Doctoral thesis for the degree of

Doctor of Philosophy (PhD) in Medical Science

PRIMARY OPEN ANGLE GLAUCOMA IN NEPAL

Exploring the Unknown

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Göteborg, Sweden

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Cover photo exemplifies a simulated vision of advanced glaucoma obscuring peripheral vision in a street view.

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This work is dedicated to all Nepalese suffering from glaucoma, a sight-threatening eye disease and to those who are devoted in preventing blindness through “Right to Sight” Vision 2020

To my loving parents

PRIMARY OPEN ANGLE GLAUCOMA IN NEPAL
Exploring the unknown

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ABSTRACT

Background: Dealing with blindness related to primary open angle glaucoma (POAG) has always been challenging due to late detection as POAG can remain asymptomatic until end stage. Most eye hospitals in Nepal conduct opportunistic screening programs for glaucoma, but no reports confirm whether screening programs achieve their goals in preventing blindness. Also, no report tells us the status of glaucoma awareness among Nepalese population.

Aims: This Thesis explored previously uninvestigated facts about POAG that are essential in preventing glaucoma blindness. It aimed to investigate the association of POAG with hypertension and diabetes. It further aimed to investigate the visual damage of POAG patients at the time of first diagnosis. This Thesis also explored knowledge about POAG, hypertension, and diabetes in a peri-urban community.

Methods: This Thesis used a mixed method approach that combined both quantitative and qualitative methods. A hospital-based case-control study investigated the association between POAG, hypertension, and diabetes. Simultaneously, we conducted a descriptive study to illustrate the clinical findings and visual damage observed at the time of POAG diagnosis. Our qualitative approach explored the knowledge of glaucoma, hypertension, and diabetes in the community.

Results: This Thesis shows an association between POAG, hypertension, and diabetes. It also reveals that very few patients knew they were high-risk for POAG when they visited a hospital. Opportunistic screening detected late-stage POAG with moderate to severe visual damage. People's in-depth knowledge of glaucoma was poor. Gender inequity was persistent in regard to knowledge, attitude, and practice of health in Nepal, and women additionally faced cultural health barriers, depriving them of adequate health care. Nepalese communities need more health awareness programs that emphasize women.

Conclusion: Studies presented in this Thesis demonstrate an association between POAG, hypertension, and diabetes. In addition, it shows that the existing glaucoma screening strategy frequently results in late detection of POAG. This Thesis also explored the gap in health literacy regarding glaucoma and gender inequity in health care, indicating a need for tailored community-based health awareness programs.

Keywords: Blindness, Primary open angle glaucoma, hypertension, diabetes, health literacy, gender inequity, health barriers.

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LIST OF THESIS PAPERS

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals.

Paper I

Suraj Shakya-Vaidya, Umesh Raj Aryal, Madan Upadhyay, Alexandra Krettek. Do non-communicable diseases such as hypertension and diabetes associate with primary open-angle glaucoma? Insights from a case-control study in Nepal.
Global Health Action 2014;6:22636.

Paper II

Suraj Shakya-Vaidya, Umesh Raj Aryal, Andrej M Grjibovski, Alexandra Krettek. Visual status in primary open-angle glaucoma: a hospital-based report from Nepal.
Journal of Kathmandu Medical College 2014;3:49-57.

Paper III

Suraj Shakya-Vaidya, Lene Povlsen, Binjwala Shrestha, Andrej M Grjibovski, Alexandra Krettek. Understanding and living with glaucoma and non-communicable diseases like hypertension and diabetes in the Jhaukhel-Duwakot Health Demographic Surveillance Site: a qualitative study from Nepal.
Global Health Action 2014;7:25358.

Additionally, this Thesis incorporates the following articles published during the study period. They are attached as Appendix I and II.

Abhinav Vaidya*, **Suraj Shakya***, Alexandra Krettek. Obesity Prevalence in Nepal: Public Health Challenges in a Low-Income Nation during an Alarming Worldwide Trend.
Int. J. Environ. Res. Public Health 2010;7:2726-2744. *Equal contribution

Umesh Raj Aryal*, Abhinav Vaidya*, **Suraj Shakya-Vaidya**, Max Petzold, Alexandra Krettek. Establishing a health demographic surveillance site in Bhaktapur district, Nepal: initial experiences and findings.
BMC Research Notes 2012;5:489-513. *Equal contribution

ABBREVIATIONS

CDR	cup disc ratio
CI	confidence interval
CPSD	corrected pattern standard deviation
CVD	cardiovascular disease
FCHV	female community health volunteers
FGD	focus group discussion
GHT	glaucoma hemifield test
HP	health post
INGO	international non-governmental organization
IOP	intraocular pressure
JD-HDSS	Jhaukhel-Duwakot health demographic surveillance site
MD	mean deviation
NCD	non-communicable disease
NGO	non-governmental organization
NHRC	Nepal Health Research Council
OPD	outpatient department
OR	odds ratio
PHCC	Primary Health Care Centre
POAG	primary open angle glaucoma
PSD	pattern standard deviation
SF	short-term fluctuation
SHP	sub-health post
VDC	Village Development Committee

PREFACE

It was mid-2008 when I met Professor Göran and Professor Bo in Kathmandu to discuss the research plan I was developing in Nepal. They both inspired me to pursue a PhD degree rather than just getting involved in research work. During that time period, research was my greatest desire, so I was slowly drifting away from clinical and academic ophthalmology toward research. I started by applying to the Nordic School of Public Health NHV (NHV) in Gothenburg, Sweden and was admitted to NHV as doctoral student in March 2009. The last five and one-half years have been a challenging journey, almost like riding a roller coaster full of jolts and upside-down turns!! Today, when I look back, those jolts were worthwhile because I learned to remain calmer with every unexpected jolt.

The real journey toward my PhD degree began with research plans and a discussion about the practical issues of undertaking a study on glaucoma and non-communicable diseases. At the same time, a doctoral students' team from Nepal (Abhinav Vaidya, Umesh Aryal, and I) were responsible for establishing the Jhaukhel-Duwakot health demographic surveillance site (JD-HDSS) in Nepal, under the supervision of Professors Bo Eriksson and Alexandra Krettek. It was not easy to begin two major additional responsibilities (glaucoma study for PhD and JD-HDSS) when I already had a pre-existing responsibility at the Nepal Medical College, including clinical and academic work in tandem with the responsibility of running the Ophthalmology Department. I frequently felt overburdened with work, and occasionally I was confused and unclear about the benefits of these extra tasks. However, the establishment of the JD-HDSS turned out to be a very important endeavor in this journey. Involvement in JD-HDSS gave me enormous exposure to field work, instilled a strong sense of team spirit, increased my ability to communicate at various levels of an administrative workforce, and built rapport with field workers and community.

It also gave me a platform, in the form of focus group discussions, to conduct the third part of my research.

The journey became even more challenging after 2011, when unavoidable circumstances forced me to relocate to the United Kingdom and take a leave of absence from my PhD studies for almost 8 months. I appreciate my supervisor Professor Alexandra Krettek for the support she provided during this very difficult period. Another shock was still to come: the Nordic Council of Ministers announced the closure of NHV by the end of 2014. My supervisor did not give up so easily; she graciously led the mission to transfer my credits to University of Gothenburg. Although the process of credit transfer was a lengthy battle of administrative procedures, I finally got transferred to the University of Gothenburg on 12th August 2013. For the second time, I completed a half-time seminar (having already completed one at NHV), which restored my confidence in no time!

The Thesis that appears here as a single book represents the pieces of information on primary open angle glaucoma (POAG) composed during the entire journey toward PhD degree. The assembled pieces depict my work, along with various insights from an extended network of colleagues at NHV and Sahlgrenska Academy, University of Gothenburg. To me, this book is almost like a "Thangka" (i.e., a depiction of Buddha's life and teaching tools) of my career that illustrates my path of learning research and research tools.

Gratifyingly, my PhD work reveals unrevealed realities about POAG in Nepal. My work may aid the development of future preventive eye care programs in Nepal. I am eager to be a part of Nepal's workforce in this endeavor, and I hope to contribute to the Nepal's mission in preventing blindness through Vision 2020: The Right to Sight.

TABLE OF CONTENTS

BACKGROUND

Glaucoma epidemiology

Glaucoma is a group of diseases characterized by optic nerve head atrophy associated with visual field damage, with normal or high intraocular pressure (IOP). It is one of the causes of irreversible blindness worldwide [1]. Primary open angle glaucoma (POAG) is the commonest type of glaucoma seen in most parts of the world, including Nepal [2-4]. In 2010, almost 45 million people were affected by POAG worldwide; 4.5 million (10%) were estimated to be blind [5]. POAG is often called "the silent thief of vision" because it is an asymptomatic disease that leads to blindness without manifesting warning signs until late stage [6].

Thus, a key aspect of preventing glaucoma blindness involves screening people in the early stages of the disease, before they develop blindness. The Asia Pacific Glaucoma Guidelines clearly recommend that glaucoma screening in low-income countries should focus on opportunistic glaucoma screening (i.e., screening all individuals older than 35 years of age who attend an eye clinic for any reason [7]. According to the American Academy of Ophthalmology, including glaucoma screening as part of a comprehensive adult eye evaluation is the most effective way to diagnose glaucoma, especially after 40 years of age and for high-risk individuals [8]. Thus, it is essential to identify individuals who are exposed to an increased risk of developing glaucoma.

Glaucoma pathogenesis

Two major theories, mechanical and vascular, have been suggested for optic nerve head damage in POAG [9]. The mechanical theory suggests that elevated IOP compresses the structure in and around the optic nerve head, altering axoplasmic flow within the nerve fibers, leading to the progressive death of axons and retinal ganglion cells, and causing excavation in the nerve head. The

vascular theory states that damage to the optic nerve head in glaucoma results from insufficient blood supply to the optic nerve. This is caused by either elevated IOP or reduced ocular blood flow to the optic nerve, due to raised systemic blood pressure or vasospasm [10-12].

The vascular theory of glaucoma pathogenesis states that hypertensive people have a higher risk of developing POAG [12]. Similarly, people with diabetes may have closure of capillaries and endothelial cell dysfunction, which in turn reduces retinal blood flow and increases their susceptibility to POAG, independent of IOP. Diabetes also impairs the auto regulation of posterior ciliary circulation, which may exacerbate glaucomatous optic neuropathy [11, 13]. Goldberg JL et al. demonstrate that surviving neurons in glaucoma do not send signals to the neuronal system, possibly inhibiting cell regeneration and probably causing the irreversible damage that occurs in glaucoma [14].

Glaucoma risk factors: link with non-communicable diseases

Age, sex, race, myopia, IOP and family history, as well as non-communicable diseases (NCDs) such as diabetes, hypertension, and obesity, are risk factors for POAG [15-17]. Most studies consistently report that risk factors like higher IOP, age above 40 years, males, and positive family history often cause POAG. However, researchers also debate whether hypertension and diabetes are risk factors for development of POAG. Some studies affirm an association of POAG with hypertension and diabetes [10, 18]; others argue against such an association [19, 20]. However, more recent reports demonstrate a significant association of POAG with hypertension and diabetes [21-24]. Nevertheless, none of these reports originated in Nepal.

Non-communicable disease

Non-communicable diseases denotes non-infectious and diseases that do not transmit from one person to another. NCDs are often called chronic diseases

because they take decades to become fully established. In other words, NCDs start at a young age and manifest later in life. Because they take a long time to establish themselves, they also provide opportunities for prevention and require long-term treatment throughout life [25]. Common NCDs seen globally include heart disease, stroke, diabetes, cancer, and chronic respiratory disease [25]. The impact of NCD is expected to rise worldwide, particularly in low- and middle-income regions where 80% of deaths currently result from NCDs [26]. Recent data show that mortality due to NCD increased by almost 8 million between 1990 and 2010, and NCD account for two of every three deaths worldwide [27].

Burden of non-communicable disease in South East Asia and Nepal

Cardiovascular disease (CVD), cancer, chronic respiratory diseases, and diabetes mellitus are major causes of mortality globally, including Asia [28]. Hypertension and diabetes are currently the leading causes of morbidity, mortality, and disability in South Asian countries like Nepal, India, Pakistan, Sri-Lanka, and Bangladesh. These diseases contribute to over 20% of the world's CVD burden [29, 30], largely due to rapid industrialization and urbanization, which lead to changing lifestyles [31]. As a direct impact of urbanization and lifestyle changes, Nepal faces a rising trend of the prevalence of obesity [Appendix I], which is considered an important risk factor for most NCDs, including hypertension and diabetes. The prevalence of diabetes and hypertension in Nepal is currently 6.3% and 33.9%, respectively [32].

The rising prevalence of NCD can have a double impact on blindness, first due to retinopathies caused by the disease itself, and second due to optic nerve head damage resulting from POAG [23, 24] and its possible association with hypertension and diabetes.

Nepal: a country profile

Nepal is a landlocked South Asian country located between China to the north and India to the east, south, and west. It has varied geographical terrain and diverse culture and ethnicity. As reported by the national population census [33], Nepal had a population of 26.5 million in 2011. Accounting for a 1.82% annual exponential growth rate, the present estimated population for 2014 is 30.9 million [34]. Male to female ratio at birth is 1.04, and life expectancy is 66 and 69 years for males and females, respectively. Although Nepal's overall literacy rate is 65.9%, male vs. female literacy is 75.1% and 57.4%, respectively.

In terms of origin, the Nepalese population is broadly classified into three major ethnic groups: Indo-Aryan, coming from India; Tibeto-Burman from Tibet; and indigenous Nepalese. These ethnic groups are further subdivided into caste systems that settle in distinct geographical areas according to migration pattern and occupation. Brahmin, Chhetri, and Kayastha (Indo-Aryan) mostly settle in valleys and mid-hills, whereas Gurungs, Newars, Sherpas, Rai, and Tamangs (Tibeto-Burman) live in valleys, high hills, and the mountainous region; indigenous groups like Tharus and Dhamies mostly live in the Terai [33]. Nepal's 125 registered population groups, or castes, speak about 123 different languages [33].

