARMD. High energy visible and ultraviolet photons produce damage to the retina by photochemical mechanism. The lesion is exacerbated by oxygen, which initiates free-radical chain reaction. There are studies which show no association with sunlight. (Tomany et al. 2004). In the current study we did not find an association of lifetime ocular UV exposure and ARMD.

There was difference noted in the rural and urban population but it did not have an association with ARMD.

5.7 Visual impairment and Blindness:

As we have dealt with ocular disorders we also looked at the incidence of visual impairment and blindness in the current population. Definitions are provided in methods section.

There were around 77 cases with visual impairment at follow-up with normal visual acuity at baseline. The causes for incident visual impairment were cataract 60 (77.9%) cases, Post cataract surgical causes like posterior capsular opacification four cases (5.2%), Glaucoma in three (3.9%) cases, Retinal Pathology seven (9.1%) cases, spheroidal degeneration two (2.6%) cases and amblyopia one (1.3%) case.

There were only seven cases with incident blindness of which five (71.4%) were due to cataract and two (28.6%) were due to posterior capsule opacification.

The burden of visual impairment or blindness in the current population was due to cataract. Vijaya et al have discussed in detail about the complete incidence and risk factors for blindness and risk factors in the CEDIS (Vijaya et al. 2014). It gives clear explanation on cataract being the leading cause of blindness in low income group of countries.

6 Strengths and Limitations

The main strengths of our study are its study design which is population based and its sampling method. To the best of our knowledge this is the first study to report UV exposure levels in a South Indian population. The large sample in the current study ensures adequate power to detect the prevalence of various eye diseases and their association with UV exposure. The study not only looked at the prevalence but also on the progression of cataract. This gave us more information on the risk factors involved in the progression of disease thus could help us plan the prevention strategies.

There are limitations in the current study where we have only recorded the presence of pterygium without grading it based on the extent of corneal involvement. We could therefore not ascertain the progression or the visual impairment due to pterygium in the current population. We also could not grade the age related macular degeneration which if done would have given us insight on the progression of the disease.

The data has been collected by administering questionnaire for the migration, task analysis and leisure activities. Thus recall bias is an issue. It was particularly difficult for those who did not have well defined work schedule. The study has the limitation of using questionnaire, as the lifetime ocular UV exposure details. Recall bias the major source of limitation for questionnaire based study has the same issue in the current study. As the questions were broader we could eliminate some amount of the bias. Indoor smoke and nutritional levels are confounders for development of cataract and they were not studied.

7 Conclusions

To the best of our knowledge the current study reports for the first time the lifetime ocular UV exposure in South India. The lifetime ocular UV exposure levels were 3.35 (IQR: 1.98) in rural and 0.33 (IQR: 0.11) in urban population. We have used the well-established Melbourne visual impairment model to calculate UV exposure. We found odds ratio 1.1, 1.1 and 1.3 with pterygium, pinguecula and spheroidal degeneration with a higher lifetime ocular UV exposure. We have noted 1.6 times increased risk with UV exposure levels beyond 4^{th} quintile for pinguecula. We also found smokeless tobacco use to be associated with all the ocular surface disorders.

In the current study we did not find an association of lifetime ocular UV exposure and ARMD. There was a difference noted in the rural and urban population but it did not have an association with ARMD.

Subjects with exposure to UV radiation are 1.2 times at higher risk for the development of pseudoexfoliation. We also found that they were1.3 times greater risk for the development of nuclear cataract at the baseline, 1.1 times for cortical cataract and 1.2 times for posterior sub-capsular cataract. When progression was analyzed it also did not show any relation with the lifetime ocular UV exposure. This can be explained by the slower rate of progression in the study group when compared to other types of cataract. Even after adjusting for the confounding factors there was no association with the lifetime ocular UV exposure and the progression of cataract.

The significant differences in the rural and urban exposure levels are an important factor for the difference in prevalence of cataract and other UV related ocular pathology.

8 Specific Contributions

To the best of our knowledge, the current study is the first to report the lifetime ocular UV exposure levels measurement in population based study in South India.

The study has reported the rural and urban difference in lifetime ocular UV exposure and provided new insights of understanding the differences in prevalence of diseases such as pterygium, pseudoexfoliation, spheroidal degeneration and cataract among the rural and urban population.

The current study is the first population based study to report the ocular disease prevalence and association with lifetime ocular UV exposure.

9 Future Scope of the study

The study has provided insights on the association of UV exposure with ocular disease such as pterygium, pinguecula, spheroidal degeneration, pseudoexfoliation, and cataract. This triggers the following questions.

1. Are there any changes at the structural level with UV exposure?
    a. Association of ocular surface or corneal integrity changes with long term UV exposure using tearscope and specular microscope
    b. Retinal pigment epithelial changes with optical coherence tomography and its association with UV exposure and dietary lutein levels
    c. Foveal changes with optical coherence tomography and its 10-2 visual field and relate its association with UV exposure
2. Is there any evidence of lens density changes with UV exposure within rural and urban population?
    a. To assess the lens densitometry using pentacam in rural and urban population
3. To investigate the relationship between dietary leutin levels and its association with AMD and UV exposure
4. To develop a self-testing model which can be used to assess the lifetime ocular UV exposure for a person
5. Assess ocular surface changes with blue light exposure
6. Clinical case control study on UV exposure levels among diseased and non-diseased in hospital based set up

10 References

Abdul-Rahman AM, Casson RJ, Newland HS, Muecke J, McGovern S, Aung TH, Selva D, Aung T. Pseudoexfoliation in a rural Burmese population: the Meiktila Eye Study. Br J Ophthalmol. 2008 Oct;92(10):1325-8.

Allingham RR, Loftsdottir M, Gottfredsdottir MS, Thorgeirsson E, Jonasson F, Sverisson T, Hodge WG, Damji KF, Stefánsson E. Pseudoexfoliation syndrome in Icelandic families. Br J Ophthalmol. 2001 Jun;85(6):702-7.

Anastasopoulos E, Topouzis F, Wilson MR, Harris A, Pappas T, Yu F, Koskosas A, Founti P, Coleman AL. Characteristics of pseudoexfoliation in the Thessaloniki Eye Study. J Glaucoma. 2011 Mar;20(3):160-6.

Arnarsson A, Damji KF, Sverrisson T, Sasaki H, Jonasson F. Pseudoexfoliation in the Reykjavik Eye Study: prevalence and related ophthalmological variables. Acta Ophthalmol Scand. 2007 Dec;85(8):822-7.

