

EVALUATION OF DEPRESSION AND QUALITY OF LIFE AMONG PRIMARY CAREGIVERS OF CHILDHOOD GLAUCOMA AND JUVENILE OPEN ANGLE GLAUCOMA

by

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DISCLAIMER

I hereby clarify that the work in this dissertation is of my own except for quotations, some figures, and summaries which have been duly acknowledged. I declare that I have no financial of interest in the instruments and the computer software used in this study.

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LIST OF ABBREVIATIONS

AD	Alzheimer Disease
BDI	Beck's Depression Index
CarCGQoL	Caregivers Childhood Glaucoma Quality of Life
CBI	Caregiver Burden Interview
CG	Childhood Glaucoma
CGRN	Childhood Glaucoma Research Network
CSI	Caregiver Strain Index
GAD-7	Generalised Anxiety Disorder Assessment
GDD	Glaucoma Drainage Device
HADS	Hospital Anxiety and Depression Score
HKL	Hospital Kuala Lumpur
HRPZ II	Hospital Raja Perempuan Zainab II
IHD	Ischemic Heart Disease
IOP	Intraocular Pressure
ITC	Iridotrabecular-contact
JOAG	Juvenile Open Angle Glaucoma
MYR	Ringgit Malaysia
MYOC	Myocilin
ONH	Optic Nerve Head
PAS	Peripheral Anterior Synechie
PACG	Primary Angle Closure Glaucoma
PCB	Perceived Caregiver Burden Scale
PHQ-9	Patient Health Questionnaire
POAG	Primary Open Angle Glaucoma
PGA	Prostaglandin Analogue
QoL	Quality of Life
RNFL	Retinal Nerve Fibre Layer
VF	Visual Field
WHO	World Health Organization
ZBI	Zarits Burden Interview

Abstract

Introduction

Childhood glaucoma (CG) and juvenile open angle glaucoma (JOAG) are rare glaucoma diseases causing 5 % of childhood blindness worldwide. CG presents at birth till age three, and JOAG is after age three. Management of these patients are chronic, lifelong and dependency on caregiver is crucial.

Objective

The aim of this study was to evaluate depression and quality of life (QoL) experienced by the caregivers of CG and JOAG patients.

Method

This is a cross-sectional, multi-centre study involving 117 caregivers of CG and JOAG. Caregivers were given two questionnaires; Malay version Patient Health-9 (PHQ-9) and Caregiver of Childhood Glaucoma Quality of Life Questionnaire (CarCGQoL). The mean scores were tabulated and analysed using simple, multiple logistic regression and Pearson correlation.

Results

Total 117 caregivers, 80 were of JOAG and 37 of CG patients. The mean age of caregivers was 41.2 ± 11.2 years with more females (58.0%) than males (41.0%). 71% of the total caregivers had depression where (51.3%) had mild depression followed by moderate depression.

Caregivers of CG had lower quality of life (56.7%) compared to JOAG (48.3%). The mean score of CarCGQoL was 2.28(0.32) and PHQ-9 was 0.74(0.32). Female caregivers were the only associated factor to low QoL.

Conclusion

There is a weak positive linear correlation between depression and the QoL of the caregivers. Female and CG caregiver's QoL are more affected, hence, psycho-social support to these caregivers should be highlighted a part of holistic management of CG and JOAG patients.

Abstrak

Pengenalan

Glaukoma pediatrik dan glaukoma juvana sudut terbuka adalah penyakit saraf optik yang jarang ditemui dan menyumbang kepada lima peratus kebutaan di kalangan kanak-kanak seluruh dunia. Diagnosa glaukoma pediatrik bermula dari kelahiran sehingga umur tiga tahun manakala glaukoma juvana sudut terbuka adalah selepas umur tiga. Penjagaan terhadap pesakit kronik memerlukan jangka masa yang panjang dan kebergantungan kepada penjaga untuk mendapatkan rawatan optimal adalah amat penting.

Objektif

Kajian ini dijalankan untuk meninjau tahap kemurungan dan kualiti hidup yang dialami oleh penjaga pesakit.

Kaedah

Kajian keratan rentas yang melibatkan tiga pusat rawatan dan 117 penjaga pesakit glaukoma pediatrik dan glaukoma juvana sudut terbuka. Penjaga diberikan dua soalan kaji selidik; Patient Health Questionnaire (PHQ 9) versi Bahasa Malaysia dan Soal Selidik Kualiti Kehidupan Penjaga Pesakit Glaukoma Pediatrik (CarCGQol) versi Bahasa Malaysia. Skor kedua-dua soal selidik dikira dan dianalisa menggunakan ujian “Simple and Multiple Logistic Regression” dan korelasi “Pearson”.