From south to north, the three distinct geographical terrains include the plains, or Terai; the middle hills and valleys, including the capital city, Kathmandu; and the mountainous region toward the north, which includes Mount Everest. From east to west, Nepal is divided into five developmental regions (Eastern, Central, Western, Mid-Western, and Far-Western) [33] to decentralize administrative power and ensure efficient operation. Apart from the developmental regions, Nepal is also divided administratively into 14 zones and 75 districts. Each district is further divided, according to the number of wards

(the smallest unit of administrative structure of Nepal), into village development committees (VDC), which include up to 9 wards, and municipalities with more than 9 wards [35].

Health care system in Nepal: lacking integration

Nepal has a strong community-based workforce, which includes over 50,000 female community health volunteers (FCHV) and more than 28,000 public health workers across the country. Their main responsibility centers on preventive care at the grass-roots level [36]. According to the institutional framework of the Department of Health Services at the Ministry of Health, VDCs and municipalities have sub-health posts (SHP) that function as the first contact point for basic health services. Each level above SHP is a referral point (e.g., SHP to health post [HP]; HP to primary health care center [PHCC]; and PHCC to district hospital, zonal hospital, and regional hospital, and finally to specialty tertiary care centers in Kathmandu (Figure 1). A Regional Health Directorate is responsible for health care in each of the five developmental regions, and District Public Health Officers/ District Public Health Offices monitor each of the 75 districts across the country [36].

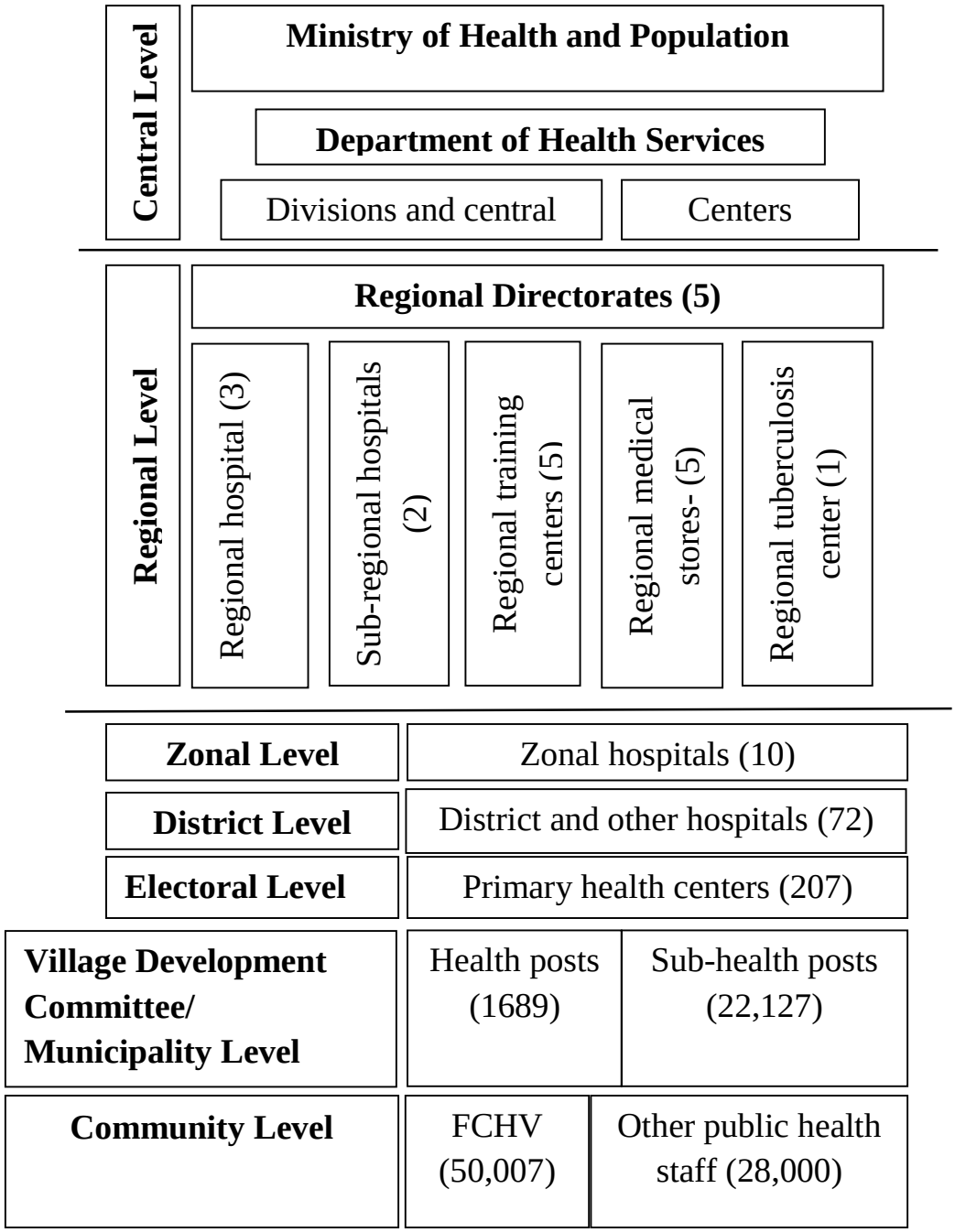

Figure 1: Organizational Structure of the Health System in Nepal. *Modified from Annual report of Department of Health services 2009/2010. FCHV, female community health volunteer.*

The eye health sector has not benefitted from Nepal's comprehensive health network due to lack of integration between eye health care and general health care [37]. Instead, eye care is a parallel system that operates independently from general health care. This is a major source of concern among eye care providers [37]. However, even general health care has been unable to address community health needs for several reasons [38]. Foremost, Nepal lacks national health insurance, and people in Nepal are financially unstable. Therefore, lack of funds prevents people from using healthcare services because they perceive a risk of poverty if they spend a large sum of money from their own pocket. Second, the health system provides only limited financial support to protect the poor and address inequities. Further, the Government of Nepal generates limited resources for the health sector and lacks an integrated approach to make health providers accountable to the public [38]. Cost for health care in Nepal is high, and most people cannot afford healthcare services. According to the latest estimate from the national health accounts, each household spends about 55% of total expenditure in health care alone [39].

Primary open angle glaucoma: a growing public health problem

Vision loss due to glaucoma is irreversible and may lead to severe disability, which will directly affect social and economic growth. Some estimates suggest that POAG comprises 74% of total glaucoma diagnoses, and Asians represent 47% of glaucoma patients worldwide [1]. In Nepal, prevalence of glaucoma ranges from 0.94% to 1.80 % [4, 40], and prevalence of POAG is 1.24% [4]. Another study from Nepal reports that POAG comprises 38.2% of all glaucoma patients diagnosed at hospital clinics [41]. A large community-based survey originating from India demonstrates that POAG prevalence in the community is threefold higher than expected on the basis of POAG detected by hospital-based studies [42]. The same study states that surveys frequently underestimate glaucoma blindness because the criteria for diagnosing blindness is often based

on visual acuity and do not consider visual fields [42]. A study from Sweden demonstrates that excluding visual field status would underestimate the prevalence of glaucoma blindness [43].

Role of preventive health care in reducing POAG blindness

Having a screening program to detect early-stage POAG may help reduce glaucoma blindness. Early diagnosis of POAG and timely initiation of treatment will prevent further damage to the optic nerve and, in turn, preserve vision. The best setting for glaucoma screening is in eye hospitals or clinics where people go for general eye complaints [7]. Additionally, if we anticipate screening a larger group of the at-risk population, including individuals with ocular as well as systemic risk factors, we would be able to reduce glaucoma blindness even better. Therefore, identifying the high-risk population would help focus screening programs on people who are at risk for developing POAG.

Current focus of eye health care in Nepal

Nepal's health care system is impoverished due to lack of human resources and financial constraints, both nationally and locally, that create barriers for the delivery and utilization of health services [44]. Although, Nepal's eye care program lacks strong support from the government, its achievements are significant in terms of human resources, infrastructure, and curative eye health, mainly due to help from national and international nongovernmental organizations (NGOs and INGOs) [37]. Compared to high-income countries, health care in Nepal focuses little on prevention [45, 46]. Eye hospitals conduct opportunistic glaucoma screening for anyone who attends eye outpatient departments (OPD) or mobile cataract camps for any complaints during surveys [4, 47]. However, no detailed reports illustrate the status of visual damage at time of diagnosis as evidence of early disease detection.

Some reports from Nepal suggest that barriers to accessing health care at community-level make it difficult for people to reach hospitals [37, 48], but the eye care program remains unable to deliver services closer to the community or to find ways to bring more people to hospitals other than cataract surgical camps [49].

Role of health awareness in preventing glaucoma blindness

Late diagnosis of glaucoma is the most important risk factor for subsequent blindness and often associates with poor knowledge regarding glaucoma [50]. To some extent, community-based health awareness programs can limit glaucoma-related blindness by influencing at-risk people to participate in periodic eye examination programs [51].

Studies on health behavior suggest that a patient's level of health awareness regarding eye care significantly contributes to increasing patients' attendance at hospitals for eye care [52, 53]. A report from Nepal suggests poor awareness regarding glaucoma among patients attending hospital [54]. Another hospital-based report from Nepal shows that promoting awareness and patient education positively influences glaucoma detection [55]. Future research should focus on evaluating glaucoma awareness in the community.

Rationale behind the Thesis

Due to rapid urbanization and changing lifestyles, the prevalence of NCDs in Nepal is rising [32]. Additionally, POAG is the most common irreversible cause of blindness in Nepal, which may have impact on economic and social development [1, 39].

In view of earlier reports originating from various countries that demonstrate an association between POAG and NCD [21-24], it would be worthwhile to investigate whether this is valid in the Nepalese context. Due to the rudimentary state of Nepal's health system, this information may serve as a

foundation for future research and trigger more POAG-focused screening programs to prevent irreversible and avoidable blindness. It may also help widen the horizon of target groups for POAG screening.

Next, eye care providers face a substantial burden in tackling the backlog of cataract surgeries and other infectious diseases, due largely to the lack of governmental support for the eye care system [37]. Consequently, providers have not been able to devote more time to evaluating the results of glaucoma screening programs in most of hospitals. Therefore, this Thesis aimed to investigate whether the opportunistic screening program for POAG detects cases before patients develop visual damage. Such knowledge will help eye care programs determine whether the POAG screening program helps prevent blindness.

Furthermore, community health awareness contributes to reducing the prevalence and complications of disease and making people more confident in self-managing their disease [51-53]. Thus, this Thesis aimed to explore the knowledge level regarding POAG, hypertension, and diabetes in a rapidly urbanizing peri-urban community of Nepal. The findings of this Thesis provide information from the perspective of community, which would be important for future research, and could form the basis of community-oriented health awareness programs.

RESEARCH AIMS

The overall aim of this Thesis was to explore the unknown facts of POAG in the context of its possible association with NCDs like hypertension and diabetes, time of disease detection, and knowledge of disease.

Specifically, I wanted to

- investigate the association between POAG and NCDs like hypertension and diabetes in the Nepalese population (Paper I);
- investigate the presenting clinical features and visual status of POAG patients at the time of diagnosis (Paper II);
- explore the knowledge of POAG, hypertension, and diabetes in a peri-urban community of Nepal (Paper III); and
- identify perceptions and potential barriers to lifestyle changes and seeking health care (Paper III).

THEORETICAL FRAMEWORK

The core theme of this Thesis is the study of POAG in terms of its association with emerging diseases such as hypertension and diabetes, vision status at the time of case detection, and knowledge regarding POAG, hypertension, and diabetes in a peri-urban community. This Thesis incorporates various health theories and concepts to explain the study of POAG (Figure 2).

Theory of Change

Because the Theory of Change explains why change is required, it helps remodel the strategic plan for health care. The process of developing a theory of change starts by focusing on a goal. A good strategic plan should be based on scientifically collected evidence that will determine whether or not the goal has been achieved. Thus, the Theory of Change helps evaluate the validity of activities conducted to meet the goals or determine possible modification to bring the goal closer [56].

Therefore, Papers I–II aimed to determine whether Nepal's hospital-based glaucoma screening programs are directed toward achieving their goal of reducing glaucoma blindness, and to explore whether there is any possible change or option that requires introduction as part of the screening program. Evaluating visual damage at the time of diagnosis would indicate whether screening programs detect POAG before blindness sets in. Determining POAG's association with hypertension and diabetes would suggest a possible path for expanding the sphere of glaucoma screening targets (Figure 2).