Arvind H, Paul PG, Raju P, Baskaran M, George R, Balu S, Sripriya S, Ramesh SV, Mukesh BN, Vijaya L, Kumaramanickavel G, McCarty C. Methods and design of the Chennai Glaucoma Study. Ophthalmic Epidemiol. 2003 Dec;10(5):337-48.

Arvind H, Raju P, Paul PG, Baskaran M, Ramesh SV, George RJ, McCarty C, Vijaya L. Pseudoexfoliation in South India. Br J Ophthalmol. 2003 Nov;87(11):1321-3.

Asokan R, Venkatasubbu RS, Velumuri L, Lingam V, George R. Prevalence and associated factors for pterygium and pinguecula in a South Indian population. Ophthalmic Physiol Opt. 2012 Jan;32(1):39-44.

Asokan, R., Vijaya, L, Kapur, S. George R,. Estimation of lifetime ocular ultraviolet (UV) exposure levels in the rural and urban South Indian population using meteorological data from Tropospheric Emission Monitoring Internet Service. *International Journal of Engineering Research & Technology (IJERT)*, 2016, 5(1), pp.374–377.

Bartholomew RS. Spheroidal degeneration of the cornea. Prevalence and association with other eye diseases. Doc Ophthalmol. 1977 Jun 30;43(2):325-40.

Bird AC, Bressler NM, Bressler SB, Chisholm IH, Coscas G, Davis MD, de Jong PT, Klaver CC, Klein BE, Klein R, et al. An international classification and grading system for age-related maculopathy and age-related macular degeneration. The International ARM Epidemiological Study Group. Surv Ophthalmol. 1995. Mar-Apr;39(5):367-74.

Brilliant LB, Grasset NC, Pokhrel RP, Kolstad A, Lepkowski JM, Brilliant GE, Hawks WN, Pararajasegaram R. Associations among cataract prevalence, sunlight hours, and altitude in the Himalayas. Am J Epidemiol. 1983 Aug;118(2):250-64.

Cameron ME, Pterygium throughout the world. *Springfiled III Cherles C Thomas*. 1965

Chylack LT Jr, Leske MC, McCarthy D, Khu P, Kashiwagi T, Sperduto R. Lens opacities classification system II (LOCS II). Arch Ophthalmol. 1989 Jul;107(7):991-7.

Chylack LT Jr, Wolfe JK, Singer DM, Leske MC, Bullimore MA, Bailey IL, Friend J, McCarthy D, Wu SY. The Lens Opacities Classification System III. The Longitudinal Study of Cataract Study Group. Arch Ophthalmol. 1993 Jun;111(6):831-6.

Collman GW, Shore DL, Shy CM, Checkoway H, Luria AS. Sunlight and other risk factors for cataracts: an epidemiologic study. Am J Public Health. 1988 Nov;78(11):1459-62.

Coroneo MT. Pterygium as an early indicator of ultraviolet insolation: a hypothesis. Br J Ophthalmol. 1993 Nov;77(11):734-9.

Cruickshanks KJ, Klein BE, Klein R. Ultraviolet light exposure and lens opacities: the Beaver Dam Eye Study. Am J Public Health. 1992 Dec;82(12):1658-62.

Delcourt C, Cougnard-Grégoire A, Boniol M, Carrière I, Doré JF, Delyfer MN, Rougier MB, Le Goff M, Dartigues JF, Barberger-Gateau P, Korobelnik JF. Lifetime exposure to ambient ultraviolet radiation and the risk for cataract extraction and age-related macular degeneration: the Alienor Study. Invest Ophthalmol Vis Sci. 2014 Oct 21;55(11):7619-27.

Delcourt C, Carrière I, Ponton-Sanchez A, Fourrey S, Lacroux A, Papoz L; POLA Study Group. Light exposure and the risk of age-related macular degeneration: the Pathologies Oculaires Liées à l'Age (POLA) study. Arch Ophthalmol. 2001 Oct;119(10):1463-8.

Delcourt C, Carrière I, Ponton-Sanchez A, Lacroux A, Covacho MJ, Papoz L. Light exposure and the risk of cortical, nuclear, and posterior subcapsular cataracts: the Pathologies Oculaires Liées à l'Age (POLA) study. Arch Ophthalmol. 2000 Mar;118(3):385-92.

Delcourt C, Cristol JP, Tessier F, Léger CL, Michel F, Papoz L. Risk factors for cortical, nuclear, and posterior subcapsular cataracts: the POLA study. Pathologies Oculaires Liées à l'Age. Am J Epidemiol. 2000 Mar 1;151(5):497-504.

Detorakis ET, Spandidos DA. Pathogenetic mechanisms and treatment options for ophthalmic pterygium: trends and perspectives (Review). Int J Mol Med. 2000 Apr;23(4):439-47.

Diffey BL, Davis A, Johnson M, Harrington TR. A dosimeter for long wave ultraviolet radiation. Br J Dermatol. 1977 Aug;97(2):127-30.

Fletcher AE, Bentham GC, Agnew M, Young IS, Augood C, Chakravarthy U, de Jong PT, Rahu M, Seland J, Soubrane G, Tomazzoli L, Topouzis F, Vingerling JR, Vioque J. Sunlight exposure, antioxidants, and age-related macular degeneration. Arch Ophthalmol. 2008 Oct;126(10):1396-403.

Forsman E, Cantor RM, Lu A, Eriksson A, Fellman J, Järvelä I, Forsius H. Exfoliation syndrome: prevalence and inheritance in a subisolate of the Finnish population. Acta Ophthalmol Scand. 2007 Aug;85(5):500-7.

Foster PJ, Seah SK. The prevalence of pseudoexfoliation syndrome in Chinese people: the Tanjong Pagar Survey. Br J Ophthalmol. 2005 Feb;89(2):239-40.

Gottsch JD, Bynoe LA, Harlan JB, Rencs EV, Green WR. Light-induced deposits in Bruch's membrane of protoporphyric mice. Arch Ophthalmol. 1993 Jan;111(1):126-9.

Gray RH, Johnson GJ, Freedman A. Climatic droplet keratopathy. Surv Ophthalmol. 1992 Jan-Feb;36(4):241-53.

Hiller R, Giacometti L, Yuen K. Sunlight and cataract: an epidemiologic investigation. Am J Epidemiol. 1977 May;105(5):450-9.

Hussain A, Awan H, Khan MD. Prevalence of non-vision-impairing conditions in a village in Chakwal district, Punjab, Pakistan. Ophthalmic Epidemiol. 2004 Dec;11(5):413-26.

Risk factors for age-related cortical, nuclear, and posterior subcapsular cataracts. The Italian-American Cataract Study Group. Am J Epidemiol. 1991 Mar 15;133(6):541-53.