Keputusan

Daripada jumlah 117 penjaga, 80 adalah penjaga untuk pesakit glaukoma juvena sudut terbuka dan 30 adalah dari glaukoma pediatrik. Purata umur penjaga ialah 41.2 ± 11.2 tahun. 71.0% daripada keseluruhan penjaga mengalami kemurungan. Taburan jantina penjaga menunjukkan lebih banyak wanita (58.0%) berbanding lelaki (41.0%). Skor min untuk versi Bahasa Malaysia CarCGQol adalah 2.28(0.32) dan untuk PHQ-9 adalah 0.73(0.32). Lebih banyak penjaga glaukoma pediatrik mengalami kualiti hidup yang rendah (56.7%). Penjaga wanita adalah factor yang berkaitan dengan kualiti hidup yang rendah.

Kesimpulan

Kajian ini menunjukkan terdapat hubungan linear positif yang lemah di antara kemurungan dan kualiti kehidupan penjaga. Kualiti kehidupan penjaga wanita dan glaukoma pediatrik lebih terjejas, oleh itu, sokongan psiko-sosial harus diberikan kepada penjaga tersebut, sebahagian daripada pengurusan holistik pesakit untuk memastikan penjagaan yang optimum untuk pesakit glaukoma pediatrik dan glaukoma juvena sudut terbuka.

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CHAPTER 1

INTRODUCTION

CHAPTER 1: INTRODUCTION

1.1 Glaucoma

1.1.1 Introduction to Glaucoma

Glaucoma is a chronic disease which is characterised with clinical progressive optic neuropathy with morphological changes of the optic nerve head (ONH) and retinal fibre layer (RNFL) with corresponding visual field (VF) defect that is consistent with glaucoma (Management of Glaucoma, Ministry of Health, 2017). The main contributing factor is intraocular pressure (IOP) as it influences the progression in the death of the retinal ganglion cells affecting visual field defect (Salmon, 2020, p. 349).

Glaucoma can be further subdivided into either open-angle glaucoma or closed-angle/angle closure based on the angle configuration. Further classification is based on the aetiology of either primary or secondary. Ethnicity, systemic comorbidities such as diabetes mellitus, hypertension, vascular disorders, pre-existing myopia, use of birth control pills, family history, and genetics are all identified risk factors for developing glaucoma. (Salmon, 2020, pp. 345-350).

1.1.2 Prevalence of Glaucoma

In Malaysia, it has been reported that 6.6% of blindness are due to glaucoma, labelled as the third leading cause of total blindness in the nation according to the National Eye Survey II (Chew et al., 2018). Worldwide projection of glaucoma burden has been predicted there would be 64.3 million people affected by glaucoma in 2013, increasing to 76.0 million in 2020, and

to 111.8 million in 2040 (Tham et al., 2014). In comparison to other Asian subregions, it is predicted that South Central Asia will experience the steepest rise in the number of people with glaucoma, from 17.06 million to 32.90 million, in 2040 and is expected to surpass East Asia (Allison et al., 2020). In Asia, the overall prevalence of glaucoma is 3.54%, and in this Primary Open Angle Glaucoma (POAG) is the most common type of glaucoma, followed by Primary Angle Closure Glaucoma (PACG) and secondary glaucoma, with prevalence rates of 2.34%, and 0.47%, respectively (Allison et al., 2020).

1.1.3 Classification of Glaucoma

Glaucoma can be classified according to the angle configuration and anatomy. For angle configuration, it is divided as open and closed angle. For open angle, it is further subdivided into primary and secondary open-angle glaucoma (Management of Glaucoma, Ministry of Health, 2017). POAG is further subclassified into POAG suspect, POAG, normotensive glaucoma, and ocular hypertension. The site of aqueous outflow obstruction is used as the reference point for the classification of secondary open-angle glaucoma. In the pre-trabecular type, outflow is obstructed by a membrane covering the trabeculum, trabecular type; obstruction occurring as a result of clogging up of the meshwork and secondary degenerative changes and post-trabecular where the trabeculum is normal but the outflow is impaired as a result of elevated episcleral venous pressure (Salmon, 2020, p. 378).

For angle closure glaucoma, closure is the occlusion of the meshwork by peripheral iris forming iridotrabecular contact (ITC) and obstructing the aqueous outflow. It can be further divided into primary and secondary. Under the PACG, the sub-entities are primary angle closure suspect in which the angle has appositional ITC with normal IOP, normal optic disc head and

normal visual field (VF). The next is the primary angle closure in which there is ITC and peripheral anterior synechiae (PAS), with IOP more than 21mmHg, normal or suspicious optic nerve head and normal VF. In the last entity, PACG, there is ITC with PAS, with IOP of more than 21mmHg, glaucomatous optic nerve head changes, and glaucomatous VF changes (Management of Glaucoma, Ministry of Health, 2017).