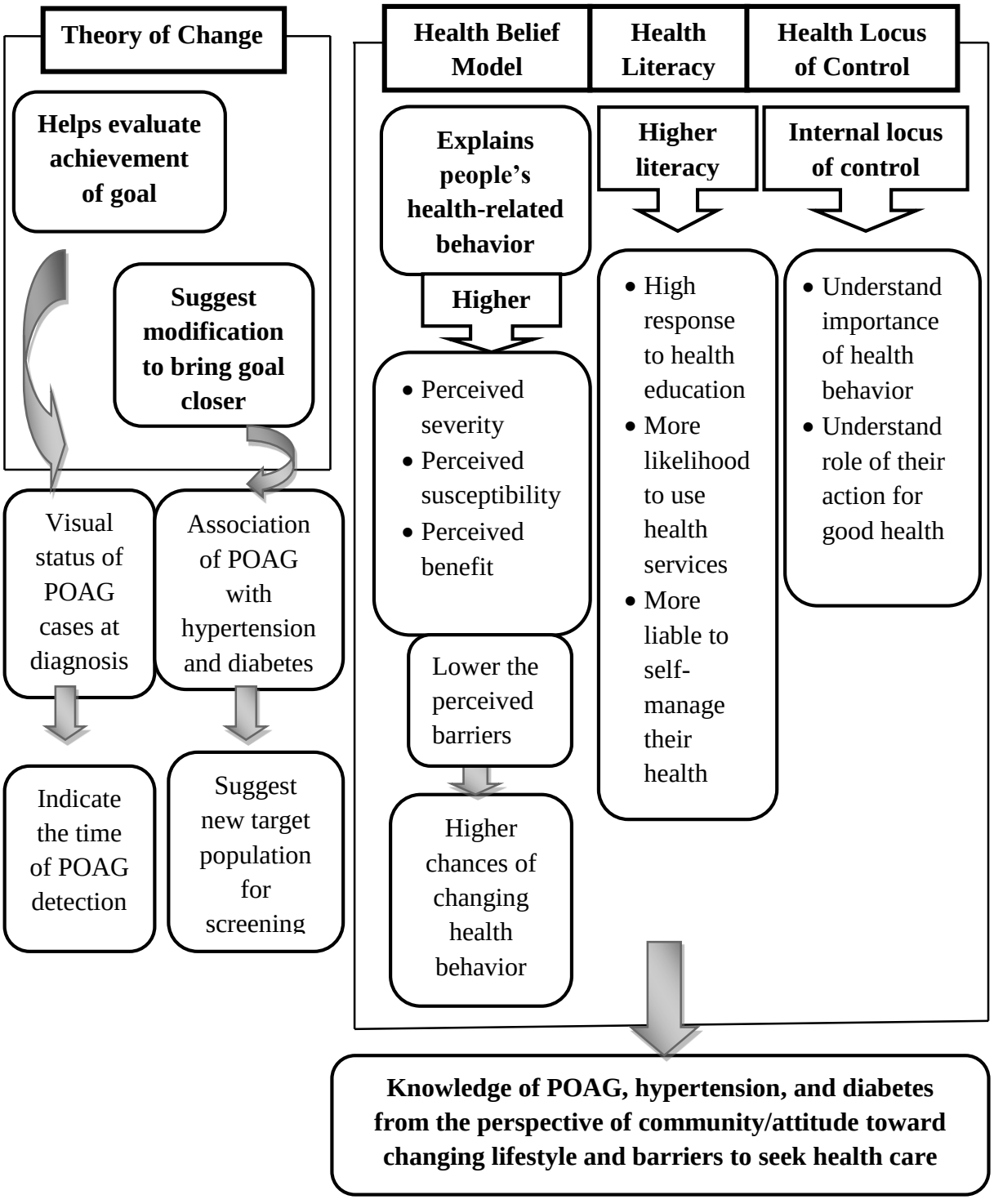

Figure 2: Models of Health Theories and Concepts used in this Thesis.
POAG, primary open angle glaucoma.

Health Belief Model

Health belief is a psychological health behavior change model that explains and predicts health-related behaviors, particularly regarding the use of health services [57]. The Health Belief Model suggests that people's beliefs about health problems, perceived benefits of action, and perceived barriers to action explain their commitment or lack of commitment to health-promoting behavior [58].

The higher the perception of various constructs of the Health Belief Model (e.g., perceived severity, perceived susceptibility, perceived benefits), the higher the chances of a change in health behavior [57]. However, perceived barriers can stop people from changing their behaviors unless the perceived benefits outweigh the perceived barriers. This theory is incorporated in Paper III, in which we explored the perception of health behavior and perceived barriers to health care among people living in a peri-urban community.

Health literacy

Low health literacy has been linked with poor health outcomes, less responsiveness to health education, less likelihood to use health services, and less likelihood to self- manage health problems [59]. Health literacy is an emerging concept that allows wider thinking regarding the content and methods used for health education [59]. Improving a population’s health literacy involves much more than simply distributing health information, although that is the primary task [56]. Community-based outreach programs can help people develop self-confidence and support others as they tackle health issues [56].

If preventing disease-related complications is the primary objective, the best approach involves bringing more people to health service providers to increase disease detection before any complications develop. This happens only if a community’s health literacy is sufficient for people to realize an existence

of complication and act accordingly to prevent complications. Therefore, Paper III also applied the health literacy theory and aimed to explore the community's knowledge regarding POAG, hypertension, and diabetes and determine any need for modifying future health promotional programs.

Health Locus of Control

Health Locus of Control refers to the extent to which individuals believe they participate in and control events that affect their health [60]. Individuals with an internal locus of control believe that their own behavior and active involvement in health care is vital to an improved outcome, whereas those with external locus of control believe that other external factors are responsible for their health outcome [60]. Another type of control that makes a person believe in both internal and external types is known as Bi-local [61]. Bi-locals handle stress and cope well with their diseases more efficiently by combining both types of control. We used this concept to investigate whether the health of people living in a JD-HDSS, peri-urban community, are governed by any of the above types of health locus of control.

CONCEPTUAL FRAMEWORK

The main concept of this Thesis is to use a mixed method approach to study POAG. To assess whether providers currently identify POAG cases early enough to prevent blindness, we designed two quantitative studies in a hospital setting to determine the association between POAG, hypertension, and diabetes and detect glaucoma-related visual damage at time of diagnosis. To explore whether low health literacy and/or perceived barriers to accessing health care cause late presentation to hospital and, consequently, delay case detection, this Thesis also evaluates knowledge of POAG, hypertension, and diabetes in a peri-urban community. Figure 3 illustrates the conceptual framework of this Thesis.

This Thesis includes three papers: a hospital-based quantitative study to investigate the association between POAG, hypertension, and diabetes (Paper I); a hospital-based quantitative study to evaluate clinical features and visual damage of POAG cases (Paper II); and a community-based qualitative study to explore knowledge related to POAG, hypertension, and diabetes (Paper III). Thus, this Thesis compares health perception between those already exposed to these diseases and those who do not have any of these diseases. It also explored possible gender differences in perception of disease and depth of knowledge about disease.

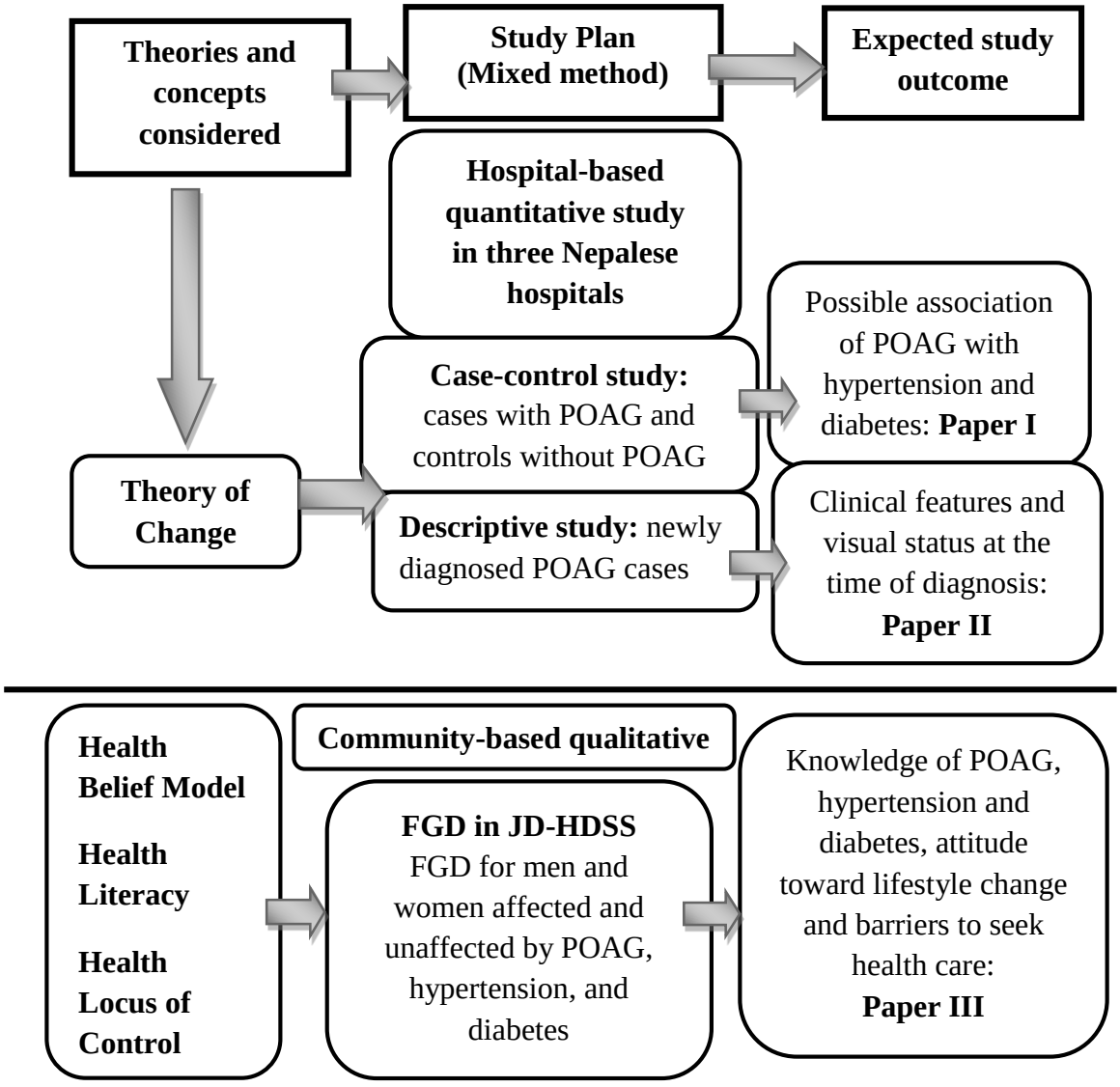

Figure 3: Conceptual Framework of Thesis and the areas of studies (Papers I–III). *FGD, focus group discussion; JD-HDSS, Jhaukhel-Duwakot Health Demographic Surveillance Site; POAG, primary open angle glaucoma.*

METHODOLOGICAL CONSIDERATIONS

Research Design

To achieve all four specific objectives, this Thesis used a mixed method approach that combines both quantitative and qualitative methods.

Papers I–II used a quantitative approach, and Paper III used a qualitative approach. We conducted a hospital-based case-control study (Paper I) to investigate the association between POAG, hypertension, and diabetes. Simultaneously and using the same sample, we conducted a hospital-based descriptive study to illustrate the clinical findings and visual damage at the time of diagnosis of new POAG cases (Paper II).

Paper III used a qualitative approach because this method is particularly effective in describing experiences and perceptions of individuals from their own perspectives [62].

Study setting

Papers I–II were conducted in three hospitals, located in the central (Kathmandu), western (Pokhara), and far-western (Geta) regions of Nepal, and covering comprising areas of mid- hills and plains to achieve a representative sample in terms of geographical terrain. Another criterion for choosing these hospitals involved the availability of the basic diagnostic facilities required for glaucoma screening. Hospitals enrolled for these studies were Nepal Medical College, a teaching hospital in Kathmandu; Himalaya Eye Hospital in Pokhara; and Geta Eye Hospital in Dhangadi (Figure 4).

Paper III was conducted in a peri-urban community situated within the JD-HDSS in the Bhaktapur district of Nepal, about 13 kilometers from the capital city Kathmandu (Figure 4).

Jhaukhel-Duwakot Health Demographic Surveillance Site

Jhaukel and Duwakot, two villages in the Bhaktapur district are located 13 kilometers from Kathmandu (Figure 4), the capital city of Nepal, and are rapidly transforming into peri-urban settlements. Although the villages' outer approach roads connect to the newly constructed Kathmandu-Bhaktapur Highway, inner sections of the villages are connected only by narrow trails. Regular means of transportation are based on busy public vehicles (e.g., buses and mini-vans). The three major ethnic groups living in JD-HDSS are Brahmin, Chhetri, and Newar.

We established the Jhaukhel-Duwakot Health Demographic Surveillance Site (JD-HDSS) as a collaborative project between academic institutes in Nepal and Sweden (Appendix II). JD-HDSS provides a setting for different studies, including research on community-based cardiovascular health literacy and behavior issues. According to the 2010 baseline census, JD-HDSS includes 2,712 households and 13,669 inhabitants (Appendix II).