Johnson GJ. Aetiology of spheroidal degeneration of the cornea in Labrador. Br J Ophthalmol. 1981 Apr;65(4):270-83.

Jonas JB, Nangia V, Matin A, Bhojwani K, Sinha A, Khare A, Agarwal S, Bhate K. Pseudoexfoliation: normative data and associations. The Central India Eye and Medical Study. PLoS One. 2013 Oct 21;8(10):e76770.

Klein BE, Klein RE, Lee KE. Incident cataract after a five-year interval and lifestyle factors: the Beaver Dam eye study. Ophthalmic Epidemiol. 1999 Dec;6(4):247-55.

Kang JH, Loomis S, Wiggs JL, Stein JD, Pasquale LR. Demographic and geographic features of exfoliation glaucoma in 2 United States-

based prospective cohorts. Ophthalmology. 2012 Jan;119(1):27-35.

Khan JC, Shahid H, Thurlby DA, Bradley M, Clayton DG, Moore AT, Bird AC, Yates JR; Genetic Factors in AMD Study. Age related macular degeneration and sun exposure, iris colour, and skin sensitivity to sunlight. Br J Ophthalmol. 2006 Jan;90(1):29-32.

Klein R, Myers CE, Lee KE, Gangnon RE, Sivakumaran TA, Iyengar SK, Klein BE. Small Drusen and Age-Related Macular Degeneration: The Beaver Dam Eye Study. J Clin Med. 2015 Mar;4(3):424-40.

Klein R, Klein BE, Linton KL. Prevalence of age-related maculopathy. The Beaver Dam Eye Study. Ophthalmology. 1992 Jun;99(6):933-43.

Krishnadas R, Nirmalan PK, Ramakrishnan R, Thulasiraj RD, Katz J, Tielsch JM, Friedman DS, Robin AL. Pseudoexfoliation in a rural population of southern India: the Aravind Comprehensive Eye Survey. Am J Ophthalmol. 2003 Jun;135(6):830-7.

Krishnaiah S, Vilas K, Shamanna BR, Rao GN, Thomas R, Balasubramanian D. Smoking and its association with cataract: results of the Andhra Pradesh eye disease study from India. Invest Ophthalmol Vis Sci. 2005 Jan;46(1):58-65.

Krishnan T, Ravindran RD, Murthy GV, Vashist P, Fitzpatrick KE, Thulasiraj RD, John N, Maraini G, Camparini M, Chakravarthy U, Fletcher AE. Prevalence of early and late age-related macular degeneration in India: the INDEYE study. Invest Ophthalmol Vis Sci. 2010 Feb;51(2):701-7.

Landers J, Henderson T, Craig J. Prevalence of pseudoexfoliation syndrome in indigenous Australians within central Australia: The Central Australian Ocular Health Study. Clin Experiment Ophthalmol. 2012 Jul;40(5):454-7.

Leske MC, Chylack LT Jr, Wu SY. The Lens Opacities Case-Control Study. Risk factors for cataract. Arch Ophthalmol. 1991 Feb;109(2):244-51.

Lester RA, Parisi AV, Kimlin MG, Sabburg J. Optical properties of poly(2,6-dimethyl-1,4-phenylene oxide) film and its potential for a long-term solar ultraviolet dosimeter. Phys Med Biol. 2003 Nov 21;48(22):3685-98.

Limburg H, Kumar R, Bachani D. Monitoring and evaluating cataract intervention in India. Br J Ophthalmol. 1996 Nov;80(11):951-5.

Liu L, Wu J, Geng J, Yuan Z, Huang D. Geographical prevalence and risk factors for pterygium: a systematic review and meta-analysis. BMJ Open. 2013 Nov 19;3(11):e003787.

Lucas RM, Norval M, Neale RE, Young AR, de Gruijl FR, Takizawa Y, van der Leun JC. The consequences for human health of stratospheric ozone depletion in association with other environmental factors. Photochem Photobiol Sci. 2015 Jan;14(1):53-87.

Luthra R, Nemesure BB, Wu SY, Xie SH, Leske MC; Barbados Eye Studies Group. Frequency and risk factors for pterygium in the Barbados Eye Study. Arch Ophthalmol. 2001 Dec;119(12):1827-32.

Maxia C, Perra MT, Demurtas P, Minerba L, Murtas D, Piras F, Cabrera R, Ribatti D, Sirigu P. Relationship between the expression of cyclooxygenase-2 and survivin in primary pterygium. Mol Vis. 2009;15:458-63.

McCarty CA, Mukesh BN, Fu CL, Mitchell P, Wang JJ, Taylor HR. Risk factors for age-related maculopathy: the Visual Impairment Project. Arch Ophthalmol. 2001 Oct;119(10):1455-62.

McCarty CA, Lee SE, Livingston PM, Bissinella M, Taylor HR. Ocular exposure to UV-B in sunlight: the Melbourne visual impairment project model. Bull World Health Organ. 1996;74(4):353-60.

McCarty CA, Mukesh BN, Fu CL, Taylor HR. The epidemiology of cataract in Australia. Am J Ophthalmol. 1999 Oct;128(4):446-65.

McCarty CA, Fu CL, Taylor HR. Epidemiology of pterygium in Victoria, Australia. Br J Ophthalmol. 2000 Mar;84(3):289-92.

Mccarty CA, Taylor HR. Pseudoexfoliation syndrome in Australian adults. Am J Ophthalmol. 2000 May;129(5):629-33.

McCarty CA, Nanjan MB, Taylor HR. Attributable risk estimates for cataract to prioritize medical and public health action. Invest Ophthalmol Vis Sci. 2000 Nov;41(12):3720-5.

Mitchell P, Smith W, Attebo K, Wang JJ. Prevalence of age-related maculopathy in Australia. The Blue Mountains Eye Study. Ophthalmology. 1995 Oct;102(10):1450-60.

Mitchell P, Wang JJ, Hourihan F. The relationship between glaucoma and pseudoexfoliation: the Blue Mountains Eye Study. Arch Ophthalmol. 1999 Oct;117(10):1319-24.

Miyazaki M, Kubota T, Kubo M, Kiyohara Y, Iida M, Nose Y, Ishibashi T. The prevalence of pseudoexfoliation syndrome in a Japanese population: the Hisayama study. J Glaucoma. 2005 Dec;14(6):482-4.

Mohan M, Sperduto RD, Angra SK, Milton RC, Mathur RL, Underwood BA, Jaffery N, Pandya CB, Chhabra VK, Vajpayee RB, et al. India-US case-control study of age-related cataracts. India-US Case-Control Study Group. Arch Ophthalmol. 1989 May;107(5):670-6.