The mechanism for the angle closure is according to its anatomical level (anterior or posterior). It can be due to relative pupillary block where the physiological aqueous flow is obstructed leading to a pressure difference between the anterior and posterior chambers with resultant anterior bowing of the iris. The iris becomes convex in shape and causes appositional contact with the trabecular meshwork, causing the block to the aqueous drainage. This also causes the formation of PAS and disease progression to PACG (Wright et al., 2016).

In non-pupillary block, commonly seen in patients with plateau iris, there is presence of some element of pupillary block, but not fully relieved by iridotomy (Salmon, 2020, p. 372). This is usually seen in younger patients who have a large or anteriorly rotated ciliary body that compresses the iris root forward against the trabecular meshwork (Pavlin et al., 1992). For secondary angle closure glaucoma usually, the aetiology is due to retro-lenticular cause, mainly lens-induced angle closure. This causes a sudden change in the lens volume or position that leads to sudden pressure rise. Other infrequent causes are retro lenticular masses pushing the angle forward causing secondary angle closure and it can also be caused by combined mechanism (Salmon, 2020, pp. 372-373).

1.2 Childhood Glaucoma and Juvenile Open Angle Glaucoma

1.2.1 Childhood Glaucoma (CG)

CG is an uncommon group of diseases that are associated with poor visual prognosis and outcomes (Aponte et al., 2010). According to the Childhood Glaucoma Research Network (CGRN), CG is diagnosed upon two or more criteria which includes; ocular parameters of IOP of more than 21mmHg, progressive axial length changes of myopia, corneal changes such as presence of Haab's striae, increased corneal diameter of more than 11 mm in new-borns, more than 12mm in those younger than one year old and more than 13mm in those more than one-year-old. Optic disc changes include progressive increase in the cup-disc ratio, cup-disc asymmetry of 0.2 and focal rim thinning and for imaging parameter is producible VF defect that is in par with glaucomatous optic neuropathy with no other external contributing factor (Thau et al., 2018).

Primary CG can be further subdivided into primary congenital glaucoma and which comprises condition that occurs in absence of any acquired or non-acquired condition with associated isolated angle abnormalities with or without iris abnormalities. This can be further subdivided into neonatal glaucoma when occurrence is in less or equal to one month old, infantile onset where the occurrence is at age of one month to 24 months and late onset is those in more than two years old upon diagnosis (Thau et al., 2018; Yu Chan et al., 2015).

Secondary CG is further subdivided into four groups; glaucoma occurring following cataract surgery in those with no preceding glaucoma, glaucoma associated with non-acquired systemic disease, glaucoma associated with non-acquired ocular anomaly and glaucoma associated with acquired conditions that are not present at birth such as trauma and uveitis (Thau et al., 2018).

1.2.2 Prevalence of CG

More than 300,000 kids worldwide suffer from CG, which is frequently linked to serious visual impairment (Senthil et al., 2019). The incidence rate in the United States is 2.29 per 100,000 people under the age of 20 with primary congenital form of glaucoma has the highest prevalence (Aponte et al., 2010). The rate of occurrence varies over the world, from 1 in 2500 births in Saudi Arabia to 1 in every 3300 births in India, amounting to 4.2% of all childhood blindness in the population of India. It is most common among people with consanguinity marriage (Senthil et al., 2019; Yassin et al., 2016).

In Malaysia, Patel *et al.* reported in children less than 15 years old in blind schools throughout Malaysia in 2011, 95% were severely visually impaired and 7.6% (34 students) were due to glaucoma (Patel et al., 2011).

1.2.3 Treatment of CG

1.2.3.1 Medical

Medical therapy in CG has a limited role as there is anterior segment dysgenesis and intraocular pressure reduction with medical therapy is shown to be effective in about 10 % of cases (Yu Chan et al., 2015). It is used as an adjunct for preparation of patients for IOP reduction prior to surgery or post-surgery (Greco et al., 2022).

First-line therapy is usually of Beta-blocker used in absence of any contraindication. It is started after excluding asthmatic/cardiac anomaly of the patient. The response was considered fair and was reported in up to 53% of children (Chang et al., 2013). It has been suggested in children,

a lower concentration of 0.25% can be given for reduced systemic side effect (Greco et al., 2022).

Second group is carbonic anhydrase inhibitors which has been reported to have fair effect, however with substantial side effect of growth suppression and metabolic acidosis (Yu Chan et al., 2015). The percentage of IOP reduction has been reported to be 25% for topical and up to 35% for systemic usage (Greco et al., 2022).