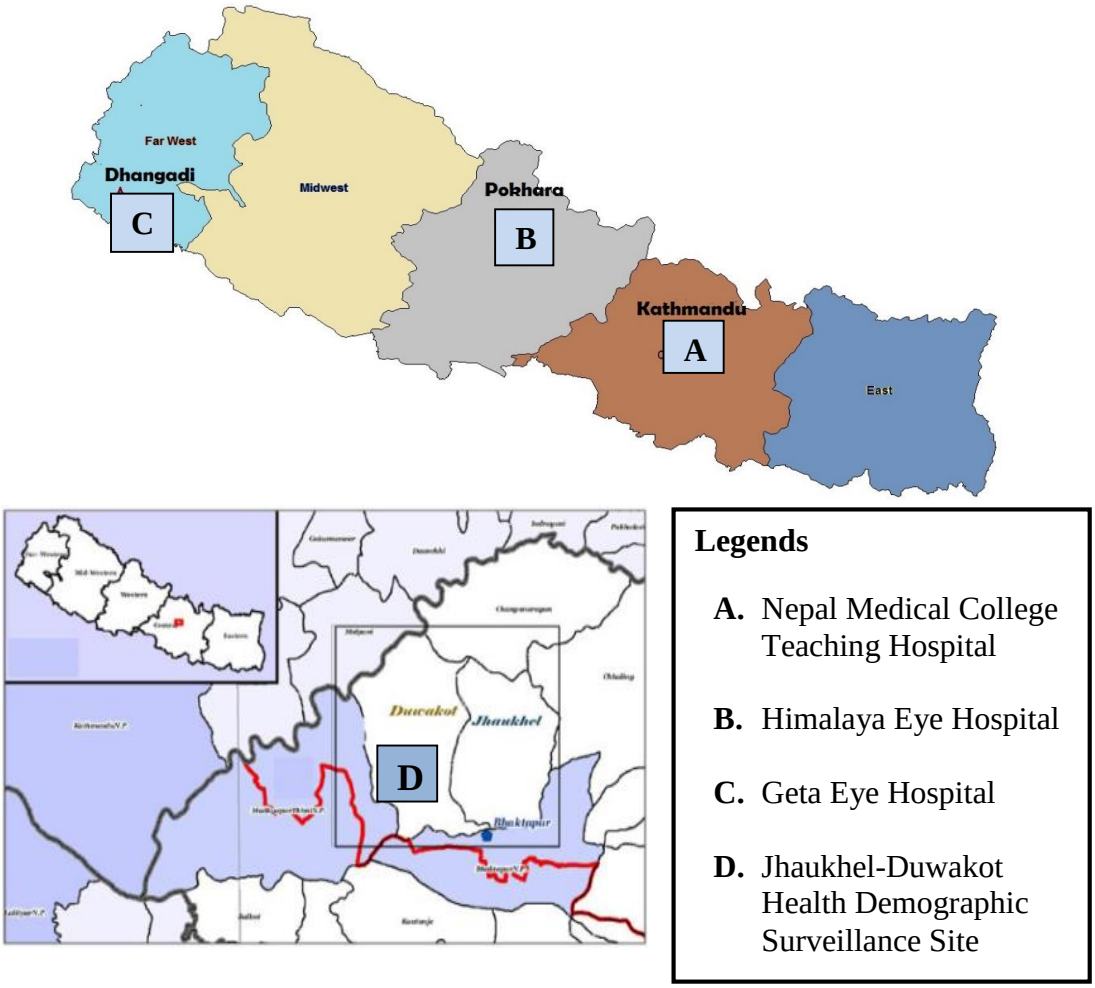

Figure 4: Map of Nepal illustrating the study settings. *Modified from "Image: Nepal districts.png" and Appendix II. Licensed under the Creative Commons Attribution-Share.*

Study Population

Newars, Brahmins, Tharus, and Gurungs, which belong to Nepal's major ethnic populations, live in distinct pockets of Kathmandu, Pokhara, and Dhangadi, where the selected hospitals are situated. Therefore, the target population in Papers I–II was adults belonging to these ethnic groups who self-reported to an eye OPD for ocular or visual problems. The target population for Paper III was residents of JD-HDSS.

Sampling technique and sample size

Papers I–II used a non-random consecutive sampling technique to enroll newly diagnosed POAG patients from the eye OPD, and recruited three age-, gender-, and ethnicity-matched controls without POAG from the same eye OPD. To calculate the sample size, we reviewed published data showing a relationship between POAG, diabetes, and hypertension [63-65]. However, we used the proportion of hypertension in control groups (0.12), with an odds ratio (OR) of 2.4 [64], and we assumed that correlation between cases and controls was 0.225 [66] because this allowed us to obtain a larger sample size. We determined the minimum required sample size (Table 1) with a power of 90% at a 95% confidence interval (CI). Paper II evaluated consecutive cases of newly diagnosed POAG enrolled as cases in Paper I.

Table 1: Sample size for Papers I–II.

Study Description	Sampling Technique	Minimum Sample Size
Paper I Case-control study	Non-random consecutive sampling technique	168 cases 504 controls
Paper II Descriptive study	Non-random consecutive sampling technique	168

In Paper III, we conducted separate focus group discussions (FGDs) for men and women. To explore any difference in knowledge, groups of men and women were further divided into participants unaffected by disease and those affected by diseases such as hypertension, diabetes, or POAG. We assigned codes to every focus group according to gender involvement and whether participants were affected or unaffected by a particular disease (Table 2).

Table 2: Focus group discussion codes and total participants in each group.

FGD Code	Subgroup Code	Subgroup Characteristic	Age (years)	Participants in 1st / 2nd FGD (N)	Total
FGD(M)	FGD(MU)	Unaffected by diseases**	25-45	9/8	17
	FGD(MA)	Affected by diseases	25-45	8/7	15
FGD(W)	FGD(WU)	Unaffected by diseases	25-45	9/9	18
	FGD(WA)	Affected by diseases	25-45	9/8	17

** Hypertension, diabetes or POAG

FGD, focus group discussion; M, men; W, women; MA, men affected; MU, men unaffected; WA, women affected; WU, women unaffected.

Study participants and enrolment

Papers I–II

Adults with newly diagnosed POAG were enrolled for Papers I–II. Individuals' ≥ 15 years of age were considered adults for this study. This age group was chosen because no reports indicate a minimum age of occurrence of POAG in Nepal. Thus, this Thesis investigated all adults with POAG. We excluded individuals with secondary glaucoma, narrow angles, previous ocular surgery, ocular pathologies that obscure the view of the optic nerve head, and pathologies that could alter IOP (e.g., uveitis and high refractive errors >5 dioptre).

Patients suspected of having POAG on the basis of large cup disc ratio (CDR) >0.4, asymmetry of CDR between two eyes which is >0.2 or intraocular pressure (IOP) ≥23 mm Hg and/or with strong family history of glaucoma were referred to the glaucoma clinic for detailed evaluation. After specific examinations confirmed the diagnosis, we enrolled these patients as "cases."

For each case of POAG, we enrolled three age-, gender-, and ethnicity-matched controls without glaucoma on the same or next day from the general eye clinic. Figure 5 shows the flow chart of the enrolment process for participants in Paper I and II.

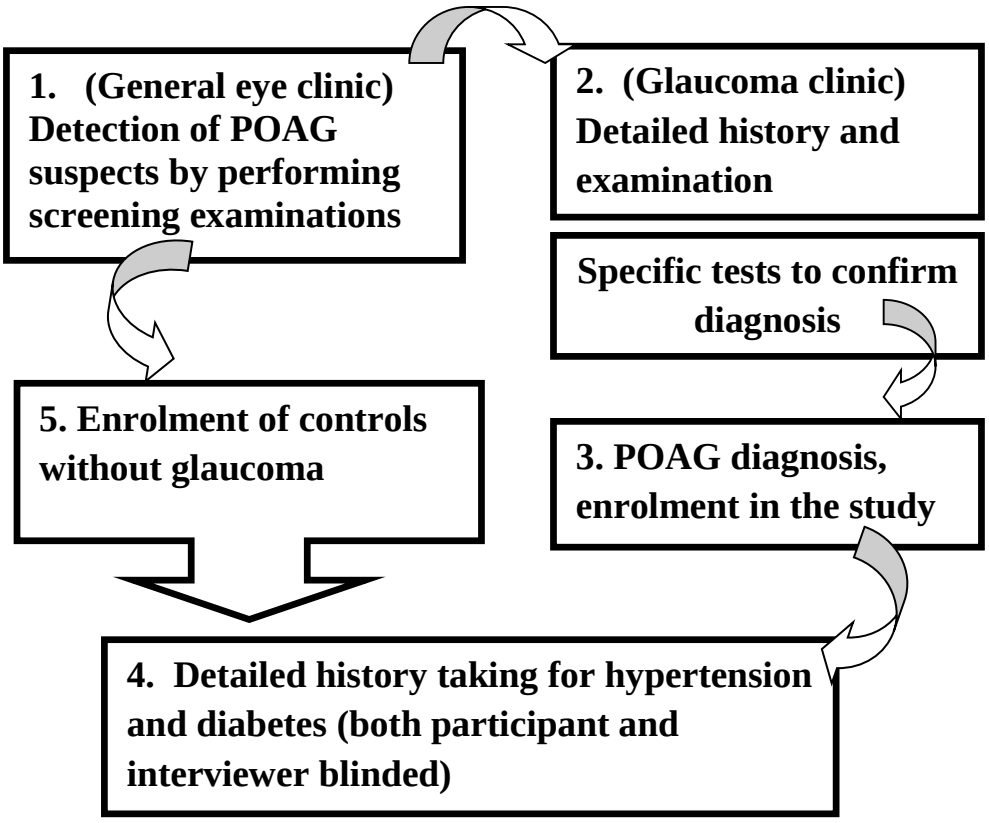

Figure 5: Flow chart showing enrolment of participants (Papers I–II). *POAG, primary open angle glaucoma.*

Paper III

Paper III aimed to explore knowledge of POAG, hypertension, and diabetes from the perspective of a peri-urban community. Thus, we considered both males and females residing in JD-HDSS, aged between 25 and 45 years, and belonging to various occupations (e.g., housewife, student, farmer, businessman teacher and so on) for enrolment. Because the study also aimed to explore

whether pre-existing diagnoses influence knowledge of POAG, hypertension, and diabetes, we carefully selected participants from distinct groups of people who are affected by POAG, hypertension, and/or diabetes, as well as healthy participants unaffected by disease.

This study enrolled individuals aged between 25 and 45 years because

- NCD accounts for 9 million premature deaths before the age of 60 years [67] (i.e., NCD occurs early in life, before clinical manifestations appear). Studies from Nepal also support the finding that demonstrates diabetes and hypertension in young individuals < 40 years of age [32, 68], justifying our inclusion;
- Nepal's demographic profile (2013) [34] shows that the highest proportion of the Nepalese population belongs to this age group; and
- the 25–45-year-old age group includes the most active people and represents the working population. Additionally, people whose job exposes them to the outer world likely will interact with more people, increasing their opportunity to gain more knowledge than other groups in the community.

Two FCHVs helped recruit FGD participants. We used the JD-HDSS database to identify potential participants and also by FCHVs directly, because FCHVs they became familiar with every household in the community when they collected data for the JD-HDSS surveys. FCHVs visited households and informed members the about the study and the FGDs. They asked household members if they would be interested in participating in a FGD and enrolled those who were interested. Presence or absence of disease was based on self-reporting, which was not reconfirmed clinically. However, self-reported disease was confirmed by supporting documentation of medical prescription. Further, all participants with a pre-existing disease took medication for the same disease.

Data-collection tools

Papers I–II

The data-collection tools for Papers I–II that included two sections of semi-structured questionnaires formatted to allow notation of clinical data. Section 1 included socio-demographic information, questions related to symptoms, duration of illness, any other history of ocular diseases and treatment, family history of ocular disease, etc. Section 1 also contained a semi-structured clinical format to note ocular findings. Section 2 was designed to collect any history of hypertension and diabetes, as well as information regarding duration of illness and prescribed medications.

Paper III

FGDs were conducted to collect data for Paper III. Data-collection tools included a digital audio recorder and note pads. Additionally, we developed a FGD guide to provide a framework for the appropriate use of core questions and probes, and to allow the moderator to conduct the FGD in a comprehensive manner. The guide included open-ended core questions covering areas such as general perceptions of health; knowledge of POAG, hypertension, and/or diabetes; change of lifestyle; and access to health care. Some examples of open-ended questions include

- "What do you understand by good health?"
- "Have you heard about non-communicable diseases?"
- "Please share your knowledge and experience about such disease with your friends in this group"
- "Have you heard about a disease called glaucoma?"
- "Can you discuss what you know about this disease with the group?"

When and where required, probing questions ensured that all issues were addressed and understood correctly.

Data collection

Clinical examination of POAG cases (Papers I–II)

To collect clinical history, a trained interviewer used a pre-designed questionnaire that included questions relating to reasons for hospital visit, symptoms, present and past illnesses, and medical history. An ophthalmic assistant used an internally illuminated Snellen's vision chart to measure presenting visual acuity for distance and near vision (with existing optical correction, if any). A trained optometrist conducted retinoscopy and subjective refraction for patients whose presenting visual acuity was > 6/6 in either eye.

I performed detail ocular examinations (e.g., detailed evaluation of the anterior segment, using a Haag-streit slit lamp; evaluation of the posterior segment; and evaluation of the optic disc, using a + 90 D lens at x16 magnification). Dilatation of the pupils was done using 1% tropicamide and 2.5% phenylephrine only when it was difficult to visualize the fundus without dilating the pupil. Vertical cup-to-disc ratio (VCDR) was measured as the parameter to determine structural damage to the glaucomatous optic nerve head. The margins of the cup were identified by viewing the point of maximum inflection of the vessels crossing the neuro-retinal rim. The vertical dimensions of the disc and cup were measured using a continuously adjustable vertical light beam and a scale calibrated in millimeters; diameters were then multiplied by magnification correction factor 1.33 for +90 D lens [69]. Any notching, disc hemorrhage, peri-papillary atrophy, or retinal nerve fiber layer defects were recorded.

Intraocular pressure was serially measured using a Goldmann Applanation Tonometer three times in both eyes, and an average of three measurements was used for data analysis; gonioscopy was done using Goldmann 3- mirror contact lens. IOP measurement was done by an ophthalmologist. An optometrist performed a visual field test, using static-

automated white-on-white perimeter (Humphrey Field Analyser, Carl Zeiss Meditec, Germany). To ensure uniformity, we used a full threshold 24-2 program. All three hospitals routinely used this program, decreasing the chance of examiner error and bias. The visual field test was repeated if the patient reliability index was unsatisfactory (i.e., fixation loss > 20% and/or false positive and false negative indices exceeding 33%) or the result of the glaucoma hemifield test (GHT) was outside normal limit.

Diagnostic criteria

In accordance with a modified Shaffer's classification, we labeled the angle of the anterior chamber as "open angle" when we observed a grade III or grade IV angle [70]. Intraocular pressure ≥ 23 mmHg was considered high and < 23 mm Hg was considered within normal range [71]. The minimum criteria for diagnosis of compatible glaucoma visual field defect was GHT exceeding normal limits, together with a cluster of four or more contiguous points with p<5% on the pattern standard deviation plot (PSD) not crossing the horizontal meridian [72, 73].

Glaucoma diagnosis was confirmed by signs of structural damage to the optic disc and compatible glaucomatous visual field defect, with raised intraocular pressure in at least one eye [7]. Diagnosis of POAG was made even without visual field changes but only when CDR was ≥ 0.7 and IOP was > 30 mmHg.