Nangia V, Jonas JB, Nair D, Saini N, Nangia P, Panda-Jonas S. Prevalence and associated factors for pterygium in rural agrarian central India. The central India eye and medical study. PLoS One. 2013 Dec 4;8(12):e82439.

Naumann GO, Schlötzer-Schrehardt U, Küchle M. Pseudoexfoliation syndrome for the comprehensive ophthalmologist. Intraocular and systemic manifestations. Ophthalmology. 1998 Jun;105(6):951-68.

Newkirk KM, Chandler HL, Parent AE, Young DC, Colitz CM, Wilkie DA, Kusewitt DF. Ultraviolet radiation-induced corneal degeneration in 129 mice. Toxicol Pathol. 2007 Oct;35(6):819-26.

Nirmalan PK, Padmavathi A, Thulasiraj RD. Sex inequalities in cataract blindness burden and surgical services in south India. Br J Ophthalmol. 2003 Jul;87(7):847-9.

Panchapakesan J, Hourihan F, Mitchell P. Prevalence of pterygium and pinguecula: the Blue Mountains Eye Study. Aust N Z J Ophthalmol. 1998 May;26 Suppl 1:S2-5.

Panday M, George R, Asokan R, Ve Ramesh S, Velumuri L, Choudhari NS, Boddupalli SD, Sunil GT, Vijaya L. Six-year incidence of visually significant age-related cataract: the Chennai eye disease incidence study. Clin Experiment Ophthalmol. 2016 Mar;44(2):114-20.

Parisi AV, Wong JC, Kimlin MG, Turnbull D, Lester R. Comparison between seasons of the ultraviolet environment in the shade of trees in Australia. Photodermatol Photoimmunol Photomed. 2001 Apr;17(2):55-9.

Parisi AV, Kimlin MG, Turnbull DJ, Macaranas J. Potential of phenothiazine as a thin film dosimeter for UVA exposures. Photochem Photobiol Sci. 2005 Nov;4(11):907-10.

Pasquale LR, Jiwani AZ, Zehavi-Dorin T, Majd A, Rhee DJ, Chen T, Turalba A, Shen L, Brauner S, Grosskreutz C, Gardiner M, Chen S, Borboli-Gerogiannis S, Greenstein SH, Chang K, Ritch R, Loomis S, Kang JH, Wiggs JL, Levkovitch-Verbin H. Solar exposure and residential geographic history in relation to exfoliation syndrome in the United States and Israel. JAMA Ophthalmol. 2014 Dec;132(12):1439-45.

Pastor-Valero M, Fletcher AE, de Stavola BL, Chaqués-Alepúz V. Years of sunlight exposure and cataract: a case-control study in a Mediterranean population. BMC Ophthalmol. 2007 Nov 26;7:18.

Pham TQ, Wang JJ, Rochtchina E, Mitchell P. Pterygium, pinguecula, and 5-year incidence of cataract. Am J Ophthalmol. 2005 Jun;139(6):1126-8.

Pham TQ, Rochtchina E, Mitchell P, Smith W, Wang JJ. Sunlight-related factors and the 10-year incidence of age-related maculopathy. Ophthalmic Epidemiol. 2009 Mar-Apr;16(2):136-41.

Pokhrel AK, Smith KR, Khalakdina A, Deuja A, Bates MN. Case-control study of indoor cooking smoke exposure and cataract in Nepal and India. Int J Epidemiol. 2005 Jun;34(3):702-8.

Raju P, George R, Ve Ramesh S, Arvind H, Baskaran M, Vijaya L. Influence of tobacco use on cataract development. Br J Ophthalmol. 2006 Nov;90(11):1374-7.

Raju P, Ramesh SV, Arvind H, George R, Baskaran M, Paul PG, Kumaramanickavel G, McCarty C, Vijaya L. Prevalence of refractive errors in a rural South Indian population. Invest Ophthalmol Vis Sci. 2004 Dec;45(12):4268-72.

Rosenthal FS, Bakalian AE, Taylor HR. The effect of prescription eyewear on ocular exposure to ultraviolet radiation. Am J Public Health. 1986 Oct;76(10):1216-20.

Rosenthal FS, Phoon C, Bakalian AE, Taylor HR. The ocular dose of ultraviolet radiation to outdoor workers. Invest Ophthalmol Vis Sci. 1988 Apr;29(4):649-56.

Rotchford AP, Kirwan JF, Johnson GJ, Roux P. Exfoliation syndrome in black South Africans. Arch Ophthalmol. 2003 Jun;121(6):863-70.

Rudkin AK, Edussuriya K, Sennanayake S, Senaratne T, Selva D, Sullivan TR, Casson RJ. Prevalence of exfoliation syndrome in central Sri Lanka: the Kandy Eye Study. Br J Ophthalmol. 2008 Dec;92(12):1595-8.

Saw SM, Tan D. Pterygium: prevalence, demography and risk factors. Ophthalmic Epidemiol. 1999 Sep;6(3):219-28.

Schaumberg DA, Christen WG, Hankinson SE, Glynn RJ. Body mass index and the incidence of visually significant age-related maculopathy in men. Arch Ophthalmol. 2001 Sep;119(9):1259-65.

Seddon JM, Rosner B, Sperduto RD, Yannuzzi L, Haller JA, Blair NP, Willett W. Dietary fat and risk for advanced age-related macular degeneration. Arch Ophthalmol. 2001 Aug;119(8):1191-9.

Segrè G, Reccia R, Pignalosa B, Pappalardo G, The Efficiency of Ordinary Sunglasses as a Protection from Ultraviolet Radiation. Ophthalmic Res 1981;13:180-187

Sekelj S, Dekaris I, Kondza-Krstonijević E, Gabrić N, Predović J, Mitrović S. Ultraviolet light and pterygium. Coll Antropol. 2007 Jan;31 Suppl 1:45-7.

Singh MM, Murthy GV, Venkatraman R, Rao SP, Nayar S. A study of ocular morbidity among elderly population in a rural area of central India. Indian J Ophthalmol. 1997 Mar;45(1):61-5.

Stein JD, Pasquale LR, Talwar N, Kim DS, Reed DM, Nan B, Kang JH, Wiggs JL, Richards JE. Geographic and climatic factors associated with exfoliation syndrome. Arch Ophthalmol. 2011 Aug;129(8):1053-60.

Storey P, Munoz B, Friedman D, West S. Racial differences in lens opacity incidence and progression: the Salisbury Eye Evaluation (SEE) study. Invest Ophthalmol Vis Sci. 2013 Apr 26;54(4):3010-18.

Taylor HR, West SK, Rosenthal FS, Muñoz B, Newland HS, Abbey H, Emmett EA. Effect of ultraviolet radiation on cataract formation. N Engl J Med. 1988 Dec 1;319(22):1429-33.