Third group is the prostaglandin analogue; generally used as second or third line and has been reported to have a poor response up to 50% to 80% (Yu Chan et al., 2015). Compliance to this group is better in view of the once daily medication usage and has been shown up to 58% responds to prostaglandin analogue as monotherapy (Chang et al., 2013).

The other available groups are of alpha-2 agonist and parasympathomimetic group, however the latter has limited use in younger age group and alpha-2 agonist are contraindicated in use among children

1.2.3.2 Surgical treatment

The natural progression CG has poor response to medical therapy. Angle surgery, followed by filtration techniques such trabeculectomy, glaucoma drainage devices, and cyclodestruction, has been demonstrated to have a favorable prognosis than other forms of surgical therapy (Beck, 2001).

i. Goniotomy

Removing the dysfunctional trabecular meshwork, goniotomy lowers IOP by causing the iris to drop posteriorly and widen the angle recess. This has shown to be beneficial in up to 90% of patients who present between three months to one year of age and in those after the age of one year old, the success rate is reported to be at 30% to 50% (Al-Hazmi et al., 2005; Ou et al., 2012).

ii. Trabeculotomy

Trabeculotomy also known as goniotomy ab externo is done in cases of hazy cornea where there is poor visualization of the angle. It is done to create a communication between the anterior chamber and Schlemm's canal by removing a part of the trabecular meshwork. This is usually done in children older than three years old and has good prognosis up to one year post surgery.

iii. Trabeculectomy

Trabeculectomy is done as second line of surgery in those with failed goniotomy or trabeculotomy. This is done with adjunct of usage of Mitomycin-C or 5-Fluorouracil. Performing this amongst children poses challenges to the surgeon is view of thick sclera and tenon, difficulty in identifying anatomical landmark of limbus and also carries a high risk of post operative infection and endophthalmitis. The success rate of trabeculectomy is reported to range from 55% to 95%, varying depending on the age of presentation as well as the type of glaucoma treated (Ou and Caprioli, 2012).

iv. Glaucoma Drainage Device (GDD)

Insertion of GDD is indicated in refractory primary congenital glaucoma. The commonly used implants include Baerveldt, Ahmed and Molteno implants. However, in children this would need adaptations including manipulation of tightness of suture closure, usage of anterior chamber maintainers and antimetabolites. It has been reported that more complications are seen compared to trabeculectomy, requiring more re-surgical intervention.

1.3 Juvenile Open Angle Glaucoma (JOAG)

JOAG is one of the rare entity of glaucoma clinically occurring in those aged more than three years old till adulthood of aged 35 to 40 years old. They present with normal looking angle structures without other ocular syndromes and on examination show optic disc excavation with high IOP, usually more than 40 to 50 mmHg. There is often a strong link and association of family history glaucoma and frequent autosomal dominant inheritance. Genetic association with myocilin (MYOC) are strongly linked to JOAG, affecting nearly 22% to 36 % of those affected (Yao et al., 2018).

The pathogenesis of JOAG is related to the MYOC mutation which affects the trabecular meshwork, including the trabecular beams and juxtacanalicular connective tissue. This increases the resistance in the aqueous outflow by causing abnormal extracellular like material in the trabecular meshwork. Clinically the angle appears normal but in histopathological findings of the trabecular meshwork there was presence of unusually thick compact tissue with extracellular deposits (Furuyoshi et al., 1997).

1.3.1 Prevalence of JOAG

Based on the Dallas Glaucoma Registry it has been shown that JOAG comprises about 4 % of CG cases (Fung et al., 2013). The percentage was similar to a centre in Nigeria accounting for 3.4% (Komolafe et al., 2011) and 1.9 % in Saudi Arabia (Obeidan et al., 2011). Another population-based study showed that the incidence of JOAG was 0.38 per 100000 residents between age the of 4 to 20 years old (Aponte et al., 2010).

1.3.2 Treatment of JOAG

The treatment regime for JOAG patients involves usage of medical therapy first then surgical intervention. Medical therapy is used as temporary measure prior to surgery as patients usually present with persistently high IOP. Studies have shown that up to 50% of patients can achieve their optimal IOP on medical therapy alone, however with the progression of the disease and the visual field, surgical intervention are needed in nearly 83 % (Selvan et al., 2021, Wiggs et al., 1995).

1.3.2.1 Medical

The medical therapy of JOAG is of similar groups of those used in the CG as mentioned earlier. Non-fixed groups are of interest to use in view of lesser side effects and some groups are contraindicated in younger age groups.