After confirming the diagnosis, we enrolled participants in the study and sent them to the interviewer, who determined any history of diabetes and hypertension. To determine whether they had hypertension and/or diabetes, controls also met with the interviewer. The interviewer completed Section 2 of the data-collection tool by noting the medical history of each respondent. Both interviewer and participant were blinded. Participants had no access to the results of any examination or diagnosis until they had completed the diabetes

and hypertension interview. The blinded interviewer received folded pages, secured with a sticker, of the clinical findings and diagnosis. A history of hypertension and diabetes was considered only if the individual provided a history of illness and was taking medication, as evidenced by a prescription.

Focus group discussions (Paper III)

SSV and BS conducted all eight FGDs in the local Nepali language and each FGD lasted approximately 60 minutes. SSV moderated all FGDs except the first, which was conducted by BS; SSV served as a note taker for that session. The first FGD was part of a pre-testing process for the FGD guide. We decided to include the pre-test FGD in the study because it did not necessitate in any major corrections in the guide.

The moderator began each FGD by greeting and thanking the participants for their participation, introducing the research team, and explaining the purpose of the FGD. Likewise, the participants briefly introduced themselves to the group. When participants appeared comfortable, the moderator asked an open-ended question (e.g., "What do you understand by good health?" or "Who do you think is responsible for your ill health?") about general health to demonstrate participants' understanding of good health and determine their beliefs about the causes of disease. Next, the moderator asked, "Have you heard about non-communicable diseases? Please share your knowledge and experience about such disease with your friends in this group." Thereafter, we inquired, "Have you heard about a disease called glaucoma? Can you discuss what you know about this disease with the group?" We also asked open-ended questions relating to NCDs and glaucoma, followed by questions related to access to health care. The moderator encouraged quiet participants to speak by addressing them with questions like, "What is your opinion?" and "Would you like to share something with us?" Probing questions were used when and where required.

All FGDs were recorded using a digital tape recorder. Additionally, the note taker recorded information about group dynamics, such as verbal and non-verbal cues, body language, and how and with whom participants interacted.

Data management and analysis

Papers I–II

Completed forms were checked carefully for completeness, and any missing data were traced in the examination unit register. Incomplete cases were excluded from the study.

We performed statistical analysis using SPSS Statistics 17 (SPSS Inc., Chicago, IL, USA); Paper I also used Stata10 software. We used both descriptive and inferential statistics for Paper I. We used descriptive statistics to calculate percentage, and mean and standard deviation (SD) to describe demographic characteristics and clinical variables. In inferential statistics, we used McNemar's test to measure the association between POAG, hypertension, and diabetes. Data were expressed in a fourfold table containing concordant and discordant pairs. We defined the case-control pair as concordant when both or neither member of the pair had been exposed to hypertension or diabetes. A discordant pair showed mixed exposure between cases and controls. Finally, we computed the odds ratio (OR) for discordant pairs (95% CI) and gender and caste groups within cases (95% CI). In Paper II, continuous data were presented as means and SD, and categorical data were presented as proportions (95% CI). We used unpaired t-tests to compare continuous variables. P value was set at 5% level of significance for both Papers.

Paper III

Our framework analysis approach [74] lies within a broad family of qualitative content analysis. Framework analysis is best used in applied health research, which aims to achieve specific information and provide outcome or

recommendation as a basis for need to change health care [75]. Importantly, framework analysis provides systematic and visible stages during data analysis. Although framework analysis is generally inductive (i.e., codes are generated from the data), this procedure also allows predetermined codes and themes [76]. This was an important feature because we were exploring specific issues.

Our framework analysis included the following steps [74, 76]:

1. *verbatim (word-for-word) transcription* of audio-recorded material was done in Nepali language and translated into English for analysis and reporting.
2. *text (data) familiarization* (i.e., carefully reading the entire transcript);
3. *theme identification,* using pre-determined and emerging issues identified during familiarization;
4. *inductive "open coding"* (i.e., textual coding of any data that might have been relevant from any perspective) [77]. Codes represented various aspects of data, such as belief, knowledge, emotion, behavior, incidents, frustration etc.;
5. *working thematic framework was developed* after coding the first two transcripts. Two researchers involved in the study worked from the initial codes and agreed upon a set of codes for all subsequent transcripts. Codes referring to similar information were grouped together into categories, and categories were grouped to form a theme or concept (Table 3);
6. *framework charting* (i.e., charting various categorical codes from different FGD sub-groups of against emerging or predetermined themes) allowed data summarization into a matrix); and

7. *mapping and interpretation*, whereby we searched for patterns, associations, concepts, similarities, and dissimilarities in our data, aided by visual displays and plots that helped us during data interpretations.

Table 3: Example of the thematic framework in Paper III.

Different codes with similar meaning	Category	Theme (Concept)
Not suffering from disease, 100% disease-free, sound mind, do not fall ill	No disease	Perceived good health
Can work without problem, can do all work, physically fit, able to do all the work you want to	Fit to work	
Energy in the body, do not feel tired, can walk without problem	Feeling energetic	
Feel hungry as usual, can eat a lot, feel like eating	Good appetite	
Sleep well at night, uninterrupted sleep	Good sleep	

Validity and reliability

In Papers I–II, we attempted to minimize inter-examiner variability by pre-testing the procedures (e.g., measuring intraocular pressure and visual fields examination) before performing actual tests. Pre-testing involved testing two or three individuals independently, using the same technique and programs, and then comparing the results. To minimize error, we serially measured IOP three times and used the average IOP for data analysis. When the reliability index was unsatisfactory or the glaucoma hemifield test (GHT) result was outside normal limit (i.e., fixation loss > 20% and/or false positive and false negative indices exceeding 33%), we repeated the visual field test to ensure reproducible findings.

Prior to data collection, we pre-tested the FGD guide in a group of eight healthy participants from the same JD-HDSS population to ensure that core questions were applicable and appropriate. To ensure that prior discussion with the researcher would not affect participants' knowledge about disease, the moderator discouraged participants from asking or discussing any health-related questions before, during, and after each FGD. Repetition of responses from one FGD to another was considered as the saturation point. Codes, categories, and themes represent the consensus of two researchers.

Ethical considerations

This Thesis work conforms to the Declaration of Helsinki for research involving humans. The Nepal Health Research Council (NHRC) approved the work in this Thesis. Table 4 shows the summary of ethical considerations.

Papers I–II

All study participants received information about the study and its purpose, as well as a detailed explanation of the examination procedure. The consent taker read an informed verbal consent to all participants, in Nepali language, and asked participants whether they understood everything. Thereafter, participants were asked whether they were willing to participate in the study. When participants answered "yes," the consent taker ticked the "yes" box and signed the form in the participants' presence. We also explained that participants could withdraw from the study at any time. POAG patients received treatment with either anti-glaucoma medication or filtering surgery. Participants who could not afford treatment were treated free of cost at the participating hospitals.

Paper III

Every FGD participant gave informed verbal consent after hearing an explanation of the FGD and its purpose. Participants also consented to the use of an audio recorder, still photography, and note taking. We explained the

reasons for such documentation, and also clarified that recordings would be destroyed following data analysis and would not be shared with another party.

Table 4: Summary of ethical considerations of Thesis.

Papers	Ethical approval	Consent	Data confidentiality	Financial cover/ benefit
I-II	Nepal Health Research Council (NHRC)	Informed verbal consent	Housed securely at Nepal Medical College Teaching Hospital (NMCTH)	Examinations done free of charge Medicines provided Follow up of visual fields advised after 6 months
III	NHRC	Informed verbal consent	Data securely placed in external hard drive and kept with researcher	FGD allowances provided

RESULTS

Paper I: Do non-communicable diseases such as hypertension and diabetes associate with primary open-angle glaucoma? Insights from a case-control study in Nepal

Among 4,463 individuals aged 15 years and above who visited the general eye clinic, 183 (4.1%) were diagnosed with POAG for the first time. Among those, 173 fulfilled the study's enrolment criteria. Controls included 510 participants who visited a hospital but did not have POAG.

Demographic characteristics

The sex ratio of POAG patients was 2.58 males to 1 female; the mean age was 58.9 (SD=14.72) years. Based on the total number of individuals belonging to each ethnic group and attending the hospital, we determined that POAG occurred more frequently among Gurung (6.2%), followed by Newar (3.5%), Brahmin (3.5%), and Tharu (3.2%). However, the difference in percentage of POAG among Brahmin, Newar, and Tharu was not significant ($p>0.05$). The odds of Gurung having POAG were 2.05 times higher than Brahmin, which was statistically significant (OR 2.05, 95% CI: 1.30; 3.24).

Association of POAG with hypertension and diabetes

We determined that hypertension and diabetes associated positively with POAG in each ethnic group (OR>1). The overall odds of having POAG increased 2.72-fold in patients with hypertension and 3.50-fold in patients with diabetes (Tables 5 and 6).

Table 5: Distribution of hypertension in cases and controls.

With POAG (cases)	Without POAG (controls)		Total	Odds Ratio (95% CI)
Hypertension	***Present***	***Absent***		
Present	42	131	173	2.72
Absent	48	462	510	(1.95; 3.88)
Total	90	593	683	

POAG, primary open angle glaucoma
Table modified from Paper I

Table 6: Distribution of diabetes in cases and controls.

With POAG (cases)	Without POAG (control)		Total	Odds Ratio (95% CI)
Diabetes	***Present***	***Absent***		
Present	53	120	173	3.15
Absent	38	472	510	(2.19; 4.54)
Total	91	592	683	

POAG, primary open angle glaucoma
Table modified from Paper I

Visual acuity

Vision was classified according to definitions by the International Council of Ophthalmology [78]. We found mild visual impairment, or normal vision, in 85.5% of POAG cases and 98.2% of controls. Among POAG cases, 6.9% had moderate visual impairment, 2.9% had severe visual impairment, and 4.7% were blind, compared to only 1.8% of controls with moderate visual impairment and none with severe visual impairment or blindness (Figure 6).

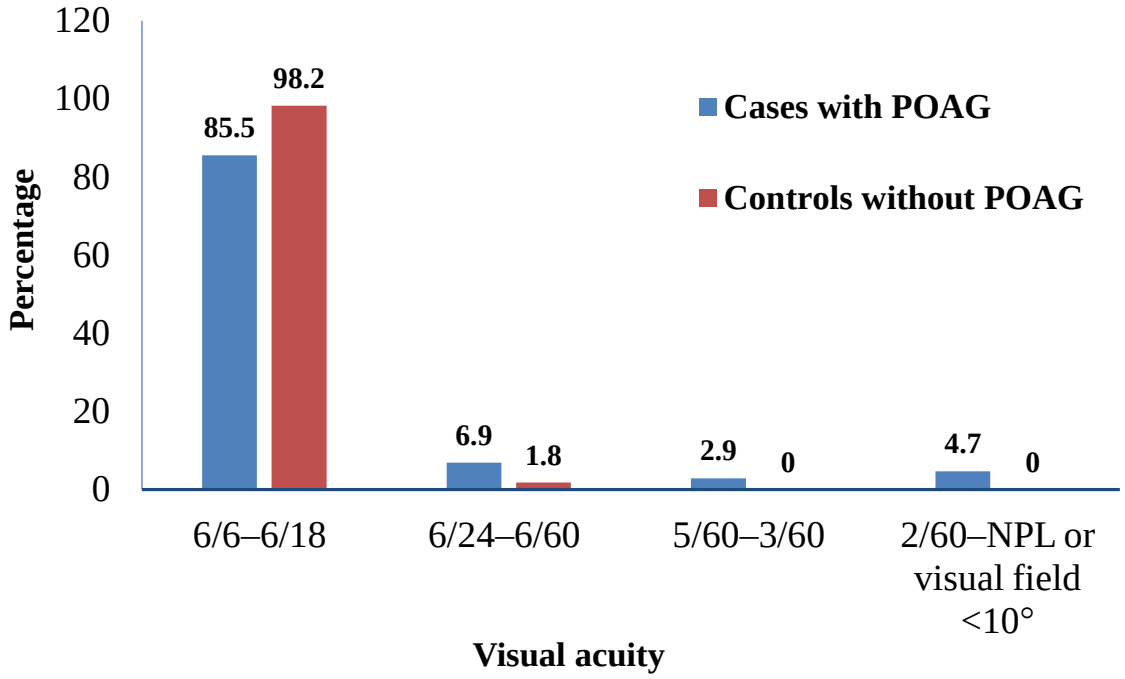

Figure 6: Best corrected visual acuity of better eye. *POAG, primary open angle glaucoma, NPL, no perception of light.*

In conclusion, POAG associates with hypertension and diabetes in the Nepalese population.

Paper II: Visual status in primary open-angle glaucoma: a hospital-based report from Nepal

Paper II explored detailed clinical features, including visual damage in terms of visual field and visual acuity, at the time of diagnosis of POAG. Among 173 POAG patients, 71.1% were male and 28.9% were female.

Reason for attending hospital

Among all POAG patients, 60.7% visited the hospital for either vision-related symptoms or other unspecific eye-related symptoms. Another 21.4% had their eyes tested while accompanying a family member to the hospital, and 9.8% came for a regular glaucoma test because they were suspected to have glaucoma earlier and/or had a positive family history of glaucoma. The remaining 8.1% were referred from other hospitals and clinics.

Clinical features

Symptoms

The commonest symptom among POAG cases was blurring of near vision, which accounted for 82.7% (95% CI: 77.1; 88.3), followed by diminished far vision (20.8%); 95% CI: 14.7; 26.8). Another 9.2% complained about reduced side vision (95% CI: 4.9; 13.5), a possible subjective visual field defect. Additionally, 40.5% (95% CI: 33.2; 47.8) complained about headache, and 24.3% (95% CI: 17.9; 30.7) had eye pain. Other complaints included watering, itching, and redness of the eyes (13.8%, 12.1%, and 10.4%, respectively). All remaining clinical symptoms (10.9%) were categorized as "others," including grittiness, heaviness, and discharge from the eye (Figure 7).