Taylor HR. Ultraviolet radiation and the eye: an epidemiologic study. Trans Am Ophthalmol Soc. 1989;87:802-53.

Taylor HR, Muñoz B, West S, Bressler NM, Bressler SB, Rosenthal FS. Visible light and risk of age-related macular degeneration. Trans Am Ophthalmol Soc. 1990;88:163-73

Thomas R, Nirmalan PK, Krishnaiah S. Pseudoexfoliation in southern India: the Andhra Pradesh Eye Disease Study. Invest Ophthalmol Vis Sci. 2005 Apr;46(4):1170-6.

Threlfall TJ, English DR. Sun exposure and pterygium of the eye: a dose-response curve. Am J Ophthalmol. 1999 Sep;128(3):280-7.

Tomany SC, Cruickshanks KJ, Klein R, Klein BE, Knudtson MD. Sunlight and the 10-year incidence of age-related maculopathy: the Beaver Dam Eye Study. Arch Ophthalmol. 2004 May;122(5):750-7.

Turnbull DJ, Parisi AV. Dosimeter for the measurement of UV exposures related to melanoma induction. Phys Med Biol. 2010 Jul 7;55(13):3767-76.

Vashist P, Talwar B, Gogoi M, Maraini G, Camparini M, Ravindran RD, Murthy GV, Fitzpatrick KE, John N, Chakravarthy U, Ravilla TD, Fletcher AE. Prevalence of cataract in an older population in India: the India study of age-related eye disease. Ophthalmology. 2011 Feb;118(2):272-8.e1-2.

Vijaya L, Asokan R, Panday M, Choudhari NS, Ramesh SV, Velumuri L, Boddupalli SD, Sunil GT, George R. Baseline risk factors for incidence of blindness in a South Indian population: the chennai eye disease incidence study. Invest Ophthalmol Vis Sci. 2014 Aug 7;55(9):5545-50.

Vijaya L, George R, Arvind H, Baskaran M, Raju P, Ramesh SV, Paul PG, Kumaramanickavel G, McCarty C. Prevalence and causes of blindness in the rural population of the Chennai Glaucoma Study. Br J Ophthalmol. 2006 Apr;90(4):407-10.

Vingerling JR, Dielemans I, Hofman A, Grobbee DE, Hijmering M, Kramer CF, de Jong PT. The prevalence of age-related maculopathy in the Rotterdam Study. Ophthalmology. 1995 Feb;102(2):205-10.

Viso E, Gude F, Rodríguez-Ares MT. Prevalence of pinguecula and pterygium in a general population in Spain. Eye (Lond). 2011 Mar;25(3):350-7.

Viso E, Rodríguez-Ares MT, Gude F. Prevalence of pseudoexfoliation syndrome among adult Spanish in the Salnés eye Study. Ophthalmic Epidemiol. 2010 Mar;17(2):118-24.

Wang F, Hu L, Gao Q, Gao Y, Liu G, Zheng Y, Liu Y. Risk of ocular exposure to biologically effective UV radiation in different geographical directions. Photochem Photobiol. 2014 Sep-Oct;90(5):1174-83.

West SK, Duncan DD, Muñoz B, Rubin GS, Fried LP, Bandeen-Roche K, Schein OD. Sunlight exposure and risk of lens opacities in a population-based study: the Salisbury Eye Evaluation project. JAMA. 1998 Aug 26;280(8):714-8.

Winkler BS, Boulton ME, Gottsch JD, Sternberg P. Oxidative damage and age-related macular degeneration. Mol Vis. 1999 Nov 3;5:32.

WHO, 2002. Global Solar UV Index–An educational tool to reduce risks of skin cancer and cataract. *Fact Sheet*.

Wong, J. C., I. Cowling, and A. V. Parisi. "Reducing human exposure to solar ultraviolet radiation." In Proceedings of the 1st Internet Conference on Photochemistry and Photobiology 1997.

Wong TY, Foster PJ, Johnson GJ, Seah SK, Tan DT. The prevalence and risk factors for pterygium in an adult Chinese population in Singapore: the Tanjong Pagar survey. Am J Ophthalmol. 2001 Feb;131(2):176-83.

www.temis.nl (Last accessed on 21st Sep 2016)

Wu KL, He MG, Xu JJ, Li SZ. The epidemiological characteristic of Pterygium in middle-aged and the elderly in Doumen County. J Clin Ophthalmol. 1999;7(1):17-8.

You QS, Xu L, Wang YX, Yang H, Ma K, Li JJ, Zhang L, Jonas JB. Pseudoexfoliation: normative data and associations: the Beijing eye study 2011. Ophthalmology. 2013 Aug;120(8):1551-8.

Appendix I

Clinical Measurement protocol

Ocular and medical history:

A detailed history pertaining to medical and ophthalmic problems is elicited. This includes details regarding use of glasses, any present or past ocular problems, any history of trauma, surgery or laser procedures to either eye, history of use of steroids and any other ocular and/or systemic medications, family history of ocular disease, details of any systemic illness and personal history. Personal history deals with history of smoking, alcohol and tobacco use.

Lensometry:

A lensmeter (Appaswamy telescopic lensometer, Appaswamy associates) is used to measure the optical power of a pair of eyeglass lenses. In this study, this is used only as a starting point for subjective refraction and for determining whether a subject's eyeglass prescription should be changed. The instrument used in this study is Appaswamy telescopic lensometer.

Refraction:

The Modified ETDRS chart (Light House Low Vision Products, New York, NY, USA) is used to test the distance visual acuity.Distance Visual Acuity Landolt's Ring Test (Light House Low Vision Products, New York, NY, USA) is used for subjects who cannot read English alphabets. The chart is placed at 4 metres and is illuminated from above so that the illumination in front of the chart is about 900lux.20 Visual acuity is checked either unaided or with the subject's spectacles, if he or she is

using any. If the visual acuity is less than 4/4 (logMAR 0.0), then the pinhole visual acuity is assessed. Objective refraction is performed with a streak retinoscope (Beta 200, Heine, Germany) followed by subjective refraction. If the subject is unable to read the 4/40 (logMAR 1.0) line, vision is checked at one metre. If he or she is still unable to identify any of the largest optotypes, perception of hand movements is looked for. If hand movements cannot be identified, the examiner checks for perception of light, which is recorded as present or absent. The right eye is examined first followed by the left eye.

Pupillary evaluation:

The pupil responses are evaluated in dim illumination.