First line of medication regime; is usage of Beta-blocker and carbonic anhydrase inhibitor group has been shown to have better retinal blood flow in JOAG patients. Compared to other paediatric glaucoma, the prostaglandin analogue group shows a better ocular hypotensive

impact in JOAG. Caution in usage of alpha-2 agonist, generally are avoided in children of less than 10 years old (Selvan et al.,2021).

1.3.2.2 Surgical treatment

It was shown in a study by Wiggs *et al.*, glaucoma filtration surgery will be required by nearly 83% of the patients who have JOAG (Wiggs et al., 1995). Surgical therapy can be divided into external/invasive that would involve external dissection of conjunctiva/sclera or micro/minimally invasive glaucoma surgeries that are done ab-interno with minimal tissue trauma (Selvan et al.,2021).

i. Trabeculectomy

Trabeculectomy has a range of variable success rate as reported by Pathania *et al.*, at one year the success rate is at 92% reducing to 80% after 5 years (Pathania et al., 2014). However, this surgery in younger age group carries a higher risk of failure in view of robust healing response in them and the age itself is a risk factor.

ii. GDD

The commonly used glaucoma drainage device are Ahmed and Baerveldt implant and it has been shown to provide with good post operative outcome. It has been reported for Ahmed valved glaucoma drainage device the rate of success is 100% at 12 months and up to 82% at 24 months (Balekudaru et al., 2014). Usage of other drainage device such as the Molteno has also been investigated, however associated with higher post operative complications.

iii. Goniotomy

This method has been reported with success rate of 77 % in JOAG patients (Yeung and Walton, 2010). It is the least invasive surgery and has fewer side effects, it improves the aqueous drainage via the conventional drainage system and spared the conjunctiva if it is needed in the future for other glaucoma surgeries.

iv. Ab interno trabeculotomy

This is performed as microcatheter/ suture aided. In a study by Grover *et al.*, this has nearly 100 % success rate in a follow up post operative up to 20 months (Grover et al., 2018). This technique has also seen clinical success among adults with advanced open angle glaucoma.

1.4 Depression and Quality of Life

1.4.1 Depression

Depression comes from the Latin word depressare or deprimere. It is characterized by the persistent sadness, empty or irritable mood which accompanied by somatic and cognitive changes that can affect a person's functional capability. They can present with depressed mood (or irritability in children) or loss of pleasure or interest for at least two weeks (Psychological Association, 2019). It is also accompanied by at least three (for a total of at least five) of the following symptoms present most days: weight loss or change in appetite, insomnia or hypersomnia, psychomotor retardation or agitation, fatigue or loss of energy, excessive/inappropriate guilt or feelings of worthlessness, indecisiveness or diminished ability to concentrate or think, and recurrent thoughts of death or suicidal ideation or suicide plan or attempt (Psychological Association, 2019). This condition can be chronic and recurrent and in

severe cases can lead to suicidal thoughts. Causes of depression is noted to be a complex interaction between social, psychological and biological factors and is very much affected by the surrounding external factors.

WHO has reported total number of people living with depression is nearly 322 million and half of these people live in the South-East Asia Region and Western Pacific Region, reflecting the relatively larger populations of those two regions. Depression is more common among females (5.1%) than males (3.6%) (Marcus et al., 2012).

In a study done in Malaysia looking into the prevalence of depression and risk factors, it has been shown that the overall prevalence rate of moderate to severe depressive symptoms are 21% accounting for one out of five Malaysians were at risk for depression. In the same study, 15% were shown to have mild depression, 11% moderate and 10% severe (Yeoh et al., 2017). This was consistent with another study by Wong et al. which reported prevalence of severe depression was at 11.3% (Wong et al, 2011).

1.4.2 Quality of Life (QoL)

QoL is also known as the representation of health status. The definition of QoL by World Health Organization (WHO) is an “individual’s perception of their position in life in regards to the context of the culture in which they live and in relation to their goals, expectations, standards and concerns” (Kuyken, 1995). QoL is a multidimensional concept that includes an individual’s health, psychological state, sense of freedom, social relationships, personal beliefs and relationship to the environment. Assessment of QoL is important for decision making in

the medical line and is has been also known as a predictor of treatment and management success (Haraldstad et al., 2019).

Caregivers are known to experience immense stress on their daily activities as a result of their caregiving regardless of status of recipient whether is a child nor an adult. The care given revolves around the general health status of the recipient, disturbance of daily activities, positive life adjustments, concerns about the costs of living and caring and household budget. These factors can impact directly to the QoL of the caregiver, by increasing their stress level, problem solving ability, fatigue, financial burden, health and wellbeing. It has been shown in other studies that poor caregiver's wellbeing can affect the recipient, child's wellbeing and QoL (Pecor et al., 2021; Phyo et al., 2020). In another study it has also be shown that there is an association between the caregiver's stress with the maladaptive behaviour of recipient (Ueda et al., 2022).