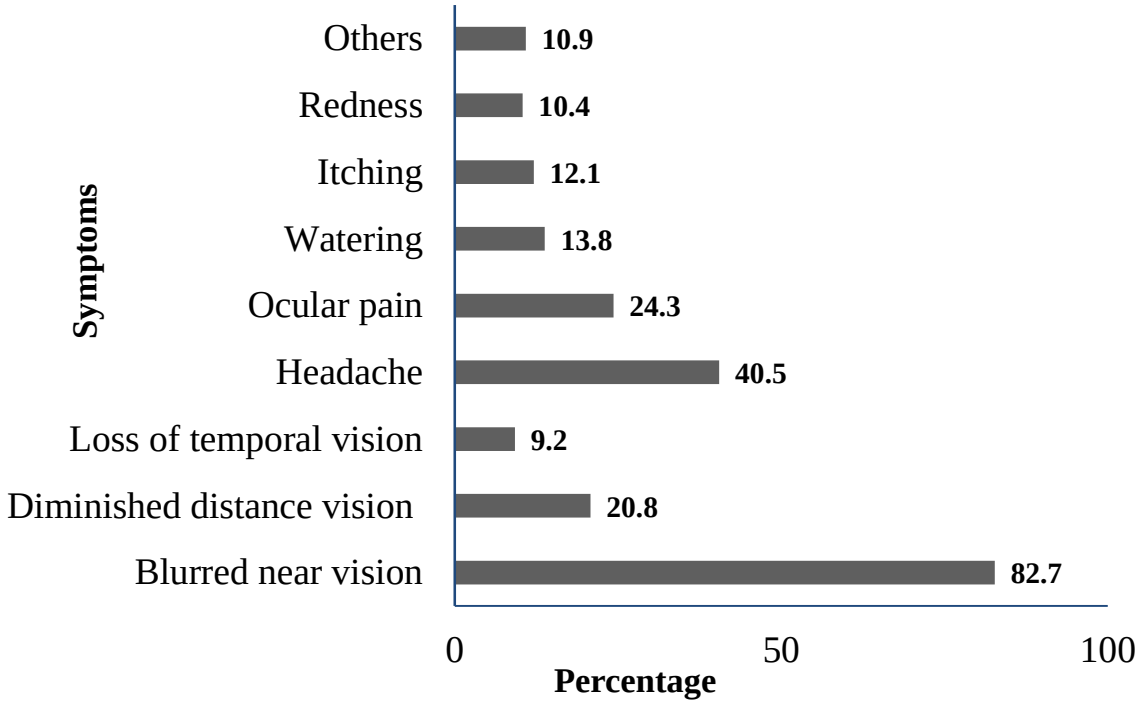

Figure 7: Presenting Symptoms of POAG patients.

Vertical cup-to-disc ratio (VCDR) and intraocula1qar pressure (IOP)

Mean VCDR in men and women was 0.7 (SD=0.18) and 0.6 (SD=0.21), respectively; p=0.999. Mean IOP in men was 27.9 mmHg (SD=3.15), compared to IOP in women (26.7 mmHg [SD=3.89]); p=0.998.

Visual fields

The mean of mean deviation (MD), an overall decibel value that indicates total visual field loss, was –13.24 (SD= –9.0). Mean pattern standard deviation (PSD) (i.e., a deviation from normal of measured visual field pattern) was 7.34 (SD=2.8), and mean short-term fluctuation (SF) (i.e., fluctuating response to test spots due to patient fatigue) was 2.52 (SD=0.9). Finally, mean corrected pattern standard deviation (CPSD) (i.e., corrected visual field pattern after subtracting SF) was 6.65 (SD=4.2).

Among total eyes undergoing a visual field test, 61.5% revealed a glaucoma hemi-field test (GHT) outside the normal limit, 18.4% showed borderline changes, 5.4% had a generalized reduction of sensitivity, and 11.9% were within the normal limit. Visual field results of nine (2.8%) eyes in five patients (both eyes in four patients and a single eye in one patient) were not incorporated in this report due to an unsatisfactory reliability index despite a repeated test. Among total eyes with POAG, 7.5% did not undergo a visual field test due to vision < 6/60 and loss of central vision.

Visual acuity

We analyzed the best corrected vision in the better eye. Among those eyes, 85.5% had mild visual impairment (95% CI 80.3; 90.8), 6.9% had moderate visual impairment, 2.9% had severe visual impairment, and 4.7% were legally blind (95% CI of 1.5; 7.8).

In conclusion, most patients visited the hospital due to either vision-related symptoms or other unspecific symptoms relating to the eye. Although the most common symptom was blurred near vision that was unrelated to POAG, 9.2% complained of diminished temporal side vision, which is a late-stage symptom of POAG. Mean IOP and mean CDR showed no gender difference. The majority of POAG cases had moderate to severe visual field loss, and 4.7% were already legally blind at the time of diagnosis.

Paper III: Understanding and living with glaucoma and non-communicable disease like hypertension and diabetes in the Jhaukhel-Duwakot Health Demographic Surveillance Site: a qualitative study from Nepal

Paper III explored knowledge of glaucoma and NCDs in a peri-urban community of Nepal. We conducted eight FGDs in the JD-HDSS, and presented our results in four main themes related to the main aspects covered in the FGDs (i.e., health and health beliefs, disease knowledge and prevention, perceptions of diseases, and coping with diseases.

Health and health beliefs

Perceptions of health

Women perceived the meaning of "good health" differently than men, but we observed no differences between those affected or unaffected by hypertension, diabetes, and/or POAG. Men described good health in various ways, including having a disease-free body, feelings of being energetic, having uninterrupted sleep, eating well with good appetite, feeling comfortable without tiredness, and not having symptoms like pain or swelling.

In comparison, women described good health as having a body fit for working, being able to undertake household responsibilities, being able to rise on time and perform household chores without any problem, having a light and comfortable body without any pain, and having normal appetite. Unlike men, women did not relate good health with absence of disease.

Perceptions of causes of disease

Regarding the causes of disease, men and women from JD-HDSS both believed that disease results from unhealthy habits and that they themselves are responsible for their good health.

On the other hand, participants also identified external factors responsible for their ill health. Men in particular believed that air pollution, inorganic

fertilizers, lack of regulations in the food market, and lack of proper governmental policies affected their health. Some men suggested that social and cultural practices negatively influenced their determination to follow recommendations for healthy habits. However, some men simultaneously expressed the possibility that self-control plays a role in changing their health behavior.

Some women believed that health was in God's hands or governed by an external evil power. They stated that some illnesses could only be cured by faith healers (i.e., mediators between the spiritual and the realistic world) or by offering sacrifices to placate the spirit.

Knowledge of the diseases and their prevention

Hypertension and diabetes

Participants were aware that hypertension and diabetes are commonly seen in their community. Regardless of health status, both men and women believed that unhealthy food habits and lack of physical activity cause these diseases. Participants described intake of sweets, salted and fatty food, adulterated cooking oil, excessive alcohol intake, smoking, physical inactivity, and mental stress as causes of hypertension and diabetes. Some women affected by hypertension and diabetes also stated that the diseases were transmitted through their parents:

> *I think diseases like diabetes and hypertension come to us through our parents. I think like this because we are seven brothers and sisters, including me. Four of us suffer from diabetes and my father died from diabetes two years ago. I am afraid that I may have given it* (the disease) *to my children as well.* (39-year-old woman with diabetes)

We observed some differences in the idea hypertension and diabetes are non-communicable diseases when transferred from parents. Some participants

stated that hypertension and diabetes transferred from parents are communicable. Participants expressed little knowledge about the role of cholesterol, but some women affected by hypertension and diabetes stated that increase body weight could be a risk factor for most non-communicable diseases, including hypertension and diabetes.

> *I feel that being fat is a disease in itself. I was absolutely fine until I delivered my first child. After this, I started putting on weight and I got this disease of sugar* (diabetes). *So I feel that excessive body weight invites all diseases.* (33-year-old woman with diabetes)

Men and women with hypertension and diabetes described the potential consequences of these diseases as paralysis of the body, loss of speech, kidney failure, sudden death, eye problems causing blindness, delayed wound healing, and infections in the body.

Participants without hypertension and diabetes knew little about these diseases and were unaware of potential complications. They described complications such as stroke, numbness of toes and fingers, and frequent infections, but were not entirely sure whether these were caused by hypertension and diabetes.

Glaucoma

Irrespective of gender and pre-existing diseases, participants were aware that glaucoma is prevalent in their community. They also perceived glaucoma as a vision-threatening, lifelong disease. Male participants who suffered from hypertension, diabetes, and/or POAG knew more about glaucoma than other participants. They described glaucoma as a genetic disease that runs in a family and requires lifelong treatment, and said that glaucoma may cause blindness and might associate with hypertension and diabetes. They also termed POAG as a sight-threatening disease.

> *My uncle has glaucoma and he is almost blind by one eye. When I went for blood pressure check-up, my doctor said that I may also get glaucoma. So I need to go to eye doctor. At that time, the doctor also told me that* (high) *blood pressure and sugar* (diabetes) *can be associated with glaucoma.* (42-year-old man with hypertension)

Although none of the female FGD participants suffered from POAG, the presence of hypertension and/or diabetes had not enhanced their knowledge about retinopathies that can be caused by hypertension and diabetes or their possible associations with POAG.

> *I don't have glaucoma so I don't know much about it. I have heard that it can cause blindness forever. I am not sure how this disease occurs. Is this similar to cataract? I have seen people getting operated for cataract but not sure whether glaucoma can also be operated.* (40-year-old woman with hypertension)

Preventive measures

Most participants were aware that healthy lifestyles and healthy food habits could prevent hypertension and diabetes. Gender and health status did not influence awareness of the general preventive aspects of hypertension and diabetes. Participants described preventive measures as active lifestyle; doing manual work; walking every day; quitting smoking; avoiding junk food; and reducing their intake of alcohol, salt, sugar, and fatty food. Additionally, some women believed that weight loss could prevent hypertension and diabetes and also prevent complications from these diseases.

Some men with hypertension and/or diabetes stated that a high cholesterol level might be a risk factor for hypertension, mentioned the necessity of regular blood tests to monitor cholesterol, and knew about the

importance of regular health check-ups. On the other hand, some men unaffected by disease expressed doubt that these diseases are preventable.

Participants did not discuss issues regarding preventive measures for glaucoma spontaneously; rather, the FGD moderator initiated such discussion with probing questions. Participants were not sure how to prevent POAG-related blindness, and even those who knew about the probable association between hypertension, diabetes, and POAG knew nothing about preventive measures. They knew that early treatment could prevent blindness, but did not know how to get treatment or when they should go for an eye examination.

> *I am not sure how blindness can be prevented. If I have no problem with my vision why would I go to an eye doctor in the first place? Well, I do not know how this works. I go to my doctor every six months for hypertension, so maybe my doctor will be able to tell me.* (42-year-old man with hypertension)

Perceptions of the diseases

Severity

Perceptions of the severity of the diseases were influenced by gender as well as pre-existing hypertension, diabetes, and/or POAG. Men with hypertension, diabetes, and/or POAG perceived these diseases as incurable, life-threatening, sight-threatening, and dangerous—diseases that require lifelong medication.

In contrast, men unaffected by disease and women with or without hypertension and/or diabetes did not consider these diseases dangerous. Instead, they described them in various ways: controlled with medication, and that one can live longer without complications if you take regular medicine. They also believed that regular medication makes one symptomless. Thus, they believed that such disease were not dangerous, but just like any other disease. Some men unaffected by disease even perceived the diseases as curable. Regardless of

health status, women perceived POAG as a blinding disease but did not consider the condition incurable (Figure 8).

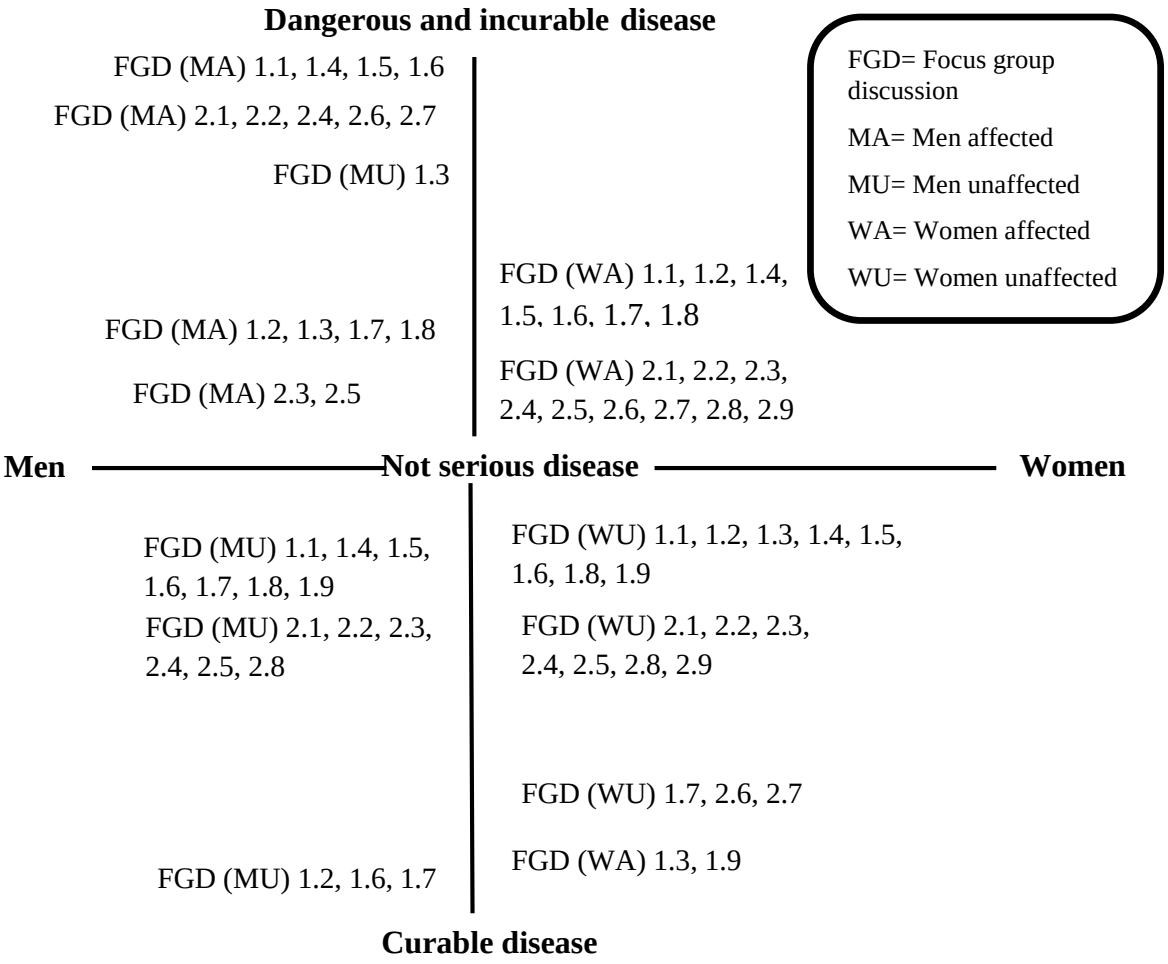

Figure 8: Mapping of perception of severity of disease. *Note: Participant's positions are plotted near vertical line representing perception against horizontal line representing gender.*

Impact

Irrespective of gender, participants suffering from hypertension, diabetes, and/or POAG consistently mentioned the impact of diseases on their lives. They described the impacts as difficulties in coping with restrictions in diet, being unable to enjoy good food, increased stress for the whole family, increased stress due to side effects of medicines, reduced work hours and subsequent

financial loss, job loss, financial constraint for treatment and hospital visits, and inability to perform their work in the office and farm with precision due to reduced vision.