Slit lamp biomicroscopy:

The Zeiss SL 130 (Carl Zeiss, Jena,Germany) slit lamp is used. Using a moderately wide beam, the eyelids, margins, lashes, canthi and puncta are systematically examined, followed by the palpebral and bulbar conjunctiva, sclera and cornea. Then, using a narrow parallelopiped beam, the cornea, anterior chamber and iris are examined for any abnormalities. Grading of peripheral anterior chamber depth is done according to the Van Herick system

Applanation tonometry:

Intraocular pressure (IOP) recording with the Goldmann applanation tonometer25 (Zeiss AT 030 Applanation Tonometer, Carl Zeiss, Jena, Germany) is performed on all subjects except in those eyes where distorted mires preclude reliable readings. After applying 0.5% proparacaine eye drops for topical anaesthesia and staining the tear film

with a 2% fluorescein strip, the IOP is recorded in each eye. By convention, the IOP is recorded first in the right eye.

Gonioscopy:

Gonioscopy is a biomicroscopic examination of the anterior chamber angle. A four-mirror size indirect gonioscopic lens is used.

Ocular biometry:

Ocular biometry, using the Alcon ultrasonic biometer (Ocuscan, Alcon Laboratories Inc, Fort Worth, TX, USA) is performed. The axial length, anterior chamber depth and the lens thickness are measured.

Grading of lens opacities:

The subject's pupils are dilated with 5% phenylephrine with 1% tropicamide eyedrops (Unimed Technologies, Halol, Gujarat, India). If phenylephrine is contraindicated, 1% homatropine eyedrops (Warren Pharmaceuticals, Mumbai, India) are used instead. Grading of lens opacities is performed using the Lens Opacities Classification System (LOCS II). With a minimum pupillary dilation of 6mm, the subjects' lenticular opacities are graded by comparison with the standard set of photographs, which are retroilluminated by mount- ing on a light box. Nuclear colour, nuclear opalescence, and cortical and posterior subcapsular opacities are graded separately.

Nuclear Cataract: The slit beam height was adjusted to the diameter of the dilated pupil and was projected at 45º to the patient's visual axis to grade the nuclear color (NC) and nuclear opalescence (N). The Nuclear Opalescence was graded on a scale of NO, NI, NII and NIII, by comparing the average opalescence and visibility of the nuclear region on the lens to the same region in the standard photographs. NO

corresponds to a clear lens, NI refers to early nuclear cataract, NII corresponds to moderately advanced cataract and NIII illustrates dense nuclear opalescence and browning. NIV was assigned for cataracts denser than NIII level and cannot assess (CA) was noted if upgradeable, anterior capsular opacity or anterior polar cataract causes shadow on the nuclear region causing difficulty in grading the opalescence.

Cortical Cataract & Posterior subcapsular: Grading of CC and PSC was done using a retro illumination setup. The CC was graded on a five scale measure (CO, CTr, CI, CII, CIII, and CIV). The grading was done by evaluating the presence of spoke like cataract and the degree of grading increased based on the density and extent of CC, as the cataract covers all the quadrants of a lens. CTr is graded if less than two spoke like opacities are observed in 6'o clock or 10'o clock positions, CI refers to slightly more advanced CC in the same location as CTr, CII grade was selected if cortical spokes obscure just over 2 full quadrants, CIII grade corresponds to CC filling approximately 50% of the pupillary region and CIV advanced opacification filling approximately 90% of the pupillary region. CV was assigned for cataracts denser than CIV level and cannot assess (CA) was noted if upgradeable. A clear lens would have grade of CO and PO for CC and PSC respectively. The PSC was graded as PO, PI, PII and PIII based on the extent of opacification on the posterior capsule. A grade of PI was given if only 3% of the posterior capsule showed opacity, PII if approximately 30% is obscured and PIII if more than 50% of posterior capsule has cataract. PIV for assigned for cataracts denser than PIII level and cannot assess (CA) was noted if upgradeable.

Fundus examination:

The binocular indirect ophthalmoscope (Appaswamy Associates, Chennai, India) is used to examine the entire ocular fundus, including the periphery. This is followed by examination of the disc and macula in greater detail using a +78 D lens (Volk Optical Inc, Mentor, Ohio, USA) at the slit lamp.

Visual field examination:

Visual field testing is performed using Humphrey Visual Field Analyser (HVFA II_ Carl Zeiss Meditec, Dublin, CA, USA). This test is done for the subjects whom it is required.

Optic disc and fundus photography:

Optic disc and fundus photography: All subjects with sufficient media clarity to permit good quality fundus photographs have optic disc photography done. The Zeiss FF450-plus fundus camera with VISUPAC digital image archiving system (Carl Zeiss, Jena, Germany) is used. One stereo-pair (non-simultaneous) of 20° optic disc photographs is taken for each eye.

Appendix II

Lifetime ocular UVR exposure questionnaire Study No: ☐

I D No: ☐☐☐☐☐☐☐☐☐ GP No: ☐☐☐☐ GPU No: ☐☐☐☐

Name: ☐ IP No: ☐☐☐☐ IPU No: ☐☐☐☐

Age/Sex: ☐☐☐ Date: ☐ Project Code: ☐ D O B: ☐

1. Have you ever worn glasses? Yes / No Year/ age began wearing _____
2. How often did you use glasses when you first received them? _____
3. How often do you wear glasses now? _____
4. How often do you wear glasses outdoor? _____
5. How old are your current glasses? _____

   Q.No 2 to 4: 1. Never 2. Less than half the time 3. Half the time 4. More than half the time 5. All the time

6. Have you ever worn sunglasses? Yes / No Year/ age began wearing
7. Are your sunglasses: Tinted Yes / No _____

   Photochromatic Yes / No _____

Location No.	Location	Start Year	End Year
1.	Town / Village/State/Country: _____	_____	_____
2.	Town / Village/State/Country: _____	_____	_____
3.	Town / Village/State/Country: _____	_____	_____
4.	Town / Village/State/Country: _____	_____	_____
5.	Town / Village/State/Country: _____	_____	_____
6.	Town / Village/ State/Country: _____	_____	_____
7.	Town / Village/State/Country: _____	_____	_____
8.	Town / Village/State/Country: _____	_____	_____
9.	Town / Village/State/Country: _____	_____	_____
10.	Town / Village/State/Country: _____	_____	_____

8. Age / year at Secondary school: _____
9. Sun gazing habit: Yes / No 9.1 For how long: _____ 9.2 Time _____
10. Any change in work pattern from outdoor to indoor in a year summer to winter: Yes / No

Name: Study ID No:

Age/ years Began wearing Glasses ________ Tinted glasses ________ Photochromics ________