In a paper by Perlin et al. there are five interlinked variables that affect the general wellbeing and the QoL of caregivers; namely contextual variables, primary objective stressors which are directly from the needs of the patients and the magnitude of the care demanded and secondary stressors such as role strain and intrapsychic strain and modulating variables (Pearlin et al., 1990). The intrapsychic strains involve parameters of self-concept and psychological state. The relentless and progressively expanding demands of caregiving, together with ensuing secondary role strains, are capable of diminishing positive elements of the caregiver themselves; increasingly vulnerability to stress outcomes.

In special interest to our study, caring for the young, parental or the caregiver stress increases with the severity of the child's disability due to the time-consuming treatment, care and rehabilitation and the subsequent economic burden (Salomone et al., 2018).

O'Dwyer et al. has reported that caregivers experience more suicidal ideation compared to non caregivers; 7.1% compared to 5.7%. It was also shown these caregivers have a poorer physical and mental health, higher levels of anxiety, lower levels of optimism and less social support (Joling et al., 2019; O'Dwyer et al., 2014).

1.5 Impact of Disease on Caregiver

Management of illness will need assistance of the caregiver especially in the younger age group and the older age group. Looking into impact of disease on caregiver in a study done by Cole *et al.*, it was noted caring for patients with Alzheimer's disease (AD) poses a large burden on both families and the healthcare community. In the study, it was shown a caregiver spends on average 14 to 43 hours weekly assisting and caregiving an AD patient, this includes both basic and instrumental activities of daily living. The prolong hours of caregiving has shown to cause negative impact on the physical, psychological, emotional, social, and financial aspects of the caregiver's life as they have to do numerous adaptations to accommodate the care recipient (Cole et al., 2014).

In another study by Mc Horney *et al.*, in managing patients with heart failure, the burden on the caregiver was seen most in situations where the caregivers were usually alone in caregiving, and had to make significant changes in their daily lifestyle to accommodate caregiving. Many caregivers expressed significant amount of stress and social and emotional isolation.

Caregivers often had to assume additional daily roles and responsibilities due to their care-recipient's functional and psychosocial limitations. This placed a burden on the caregiver which in most had their own problems to deal with as well as impact to physical health, stress and insomnia. Nearly half of the caregivers at 46.2% reported symptoms such as stress, anxiety, and dread-ness followed by being impatient at 42.3% and altering or reducing social and family interactions at 20%. Thirty-eight percent of caregivers exhibited frustration, and 34.6% displayed physical fatigue or weariness (McHorney et al., 2021).

Disease impact on caregivers has been studied extensively in certain disease group such as chronic kidney disease and those in need of haemodialysis. In a systemic review done looking into caregiver burden in these cases, the most common tools used to measure caregiver burden were the Zarits Burden Inventory in 29 studies, Caregiver Burden Scale in four studies, Novak and Guest Care Burden Questionnaire in three studies with one study using the Oberst Caregiving Burden Scale, Caregiving Stress Appraisal and the Caregiver Strain Index (Alshammari et al., 2021). The majority of the included studies reported among the caregivers whom have patients under care undergoing haemodialysis, they tend to experience moderate to severe levels of burden. Age was a significant factor affecting the caregiver's burden. The level of burden did not differ according to the country and was added on by other factors such as the demographic profile of caregivers and patients, disease-related, caregiving-related , surrounding external , and psychological factors (Alshammari et al., 2021).

Looking into burden and its contributing factors among the caregivers of chronic kidney disease by Joseph *et al.*, it showed that 68.6% of the caregivers had at-least mild to moderate level of burden placed on them. Associated factors were gender of caregiver; female, lower

educational level, older age and poor employment support ; either unemployed, lower employment profile . The burden was also to be higher in those caring for patients with multiple comorbidities and longer duration of disease (Joseph et al., 2021).

In another study by Hanspal *et al.*, looking into 152 caregiver burden of those caregiving for patients on haemodialysis with diabetes mellitus type II using the caregiver burden scale, level of moderate burden was perceived by the caregivers in 53.9%, followed by 36.2% of severe and only a small amount of 3.9% perceived as mild burden. Significant associated factors studied were unemployment ($p=0.042$), inability to have personal health insurance ($p=0.002$) and when the delay in treatment ($p= 0.012$) (Hanspal et al., 2021).

1.5.1 Impact of Childhood Disease on Caregiver

Childhood disease mainly affects the family which can be the parents or the elders of the family as well as the siblings. Child's ability to adapt and cope with illness is much influenced by their caregiver and family members. This has become an important point in developing the need for family assessment as it allows the clinician to be able to identify which family will be needing family education and further support system such as psychological care. In accordance to this, Darwish *et al.* reported that caregivers are not able to deal stress factors that contributes to consequences of family facing more physical, psychological, and financial stress. (Darwish et al., 2020).