Additionally, women diagnosed with hypertension and/or diabetes felt that family members treated them unfairly. They said that in-laws considered diagnosis as a way to avoid household work, and expected them to do all the household chores and heavy farm work even when they were not well. Furthermore, they felt that husbands did not support them in fighting for their rights and gave little time to their wife's health care, even to accompany them to the hospital. Men and women without hypertension, diabetes, and/or POAG believed that these diseases could have a substantial impact on life but had no in-depth knowledge in this regard.

Coping with the diseases

Attitude and practice toward changing lifestyle

Men with hypertension and/or diabetes said they attempted to change their lifestyle by doing exercises, walking, and reducing salt and alcohol intake, but they did not take those actions on a regular basis. They believed that changing their lifestyle was difficult, but said they were ready to do so to make their life better.

Men without hypertension and/or diabetes knew about recommendations concerning food, exercise, tobacco, and alcohol, but believed it was not easy to change their lifestyle and not crucial for them to do so because they doubted such recommendations could prevent disease. They said that knowing what to do was easy, but practicing the recommendations was much more demanding because it was difficult to give up long-standing habits. Some did not want to give up good food by reducing their intake of salt, sugar, and alcohol, but would do so in the future if they were diagnosed with the disease.

The presence or absence of disease did not influence women's view of changing their lifestyle. They said that cooking and preparing different meals meant more work in the kitchen, so they would eat whatever they cooked for the family. Some women giggled while discussing physical exercise. Women perceived that exercises are meant only for men. They also listed several reasons that it was impossible for them to exercise regularly or go for a walk. First, they had too much work at home, leaving no time for exercise. They also said that exercise was socially unacceptable for women. Moreover, even if a woman tried to change her lifestyle, her family would not support her.

> *Women doing exercise is not acceptable in our society, it is just meant for men. I know we should be doing this, but our family members will never support us. Walking is probably good for us but where is the time? We are tied up in household work so much that we can hardly find free time for ourselves.* (35-year-old healthy woman)

Some women said they would have to overcome many barriers, including their children's happiness, if they wanted to take care of their own health. One woman wondered if she should change her lifestyle by ignoring her family's happiness:

> *Forget about in-laws; if I start taking a one-hour walk every day, even my children will not be happy with me. Everyone at home expects me to have their food, clothes, tea and snacks ready for them in time, and if I start taking care of myself I will be late for all these household chores. If I really want to change my lifestyle, I will have to ignore the happiness of my family. I am not sure whether I should do this for my health.* (44-year-old woman with diabetes)

Barriers to accessing health care

Participants discussed several barriers to accessing health care. Men and women perceived such barriers differently, but neither gender was influenced by the presence of hypertension, diabetes, and/or POAG. Some common barriers described by both men and women included lack of knowledge about the disease, expense, lack of funds for health care, and long waiting times at the hospital.

Some men stated that people exhibit a casual attitude toward health and seeking health care. Additionally, some said their community lacked proper information about where people could go for proper health care or identified the best physician for a particular disease. Apart from the barriers mentioned above, women said they faced additional obstacles to access health care, including a lack of education and health awareness; cultural barriers, including their lack of decision-making power; confidence to travel alone; and independence to spend money.

> *Nothing is in women's hands. Since we do not contribute to household earnings we cannot spend as we like. To make it worse, I cannot even travel alone to hospital for check-ups. My mother in-law decides whether I should go or not, and my husband takes me to hospital.* (40-year-old woman with diabetes)

DISCUSSION

This Thesis provides a deeper understanding regarding the context of POAG in Nepal that might help define future blindness prevention programs.

Among all NCDs, hypertension and diabetes are rapidly emerging causes of mortality and morbidity in Nepal [32, 68]. There has been an ongoing debate regarding the possible association between POAG, hypertension, and diabetes and the ethnic variation regarding such associations [19, 20, 23, 24]. Paper I aimed to explore whether there is a possible association between POAG, hypertension, and diabetes in the Nepalese population. Paper II delineated the time of POAG detection through opportunistic glaucoma screening in Nepal. Considering the role of health awareness in detecting early-stage POAG to prevent from blindness, I also conducted a qualitative study (Paper III) to explore health knowledge regarding POAG, including its possible risk factors (i.e., hypertension and diabetes).

Demographic profile of POAG patients

Although an almost equal number of males and females visited the hospital during the study period, POAG frequency was 2.5-fold higher in men than in women. Some studies suggest that POAG affects men more frequently, but other reports observed no difference between genders [79-81]. In our study, the reason that more men have POAG could be due to fact that women in Nepal utilize health services less frequently than to men [82]. While reasoning critically against the fact that blindness is twice as common in women as in men [83], women's hospital visitations should have been twice that of men, but the numbers were almost equal in this study (Paper I). Our results indicate that only 50% of women visit a hospital, and another 50% do not go to a hospital for their eye problems.

POAG increased with age, but declined in participants > 75 years. Earlier reports show fewer POAG cases after people reach 75 years of age [81, 84]. In Paper I, the lower rate of POAG in this age group might reflect the low average life expectancy in Nepal [85].

Similar to a previous report, Paper I also demonstrates an ethnic difference in the prevalence of POAG, with higher prevalence in Gurungs compared to the other ethnic groups [79].

Exploring unknown facts of POAG

Association of POAG with hypertension and diabetes and impact on blindness

Paper I revealed a possible association between POAG and hypertension (OR 2.72), concurring with the Blue Mountains Eye Study [9] and the Rotterdam Study [86]. Paper I also revealed that POAG might associate with diabetes, which corresponds with a report that demonstrates a similar association [84]. Although some studies contradict an association between POAG, hypertension, and diabetes [19, 20], current studies challenge those conclusions [21-24]. These disparate results could be explained by racial and ethnic variation [87-89].

Hypertension and diabetes are the leading causes of morbidity, mortality, and disability in South Asian countries, including Nepal, and contribute to over 20% of the world's CVD burden [29-31]. An association between POAG, hypertension, and/or diabetes could represent a double burden for the prevalence of blindness, because (i) retinopathies as a result of hypertension and diabetes, and (ii) optic nerve head damage due to POAG can both lead to blindness [23, 24]. Thus, targeting the Nepalese population with hypertension and diabetes for a glaucoma screening program would provide dual benefits by detecting (i) retinopathies related to hypertension and diabetes, and (ii) POAG

related optic nerve head damage, if any exist. Both strategies would help reduce the prevalence of blindness.

POAG: detection by chance

Aiming to detect early-stage POAG and thus reduce the risk of blindness, hospitals in Nepal conduct eye screening for all patients who come to the eye OPD for consultation. Paper II aimed to investigate the clinical features and visual status of POAG at the time of diagnosis. The South East Asian Glaucoma Interest Group reports that most POAG in Asian countries is detected incidentally when patients come to hospital for eye problems other than glaucoma [7]. Likewise, 60.7% of POAG cases in our study visited hospital for eye problems relating mostly to vision and unspecific symptoms indicating incidental detection of disease. Unexpectedly, another 21.4% of our participants had no eye problems, but they took the opportunity to have their eyes tested while accompanying a family member at the hospital. Such people might easily have been missed, emphasizing the importance of periodic eye examinations, especially for high-risk individuals and even if they are currently asymptomatic [90].

In our study, only 9.8% of participants came for periodic eye examinations, either because they were suspected to have glaucoma during an earlier examination or due to a family history of glaucoma. Thus, only a limited number of participants knew they were at risk for glaucoma; this contradicts a western report [91]. The small number of people receiving a regular glaucoma test may have resulted due to barriers to seeking health care in the community [82]. This would not be surprising for a country like Nepal because, unlike many high-income countries, it lacks a national health screening policy [92, 93] that brings people to hospital for regular check-ups. Additionally, Nepal lacks national health insurance, which prevents higher spending from public accounts but often explains why people do not seek health care [94]. Physicians referred

another 8.1% of participants for eye examination, less than expected considering Nepal's rising burden of NCDs [95].

Because POAG is asymptomatic until it reaches its end stage, detection is often accidental, occurring when patients visit the hospital for other, nonspecific symptoms or seek a simple eye test to obtain a prescription for eyeglasses [96]. This was clearly reflected in our study; 82.7% of POAG cases visited the hospital because they experienced difficulty with near vision. Another tertiary hospital in Nepal reported similar findings among newly diagnosed POAG patients in the hospital's eye OPD [41]. This finding was not unexpected because most of our participants were ≥ 40 years of age and likely would need glasses for presbyopia.

Only 20.8% of our participants complained about diminished distance vision. This was expected because POAG spares central vision until the late stage of the disease. Thus, POAG patients often have good distance vision and do not notice declining peripheral vision [97]. Surprisingly, we found that 9.2% of POAG patients presented with decreased temporal side vision, indicating a probable loss of peripheral vision [96]. The visual field test report reconfirmed this finding, showing significant peripheral visual field loss in such patients. People with glaucoma recognize peripheral vision loss only at the late stage of the disease, when severe damage to the visual field obviously obscures peripheral vision [96]. Furthermore, 40.5% of our participants complained of headache and 24.3% had eye pain, possible early symptoms of POAG [96]. Hospitals often overlook such symptoms because they can result from many other conditions (e.g., tiredness and migraine, or cluster, headaches) [98].

POAG patients described various other eye symptoms, including watering, itching, redness, grittiness, heaviness, and discharge. Although such symptoms do not associate with POAG, they are worth mentioning because they brought people to the hospital and provided an opportunity for glaucoma

screening. The guidelines of the American Academy of Ophthalmology recommend a comprehensive eye evaluation for every adult as an effective way to diagnose glaucoma, especially in high-risk individuals [99]. Our study mostly detected POAG in patients who were ≥ 35 years of age, suggesting that every adult who is ≥ 35 years old and attends an eye OPD should have an opportunity for glaucoma screening, irrespective of symptoms.

Concurring with earlier reports, mean VCDR and mean IOP in our study did not differ between men and women [100, 101]. Mean of MD revealed decibel value of the retinal threshold as low as -13.24 (SD=-9.0) dB, indicating a considerable loss of visual field; MD equaling -2.00 dB or less is considered to indicate a sufficiently reduced retinal threshold to suggest glaucoma [102]. The finding of visual field test in Paper II is similar to earlier reports [103, 104]. Mean PSD was 7.34 (SD=2.8) dB, suggesting variability in the patient's response or actual visual field abnormality [102]. We excluded variations in patients' response by assessing the mean CPSD, which at 6.65 (SD=4.2) dB represented an irregular visual field pattern resulting from actual field loss after deducting the SF or variability of the patient's response to the test [102]. The visual field report in Paper II showed mean SF of 2.52 (SD=0.9), which is slightly higher than earlier reports [103, 104]. However mean CSPD was similar to that reported earlier [103, 105].

Late diagnosis of POAG leads to considerable visual damage

Visual status of POAG patients is represented by both visual fields and visual acuity. Among all POAG patients undergoing a visual field test, 61.5% had GHT outside the normal limits, clearly indicating late-presentation disease with visual field damage. However, the visual fields of 38 eyes (11.9%) were within normal limits. They were diagnosed as POAG on the basis of large VCDR (≥0.7) and IOP higher than 30 mmHg, suggesting early detection of disease before any visual field changes took place. In this respect, our results disagree

with an Indian study [106] that reports 75% of eyes outside the normal limit and 25% with either borderline or generalized reduction of sensitivity. This difference could be due to the fact that our study was conducted among individuals who visited the hospital for general eye problems and were screened for glaucoma. Consequently, they may have been identified at an earlier stage of the disease. Of total eyes, 7.5% of those with POAG could not be considered for a visual field test due to poor vision or loss of central vision, results that concur with results originating in India [106]. Mean MD as low as -13.24 dB, mean PSD=7.34 dB, and 61.5% of total eyes showing GHT outside the normal limit indicate that most POAG participants already had moderate to severe damage in their visual fields when diagnosed for the first time.