Life periods since school leaving ________

			Day time activities				Leisure time activities			
Col 1		Col 2	Col 3	Col 4	Col 5	Col 6	Col 7	Col 8	Col 9	Col 10
Period	Activity	Year	Hours	Hat/ Turban	Sun gls	Gls	Hours	Hat/ Turban	Sun gls	Gls
_____	Tasks: ________	Begin – end: ______	_____	_______	______	_____	_____	_______	______	_____
_____	Tasks: ________	Begin – end: ______	_____	_______	______	_____	_____	_______	______	_____
_____	Tasks: ________	Begin – end: ______	_____	_______	______	_____	_____	_______	______	_____
_____	Tasks: ________	Begin – end: ______	_____	_______	______	_____	_____	_______	______	_____
_____	Tasks: ________	Begin – end: ______	_____	_______	______	_____	_____	_______	______	_____
_____	Tasks: ________	Begin – end: ______	_____	_______	______	_____	_____	_______	______	_____
_____	Tasks: ________	Begin – end: ______	_____	_______	______	_____	_____	_______	______	_____
_____	Tasks: ________	Begin – end: ______	_____	_______	______	_____	_____	_______	______	_____
_____	Tasks: ________	Begin – end: ______	_____	_______	______	_____	_____	_______	______	_____
_____	Tasks: ________	Begin – end: ______	_____	_______	______	_____	_____	_______	______	_____
_____	Tasks: ________	Begin – end: ______	_____	_______	______	_____	_____	_______	______	_____
_____	Tasks: ________	Begin – end: ______	_____	_______	______	_____	_____	_______	______	_____
_____	Tasks: ________	Begin – end: ______	_____	_______	______	_____	_____	_______	______	_____

Col 3 & Col 7 : Number of hours spent outside

Col 4, Col5, Col 6, Col 8, Col 9, & Col 10: 1. Never 2. Less than half the time 3. Half the time 4. More than half the time 5. All the time (out of the number of hours spent outside)

LIST OF PUBLICATIONS/PRESENTATIONS

Publication from thesis:

1. **Asokan R**, Vijaya L, Kapur S, George R. Estimation of Lifetime Ocular Ultraviolet (UV) Exposure Levels in the Rural and Urban South Indian Population using Meteorological Data from Tropospheric Emission Monitoring Internet Service. International Journal of Engineering Research & Technology (IJERT). 2016 Jan Vol 5(1): 374-77.

2. Vijaya L, **Asokan R**, Panday M, Choudhari N. S, Ramesh SV, Velumuri L, George R. Six-Year Incidence and Baseline Risk Factors for Pseudoexfoliation in a South Indian Population: The Chennai Eye Disease Incidence Study. Ophthalmology. 2015 Jun;122(6):1158-64.

3. **Asokan R**, Venkatasubbu RS, Velumuri L, Lingam V, George R. Prevalence and associated factors for pterygium and pinguecula in a South Indian population. Ophthalmic Physiol Opt. 2012 Jan;32(1):39-44.

4. Vijaya L, **Asokan R**, Panday M, Choudhari N. S, Sathyamangalam R.V, Velumuri L, George R. The Prevalence of Pseudoexfoliation and the Long-term Changes in Eyes with Pseudoexfoliation in a South Indian Population. J Glaucoma. 2016 Jun;25(6):e596-602.

5. Panday M, George R, **Asokan R**, Ve Ramesh S, Velumuri L, Choudhari NS, Boddupalli SD, Sunil GT, Vijaya L. Six-year incidence of visually significant age-related cataract: the Chennai Eye Disease Incidence Study. Clin Exp Ophthalmol. 2016 Mar;44(2):114-20

Book Chapter (related to thesis): "Santanam's Text book on Occupational Optometry, 2015" Elite School of Optometry, Gnanodaya Press

Chapter on Electromagnetic radiation

Chapter on Occupational Lenses

Chapter on Workmen compensation

Research Awards for works related to thesis:

- **2011: "Best paper award"** in X Dr E Vaithilingam Memorial Scientific Session
- **2012:** Ruby Banik Memorial Award for the **"Best Researcher in Clinical science"**
- **2013: "ESO Alumni Association Award"** for the Best Research Publication
- **2013:** Travel grant for **ASIA ARVO - IC**
- **2014: "ESO Alumni Association Award"** for the Best Research Publication
- **2014:** Dr S Ramakrishnan and Smt. Bhagavathy Endowment Award for "**Occupational eye/vision related research."**
- **2014: "Best paper award"** in Public health session - All India Optometric Conference
- **2015: "ESO Alumni Association Award"** for the Best Research Publication

Conference presentations related to thesis:

1. Poster and poster in brief presentation on the "The prevalence of Pterygium and Pinguecula in a south Indian population" at **ASIA ARVO**, January 2009, Hyderabad
2. Presented on "The quantification of ocular UV exposure and its association with the progression of cataract" in the **Ruby Banik Memorial award** for best research in clinical science (in house) in September 2009, Chennai.
3. Presented on "Quantification of ocular ultraviolet-B radiation exposure in a South Indian population and its association with the progression of cataract" in **ESO International Vision Science and Optometry Conference** (EIVOC) August 2010, Chennai
4. Poster presentation on "Prevalence of cataract in different geographical location" in **X Dr E Vaithilingam Memorial Scientific Session**, August 2011, Chennai.
5. Presented on "Six year Incidence of Visually Significant Age -Related Cataract: The Chennai Eye Disease Incidence Study" in the **Ruby Banik Memorial award** for best research in clinical science in September 2012, Chennai.

6. Poster presentation on “Prevalence and Causes of Low Vision and Blindness in an Urban Population – The Chennai Glaucoma Study” **IAPB Ninth General Assembly**, September 2012, Hyderabad.
7. Poster presentation on “The association of ocular UV exposure and the progression of cataract in south Indian Population” in **Association of Research in Vision and Ophthalmology,** May 2013, Seattle.
8. Presented on “Six year incidence and causes for visual impairment among rural and urban south Indian population” at ASIA ARVO October 2013, New Delhi.
9. Presentation on “Comparison of Participants vs Non Participants in the Chennai Eye Disease Incidence Study over Six Year Follow Up” **36th All India Optometric Conference** September, 2014, Agra
10. Presented on “UV Exposure and Ocular Surface disorders” at **ESO International Vision Science and Optometry Conference** (EIVOC) August 2015, Chennai
11. E-Poster presentation on “Lifetime ocular UV exposure levels in the rural and urban south Indian population and its relation to their occupation” at **66th National Conference of Indian Association of Occupational Health (OCCUCON)** 2016, Bangalore

Other Publications:

1. Philomenadin F.S, **Asokan R**, George R, Lingam V, Sarangapani S. Genetic Association of SNPs near ATOH7, CARD10, CDKN2B, CDC7 and SIX1/SIX6 with the Endophenotypes of Primary Open Angle Glaucoma in Indian Population. PLoS One. 2015 Mar 23;10(3)
2. Panday M, George R, **Asokan R**, Ramesh SV, Velumuri L, Choudhari NS, Boddupalli SD, Sunil GT, Vijaya L,. Six-year incidence of ocular hypertension in a South Indian population: the Chennai eye disease incidence study. Br J Ophthalmol 2014;0:1–5.
3. Vijaya L, **Asokan R**, Panday M, Choudhari NS, Ramesh SV, Velumuri L, Boddupalli SD, Sunil GT, George R. Baseline risk factors for incidence of blindness in a South Indian population: the chennai eye disease incidence study. Invest Ophthalmol Vis Sci. 2014 Aug 7;55(9):5545-50.