In similar age group of children, looking into the impact of childhood psoriasis of the QoL of the caregivers, study by Zychowska *et al.*, showed that caring for a child with psoriasis may be

time-consuming, affect physical well-being of the caregiver and causing emotional distress. The treatment and care itself increases the household expenditure and these factors causes depression at 36% as well as anxiety at 36% among parents of children with psoriasis (Manzoni et al., 2013; Żychowska et al., 2020).

In childhood ocular disease, the commonest ocular malignancy is retinoblastoma. Parental coping mechanism, depression, caregiver burden and social support has been studied in some studies. Providing direct care, carrying out difficult medical or nursing procedures, adjusting to changes in daily routines, and balancing the need to offer emotional support to the patient and other family members are all associated to depression levels.

In a study by Wang et al using four questionnaires; a sociodemographic questionnaire, Becker Depression Inventory, Caregiver Burden Inventory and Social Support Rating Scale, showed depression among the caregivers of children with retinoblastoma showed 51.3% were depressed; 23.1% were mildly depressed, 10.3% moderately and 17.9% severely depressed. In the same study it was correlated that greater depression was associated with higher caregiver burden with a relation coefficient $r=0.394$, and $p<0.05$ (Wang et al., 2016). Gelkopf *et al.*, reported that in caregivers of retinoblastoma, they tend to have higher than normal anxiety levels upon diagnosis of retinoblastoma and up to total of 77% experience depression at some point of the caregiving (Gelkopf et al., 2019).

1.5.2 Impact of CG and JOAG on Caregiver

Impact on caregivers of CG has been investigated, however studies on caregiver of JOAG has not been established as of yet. Study done by Dada *et al.*, using the Caregiver Burden Questionnaire, it was shown mean burden score was 37.8(10.9) showing an overall moderate aggregate burden among the primary caregivers of patients with congenital glaucoma. Severe aggregate burden was seen in 5% of the caregivers. Depression was assessed using the Patient Health Questionnaire-9 (PHQ-9), showed the mean depression severity index score was 8.90(5.14), in which total 69% of the caregivers were found to have depression, 22% had moderate depression and 11% had severe. Significant factors contributing to the burden aggregate such as; socioeconomic, emotional, and aggregate burden increased severity of depression ($p<0.0001$)(Dada et al., 2013).

In another study by Kantipuly *et al.*, Caregivers Congenital Glaucoma Quality of Life Questionnaire (CarCGQoL) was used to assess QoL. Items related to anger, self-confidence, irritability, appetite and interest in leisure activities had the lowest scores. Child's age and duration of disease were significantly associated with CarCGQoL scores. Depression was assessed using the PHQ-9, there was negative correlation between the CarCGQoL and PHQ scores with $r=-0.66$ and $p<0.01$ (Kantipuly et al., 2019).

In accordance with this, Alqurashi *et al.*, also reported that the QoL of caregivers of children with glaucoma was poor and could be influenced by caregivers' relationship to patients, additional children with glaucoma in the family, and level of patients' vision in the better eye (Alqurashi et al., 2019).

Wy et al. reported in their study, in Korean caregivers of children with glaucoma, 23.6% and 20.0% had varying degrees of depressive and anxiety symptoms accordingly. The indicative factor attributing to the caregiver's depressive and anxiety symptom was the number of glaucoma surgeries and vision in better eye of the children (Wy et al., 2022).

1.6 Evaluation of Depression and QoL on the Caregivers

Caregivers stress, depression and QoL can be evaluated with standardized, validated questionnaires and interviews, the parameters play a key component in the psychological distress faced by them (Psychological Association, 2019). It can be done as quantitative with usage of assessment tools or qualitative where it can be based on interview (Knight et al., 2022).

1.6.1 Evaluation Tools

1.6.1.1 PHQ-9

PHQ-9 is a nine-item self-administered questionnaire which looked into depressive symptoms experienced by patients during the two weeks prior to answering the questionnaire. The scores range from 0 to 27, as each of the nine items was scored from 0 (not at all) to 3 (nearly every day). PHQ-9 scores of 5,10,15, and 20 represented mild, moderate, moderately severe, and severe depression, respectively. It is a widely used instrument in assessing level of depression among caregiver (Kroenke et al., 2001; Sherina et al., 2012).