An evaluation of visual acuity revealed that 85.5% of total POAG patients had normal to mildly impaired vision, which is not unusual in POAG cases. POAG often damages the visual field from the periphery toward the center. Thus, the patient will not recognize loss of visual field unless they lose vision in the central field. Additionally, 4.7% of our participants were legally blind at the time of diagnosis. Although this proportion is small, extrapolating that number in relation to the adult Nepalese population aged ≥ 35 years (44.9 % or 13.6 million) could have a substantial impact on the prevalence of blindness [34]. Considering the lowest proportion of POAG (3.25%) revealed in Paper I, POAG could affect 443,607 people in Nepal; among those, 4.7% (20,849) may likely develop irreversible blindness due to POAG.

Concept of health from the perspective of the JD-HDSS community

Paper III explored knowledge regarding glaucoma, hypertension, and diabetes in people living in JD-HDSS, a peri-urban community in Nepal. It also investigated whether pre-existing hypertension, diabetes, and/or POAG influence knowledge of disease. Foreseeing the cultural norms of Nepal (i.e.,

women have difficulty expressing their views in front of men), we conducted separate FGDs for men and women 107].

Men and women perceived the meaning of "good health" differently, but we observed no difference between groups affected or unaffected by disease. Men described good health as the absence of disease, whereas women connected good health with ability to work and undertake household responsibility. This finding is similar to a previous study [108], suggesting that women often prioritize their housework over their own health. Nepalese women considered their health less important than fulfilling their family and household responsibilities. According to the hypothesis of the Health Belief Model [57], health behavior changes only when a person recognizes a health threat. Therefore, women in JD-HDSS are less likely to change health behaviors like self-care and preventive measures because they do not consider their health as important as their household chores.

Health locus of control as perceived by JD-HDSS community

Paper III demonstrated combined health locus of control, and that opinion did not vary between men and women. However, a study from Israel reports a predominance of external health locus of control among women [109], possibly due to variations in culture, age of study participants, and/or data collection methods. The Israeli study enrolled participants aged 50–75 years and collected data via telephone interviews. In contrast, we enrolled participants' aged 25–45 years and collected data via FGD. The concept of health locus of control illustrates that people with a combined locus cope more efficiently with disease and stress, compared to those with either internal or external locus of control [60]. This may suggest that people living in JD-HDSS would be better able to handle their health issues if they received need-based health education.

Both men and women believed that their health is in their own hands (i.e., they are responsible for their own health). Among men, the locus shifted toward social and cultural practices believed to affect their determination to follow healthy health habits.

In contrast, some women believed that health is the hands of God or an unseen power. Both findings concur with a previous study, which also showed mixed belief in health locus of control [110]. These findings of externalizing health locus of control could be explained by the human tendency to blame others for threatening events [111].

Knowledge of hypertension, diabetes, and POAG

People living in JD-HDSS were aware of a rising prevalence of hypertension and diabetes in their community, and they also believed that such diseases result from an inactive lifestyle and unhealthy diet. In contrast, a study from a rural community in Pakistan demonstrates poor awareness regarding these diseases [112]. Female participants believed that obesity could increase their risk of developing hypertension and diabetes, whereas men did not associate obesity with hypertension and diabetes. Similarly, a study from Tanzania shows that men underestimate their body weight and do not perceive obesity as a health threat, compared to women [113]. Another study reports that women are more conscious of their appearance/bodies, compared to men [114].

Compared to healthy participants, participants suffering from hypertension and diabetes showed greater knowledge regarding the consequences of disease, perhaps due to curiosity about their own disease. However, better knowledge could also result from frequent hospital visits and interaction with doctors or other people suffering from similar diseases. It may also indicate good health information received from the hospital information center. Similarly, a study from Malaysia demonstrates that

people with pre-existing diseases know more about the potential consequences of their disease [115].

All participants from JD-HDSS were aware of glaucoma and its prevalence in their community. In contrast, earlier studies from India and Ethiopia report poor community awareness of glaucoma: their participants said they had never heard about glaucoma [116, 117]. This difference in awareness level could be explained by variations in study design and study setting. In earlier studies, data were collected during face-to-face interviews in rural settings. Nonetheless, in our study men suffering from POAG, hypertension, and/or diabetes and those with a family history of glaucoma exhibited more knowledge about POAG. Positive correlation between pre-existing disease and knowledge of disease has been shown by another study from India [118].

Gender inequality and health

We observed gender inequality in various aspects of health-related issues, such as perception and knowledge of disease, attitude toward health behavior and practice of healthy lifestyles, sympathy and love from family members, and opportunities to access healthcare services.

Unlike men, women from JD-HDSS, regardless of health status, did not perceive hypertension and diabetes as life threatening or dangerous diseases. Apart from this, women also lacked in-depth knowledge regarding POAG, compared to men. Because there is a positive relationship between pre-existing disease and knowledge, we expected that women with hypertension and diabetes would know more and understand the severity and consequences of having these diseases [115]. A study from India also reports a poor level of awareness of disease in women [119]. In the context of Nepal, this difference is unsurprising, because most women in Nepal are less

educated and only exposed to their own personal space, (i.e., they are often not outgoing and thus less exposed to a learning environment [120].

This Thesis demonstrated that men and women in Nepal have different attitudes toward health. Although they knew about the health benefits of changing lifestyle and regardless of whether or not they suffered from disease, women were reluctant to change their lifestyle. This reluctance associated with perceived social and cultural barriers, including lack of spousal and family support. Another study from Nepal demonstrates similar results, suggesting inadequate family support for women when they were ill [121]. An earlier study from USA also reports that women feel their spouse will not support lifestyle changes [122]. The findings reported here suggest that women who lack family support face more barriers to changing their lifestyle and procuring treatment for disease that may lead to increased morbidity and mortality in a peri-urban community [123, 124]. An earlier study demonstrates similar findings and reports poorer health outcome in people with diabetes who exhibit unwillingness to change health behavior [125].

Our study demonstrated that women face additional cultural barriers to accessing health care, apart from community-wide educational, institutional, and economic barriers. A policy brief published by a Nepal gender and eye health group reports that Nepalese women utilize healthcare services less frequently than men [82]. The policy brief also describes barriers faced by women at various levels (e.g., household and family, healthcare facilities, and service providers). A previous study from Nepal reports a lack of decision-making power, which renders women unable to access healthcare services without permission from family members [126]. This Thesis suggests that gender inequalities in JD-HDSS limit women's ability to seek health care,

compared to men. In addition, cultural barriers suggest a significant need for health education programs tailored specifically to women.

Aspects of health learned from the Thesis

Role of family and culture in tackling health issues

Although, Paper III did not specifically explore the socio-cultural aspects of health, findings from the FGD focused attention on socio-cultural values and their importance in tackling health issues in the community. Our study participants described how diseases affect the entire family in terms of stress, financial burden, change in food habits, leading healthy lifestyle, etc. Despite adequate knowledge about disease and preventive measures, the women in our study were reluctant to change their lifestyle in the face of several cultural barriers. This finding indicates that health is not just about a single person; rather, health is influenced by several cultural and social factors. Previous studies demonstrate that individualized approaches to changing health behavior are inappropriate, and interventions designed to reduce disease prevalence should also consider the role of culture and family [127, 128]. Therefore, the process of exploring disease knowledge and understanding the approach to health care in the community should focus on the entire society as well as family and cultural norms. As a theoretical basis, PEN-3 model is probably the best way to explore health-related issues in the community [129].

Valuing culture for better understanding of health (PEN-3 model)

Understanding health issues from a community perspective is difficult, and a full exploration of community health issues requires a connection between, family, culture, and health. The PEN-3 cultural model helps comprehend the relationship between health and culture in the community by focusing on three interrelated domains: (i) relationships and expectations, (ii) cultural empowerment, and (iii) cultural identity [130]. The model uses a “bottom up”

approach (i.e., community members actively delineate their health problems and identify the needs that may affect their health in a positive manner [131]. This Thesis discusses health issues that are closely amalgamated with culture and family, and the PEN-3 model is probably the best approach to address future health-related behaviors in the Nepalese community.

Community participation for better health outcome

This Thesis demonstrates how family, social, and cultural norms influence health behavior, and suggests adopting "community-lead" health promotion programs rather than programs led by a health promoter. We also show gender inequality in several aspects of health issues (e.g., perception of health, knowledge about disease, attitude toward health, and practice of healthy habits). To create positive health changes and reduce the gender gap, the community must recognize existing health issues, define needs that help achieve good health, and identify factors that affect the well-being of every community member [132]. Achievable only through community participation and a community-led health approach, these require active community involvement in health programs at each step, from decision making to baseline survey, planning, and eventually program implementation [133]. This approach likely will make people more responsible for their own health, instill a sense of belonging, help visualize unseen problems affecting health, and empower the community and its people by enhancing their knowledge and skills through participation [134].

Community participation and a community-led health approach are not new concepts. The World Health Organization has advocated this approach for decades [135], and many countries have already implemented such programs [132, 136, 137]. Indeed, nongovernmental organizations in Nepal have already used this approach to promote health care in a few villages, but community

participation was unsatisfactory, and benefits were limited due to inadequate financial support [138].

Implications of the Thesis for future health policies

Despite minimal support from the government, eye care services in Nepal have made significant gains in curative eye health. Until now, Nepal has focused on prevention, largely in response to a substantial backlog in cataract surgery, tackling infectious diseases like trachoma, and nutritional blindness resulting from vitamin-A deficiency [37]. Nepal lacks consistent community-based eye awareness programs and has a poor referral system for health care. The poor referral system may result from a lack of integration between healthcare networks at different levels of health system. However, the Ministry of Health and Population has begun the process of integrating eye care into general health care, and this action may improve the eye health care in Nepal in coming days [139].

This Thesis was not driven by health policy research and did not specifically investigate health policy issues pertaining to POAG and NCD. However, it could lay the foundation for envisioning future eye care services in Nepal and health awareness programs in the community.

The findings of this Thesis may serve as a basis for formulating future health care policies. The association between POAG, hypertension, and diabetes described here shows that the existing strategy of glaucoma screening programs may need to encompass a larger target population, including hypertensive and diabetic patients from medical OPD. The poor record of physician referrals for eye screenings for patients with hypertension and diabetes was a troubling finding of this Thesis. An earlier report analyzing Nepal's National Health Policy 1991[140] also supports my finding of lower referral rates. Although a health policy for NCD, recommended by the Ministry of Health, clearly mandated eye screening for

hypertension and diabetes patients focus on preventing blindness [141], the resulting referrals were not proportionate to disease prevalence [140]. Therefore, this Thesis may also help trigger the process of strengthening the health referral system in Nepal.

The finding that POAG patients present late to hospitals with substantial visual damage indicates that current opportunistic screening programs for glaucoma do not bring people to the hospital in time. This Thesis adds insight to the fact that Nepal must find another way to get its people needed medical attention before they lose their vision. This insight may aid the development of more community-oriented health promotion programs.

Findings of gender inequality in various aspects of health issues in the JD-HDSS community and the health behavior of people influenced by family and cultural values may signal researchers and policy makers to change their approach in future research and program implementation. Changing from researcher- to community-oriented strategies and from promoter- to community-led health promotions would increase community members' responsibility for their own health and increase their health management skills [133]. Further, this Thesis demonstrated that women in Nepal lack decision-making power, even regarding their own health, thus increasing their vulnerability. An earlier study demonstrating a similar condition for women in low-income countries supported our observation [142]. This finding may guide future policy makers to develop tailored health awareness programs to further empower women.

CONCLUSIONS

This Thesis demonstrates an association between POAG, hypertension, and diabetes. Most POAG cases described here were detected incidentally, when study participants went to a hospital eye clinic for other eye problems. Few participants were aware of being at high risk for POAG. Although the prevalence of hypertension and diabetes is increasing in Nepal, physician referrals for eye screenings were limited. POAG cases were detected at a late stage of the disease, when moderate to severe vision damage had already occurred. People from the JD-HDSS community were aware of the rising burden of hypertension, diabetes, and glaucoma, but lacked knowledge about POAG. The studies included here observed gender inequality in various aspects of health, including knowledge of diseases, attitude toward health, practice of healthy lifestyle, and access to seeking health care. Because women in Nepal face more barriers to health care than men, the government should develop community-oriented and -tailored health awareness programs and reduce the gender gap in health care.

FUTURE PERSPECTIVES

As demonstrated here, late detection of POAG and the association of POAG with rapidly emerging diseases like hypertension and diabetes raise new questions about the target population for glaucoma screening programs. Should we expand the target population for POAG screening? Rather than limiting ourselves to opportunistic screening for individuals who visit eye hospitals, should we attempt to tackle this problem differently by simultaneously conducting community awareness programs that bring more people to the hospital? Before answering these questions, we may want to demonstrate the effect of such an approach.

Additionally, although men and women were aware of good health habits, practice in real life was far from within their reach, especially for women. Therefore, the challenge lies in educating women who are busy with household work most of the time and already face several barriers to health care. Future research should focus on community-based health promotional activities, with greater emphasis on building women's confidence in their ability to overcome barriers to health care. Achievement of this goal can only occur by actively involving the community in these endeavors and making them more responsible to bring about changes in community health status.

In addition, this Thesis demonstrated how disease affects family and cultural value, rather than just an individual. This impact indicates the need for far-reaching vision in considering the realities within the family, society, and culture, which ultimately govern the health of every individual. Thus, individual-based approaches to changing health behavior are inappropriate. Future research should use the PEN-3 model as a theoretical basis, focusing on three interrelated domains—relationships and expectations, cultural empowerment, and cultural identity—to explore the cultural values of health behavior in the community.

A pilot study using the PEN-3 model to explore health from the perspective of the community can be conducted in the JD-HDSS. Next, a community-led health promotion program could involve peripheral levels of the health system (i.e., the “community level”) and the village development committee (Figure 1) in an exploration of whether community-oriented and tailored programs help change the health behavior and health status of people living in the JD-HDSS.

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