4. Mazumdar D, Pel JJ, Panday M, **Asokan R**, Vijaya L, Shantha B, George R, Van Der Steen J. Comparison of saccadic reaction time between normal and glaucoma using an eye movement perimeter. Indian J Ophthalmol. 2014 Jan;62(1):55-9
5. Vijaya L, **Rashima A**, Panday M, Choudhari NS, Ramesh SV, Lokapavani V, Boddupalli SD, Sunil GT, George R. Predictors for incidence of primary open-angle glaucoma in a South Indian population: the Chennai eye disease incidence study. Ophthalmology. 2014 Jul;121(7):1370-6.
6. Jonas JB, George R, **Asokan R**, Flaxman SR, Keeffe J, Leasher J, Naidoo K, Pesudovs K, Price H, Vijaya L, White RA, Wong TY, Resnikoff S, Taylor HR, Bourne RR; Vision Loss Expert Group of the Global Burden of Disease Study. Prevalence and causes of vision loss in Central and South Asia: 1990-2010. Br J Ophthalmol. 2014 May;98(5):592-8.
7. Vijaya L, George R, **Asokan R**, Velumuri L, Ramesh SV. Prevalence and causes of low vision and blindness in an urban population: The Chennai Glaucoma Study. Indian J Ophthalmol. 2014 Apr;62(4):477-81.
8. Choudhari NS, George R, Sathyamangalam RV, Raju P, **Asokan R**, Velumuri L, Vijaya L. Long-term change in central corneal thickness from a glaucoma perspective. Indian J Ophthalmol. 2013 Oct;61(10):580-4.
9. Vijaya L, **Asokan R**, Panday M, Choudhari NS, Ramesh SV, Velumuri L, Boddupalli SD, Sunil GT, George R. Six-Year Incidence of Angle-Closure Disease in a South Indian Population: The Chennai Eye Disease Incidence Study. Am J Ophthalmol. 2013 Dec;156(6):1308-1315.
10. Ronnie G, Ve RS, Velumuri L, **Asokan R**, Vijaya L. Importance of population-based studies in clinical practice. Indian J Ophthalmol. 2011 Jan;59 Suppl:S11-8.
11. Vijaya L, George R, Arvind H, Ve Ramesh S, Baskaran M, Raju P, **Asokan R**, Velumuri L. Central corneal thickness in adult South Indians: the Chennai Glaucoma Study. Ophthalmology. 2010 Apr;117(4):700-4.
12. Vijaya L, George R, **Rashima A**, Raju P, Arvind H, Baskaran M, Ve RS. Outcomes of cataract surgery in a rural and urban south Indian population. Indian J Ophthalmol. 2010 May-Jun;58(3):223-8.

Brief Biography of the Candidate

Ms Rashima Asokan, completed BS Optometry and M Phil In Optometry from Elite School of Optometry and Birla Institute of Technology and Science (BITS, Pilani). After completing BS optometry she joined Sankara Nethralaya as Optometrist and was also involved in teaching at Elite School of Optometry. She joined the Chennai Glaucoma Study in 2007, one of the largest epidemiological study groups in India. She was also involved in clinical research in glaucoma. She, along with the study team has published their works in many national and international peer reviewed journals and currently holds 17 peer-reviewed publications. She has presented in many national and international conferences and received awards. Her research area includes UV radiation and its effect on eye, Glaucoma, Occupational ocular disorders, Innovative education models in Optometry. She also received Best Research publication award consecutively three years for her research in optometry. She also holds as reviewer for international journal.

She also mentors the clinical internship at Elite School of Optometry and also guides undergraduate and post graduate research works. For her innovative teaching methods she has received the best faculty awards thrice from Elite School of Optometry. She also has received endowment awards for optometry related educational training. Currently she is enrolled in PhD Programme under BITS, Pilani.

Brief Biography of the Supervisor

Dr Ronnie J George is currently the Director - Research, Vision Research Foundation and Senior Consultant at Sankara Nethralaya. He completed his MBBS from St John's Medical College,Bangalore in 1993, Diploma in Ophthalmology from Christian Medical College, Vellore in 1998, MS (Ophthalmology) from Christian Medical College, Vellore in 2001and Diplomate National Board of Education, New Delhi, 2001. He joined as consultant at Sankara Nethralaya in 2001. He has contributed to the field of glaucoma significantly. He has played an important role in the designing and execution of four population based studies in India that includes the Chennai Eye Disease Incidence study. His work has helped to estimate the burden of glaucoma in India. He has more than 90 peer-reviewed publications in various national and international journals. He is a member in Associate Advisory Board of the World Glaucoma Association (WGA) and a member, Promulgation Committee, World Glaucoma Association (WGA). He invested considerable amount of time in research. In this capacity he guides scientists from various subspecialties of ophthalmology.

Brief Biography of the Co-supervisor

Prof. Suman Kapur is currently Professor at Smt Sarla Birla and Sh. B. K. Birla Chair and Head Department of Biological Sciences, Birla Institute of Technology and Science Pilani, Hyderabad Campus. She finished her B.Sc (Hons) from Kirori Mal College, Delhi University, Delhi in 1977. She finished her M.Sc (Med. Biochemistry) in 1980 and PhD in Biochemistry (1987) from All India Institute of Medical Sciences, New Delhi. She has several funded projects (Ongoing 5 and completed 09) and received over Rs 60 million as funds. To her credit she has six patents filed and more than 150 conference presentations and invited talks. She has more than 80 peer reviewed papers in National and International Journals and Four Books and Eight Book Chapters

She is also an editorial board member for Journal of Tropical Agricultural Science (JTAS), Member Board of Editors, Internet Journal of forensic Medicine and Toxicology and reviewer for International journals such as Eye (Nature Publications), BiOMARKERS, USA and National journals such as IJBB, IJCB, Cell and Tissue Research, etc