1.6.1.2 CarCGQoL

CarCGQoL is a self-administered questionnaire with 20 questions. Each question has four scale Likert options, to choose from. The questionnaire evaluates QoL of the caregiver, looking into anxiety and emotional burden. Rasch-calibrated scores were used to analyse the CarCGQoL score. A negative CarCGQoL score indicates lower QoL (worse) thus translating to higher level of emotional burden and anxiety. Positive CarCGQoL score indicates better QoL thus translating to low levels of emotional burden and anxiety (Gothwal et al., 2015).

1.6.1.3 Other Evaluation Tools

i. Zarits Burden Interview (ZBI)

ZBI is one of the most commonly used instruments to assess caregiving burden in clinical and research settings. It is a 22-item self-reported instrument that assesses caregiver's burden with each item on a five-point Likert scale, ranging from 0 = 'never' to 4 = 'nearly always. Item scores are added up to give a total score ranging from 0 to 88, with higher scores shows higher burden (Luo et al., 2010). The scale measures physical, emotional, and financial aspect of caregiving. The other parameters investigates are time schedule, physical health, mental and psychosocial burden (Al-Rawashdeh et al., 2016; Yanny et al., 2020).

ii. Caregiver Burden Interview (CBI)

CBI is another commonly used tool where there are 24 questions divided into five domains; time-dependence, developmental, physical, social and emotional burden. Each item is given a score between 0 (not at all descriptive) to 4 (very descriptive),

where higher scores indicate greater caregiver burden. This tool gives assesses the domains of lives of caregivers which impacts caregiving (Novak and Guest, 1989; Valer et al., 2015).

iii. Caregiver Strain Index (CSI)

CSI is a 21-item self-report instrument addressing the impact of caring for a child with emotional and behavioural problems. The caregiver is asked to rate how problematic each event or emotion was because of their child's issues over the previous six months.. Responses are scored on a five-point scale ranging from not at all to very much a problem (Maria Brannan et al., 1992). It has been shown the questionnaire has good internal consistency, reliability and construct validity (Yang et al., 2021).

iv. Perceived caregiver burden scale (PCB)

PCB scale is a 31 item self-reported questionnaire evaluating the perceived load of the caregiver across five domains: financial effect, scheduling impact, experience of abandonment, health impact, and sensation of entrapment. A higher score reflects a greater sense of burden. Other domains assessed are physical health, mental health, social situation, finance, and sleep (Stommel et al., 1990; Yanny et al., 2020).

v. Generalised Anxiety Disorder Assessment (GAD-7)

GAD-7 is a 13-item questionnaire was developed looking into how often patients during the last two weeks, they were bothered by each symptom of anxiety. Response options were “not at all”, “several days”, “more than half the days”, and “nearly every

day” scored as 0, 1, 2, and 3 respectively. Assessment of duration of anxiety symptoms was also included (Spitzer et al., 2006). Seven domains were assessed which were feeling worried, apprehensive, or on edge, not being able to stop or control worrying, worrying excessively about many issues, having difficulty relaxing, being restless, being quickly aggravated, and fearing that something terrible may occur (Johnson et al., 2019).

vi. Beck Depression Inventory (BDI)

BDI is a 21-item, self-report rating inventory that measures characteristic attitudes and symptoms of depression. A response of 0 to 3 is given for each of the four intensifying answer options, and the overall score is compared to a key to identify the severity of the depression (Basker et al., 2007; Cho et al., 2021). There is an updated version known as Beck Depression Inventory II created in 1996 where it looks into major depression symptoms according to diagnostic criteria listed in the Diagnostic and Statistical Manual for Mental Disorders (García-Batista et al., 2018).

vii. Hospital Anxiety and Depression Scale (HADS)

The HADS, which has two subscales for anxiety and depression, is used to assess psychological discomfort in individuals who are not receiving psychiatric treatment. It contains seven questions for anxiety and seven questions for depression, with a four-point answer scale for each topic. The anxiety and depression scores ranged from 0 to 21 (Snaith, 2003; Stern, 2014). Total score of 11 or higher indicates definitive anxiety and depression, a score of eight to ten being possible and score less than seven is normal (Djukanovic et al., 2017; Yahya and Othman, 2015).

1.7 Rationale of the study

CG and JOAG is an ocular disease of children and young adult. The caregiver has a very important role in terms of accepting the diagnosis, care given to the recipient and chronic and long-term follow-up. This increases the care burden on the caregiver causes depression and directly affecting their QoL. The assessment of the caregiver is crucial as for the outcome and prognosis of the CG and JOAG patients depends on the caregiver's effort in caring. If this parameter is neglected, it affects the outcome of the treatment given to patients of CG and JOAG. We aim to look into the level of depression and the QoL of these caregivers for a comprehensive management of patients of CG and JOAG. As we evaluate these parameters, we believe it helps in management in the illness as role the caregivers are crucial for their morbidity and survival of these patients.