PREVALENCE OF HYPERTENSIVE RETINOPATHY IN PATIENTS WITH PREGNANCY-INDUCED HYPERTENSION ADMITTED AT PARIRENYATWA GROUP OF HOSPITALS

BY

BATSIRAI LIZZIE CHIMERA MUCHEMWA

STUDENT NUMBER R032823M

THESIS SUBMITTED IN PARTIAL FULFILMENT OF THE DEGREE OF MASTERS OF MEDICINE (OPHTHALMOLOGY) UNIVERSITY OF ZIMBABWE COLLEGE OF HEALTH SCIENCES

SUPERVISOR

PROFESSOR R. MASANGANISE

CONSULTANT OPHTHALMOLOGIST

COLLEGE OF HEALTH SCIENCES

DEPARTMENT OF OPHTHALMOLOGY

UNIVERSITY OF ZIMBABWE

JUNE 2017

ABSTRACT

Background: Pregnancy-induced hypertension (PIH) is a spectrum of disorders associated with significant fetal and maternal morbidity and mortality. It is a multisystem disorder which does not spare the visual system. Some effects of PIH on the retina (hypertensive retinopathy) and choroid (hypertensive choroidopathy), can be potentially blinding if not recognised and managed promptly though in the majority of patients there is resolution within six weeks post-partum without sequelae. As the eye is the "window to one's body", the presence of hypertensive retinopathy can predict fetal outcomes, severity and likelihood of progression of pregnancy-induced hypertension.

Objectives: This study sought to:

- Determine the prevalence of hypertensive retinopathy in patients with PIH presenting at Parirenyatwa Group of Hospitals.
- Establish the severity of hypertensive retinopathy in the study population.
- Identify associations between hypertensive retinopathy with age, parity, previous history of PIH, blood pressure (systolic and diastolic), degree of proteinuria and the presence of the Human Immunodeficiency virus (HIV) in the study population.
- Identify sight-threatening complications associated with hypertensive retinopathy in the study population.

Study design: This was a hospital based cross-sectional study and was carried out from the 8th of September 2016 to the 31st of March 2017.

Methods: Participants were selected by convenience sampling from patients admitted at Mbuya Nehanda Maternity Hospital. Eligible patients were pregnant women from 24 weeks gestation onwards with a diagnosis of PIH.

Patients unwilling to participate in the study, those with pre-existing hypertension, media opacities and systemic illnesses which caused retinal pathology similar to hypertension were excluded from the study. Data was collected using a specially designed study tool.

All subjects had a medical history taken and an ocular examination which included visual acuity, anterior segment examination and a dilated fundus examination with both the direct and indirect ophthalmoscope. Fundus photographs were taken for selected cases. The Keith-Wagener-Barker classification of hypertensive retinopathy was used for grading of retinopathy. An overall grade of the hypertensive retinopathy was assigned to each patient on the basis of the eye with the most severe changes.

Results: A total of 163 patients were recruited. Seventy-five patients (46%) had gestational hypertension, 74 (45.4%) had pre-eclampsia and 14 (8.6%) had eclampsia. A total of 111 subjects (68.1%) had clinically evident hypertensive retinopathy.

Fifty-eight participants (52.3%) had grade 1 changes, 32(28.8%) had grade 2 changes, 17(15.3%) had grade 3 and 4(3.6%) had grade 4 hypertensive retinopathy respectively.

There was a statistically significant positive association ($p<0.05$), between hypertensive retinopathy and blood pressure (both systolic and diastolic), proteinuria, severity of PIH, duration of PIH since diagnosis and parity. There was no significant association ($p>0.05$), between hypertensive retinopathy and HIV status, visual acuity, gestation and maternal age. None of the patients had retinal detachment or choroidopathy.

Conclusion: The prevalence of hypertensive retinopathy was significantly high in our study population in comparison to other studies. Positive risk factors for developing hypertensive retinopathy in our study population included high blood pressure, severity of PIH, proteinuria, duration with PIH and increasing parity. However, the majority of patients did not have sight threatening complications.

ACKNOWLEDGEMENTS

I would like to express my gratitude to all the people who assisted me in preparing for this thesis. These include my supervisor Professor R. Masanganise for his guidance from the planning, execution and write-up of this study.

I would also like to acknowledge the helpful input from the consultants at Sekuru Kaguvi eye unit who include Mr A.F. Mukome, Dr A. Kufa, Dr B. Macheka, Dr D. Sibanda, Dr Y. Jaya and Dr J. Washaya. I would like to thank Dr D. Ute, Dr M. Kawome, Dr K. Zimudzi and Dr P. Madzima for their input.

I would also like to acknowledge Dr S. Mangombe who allowed me to use his panoptic fundoscope.

Assistance with biostatistics was provided by Ms J. Dzangare.

Many thanks go to the patients who agreed to take part in this study.

Lastly, I would like to thank my family, especially my husband, for their patience and unwavering support.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF APPENDICES

ABBREVIATIONS

APGAR	Appearance, Pulse, Grimace, Activity, Respiration
A-V	Arterio-Venous
D	Diopter
HIV	Human Immunodeficiency Virus
JREC	Joint Research and Ethics Committee
P	p value
PGH	Parirenyatwa Group of Hospitals
PIH	Pregnancy-Induced Hypertension
RPE	Retinal Pigment Epithelium
SKH	Sekuru Kaguvi Hospital
SS	Sample Size
TX	Texas
USA	United States of America

CHAPTER 1: INTRODUCTION

1.1 INTRODUCTION

Pregnancy-Induced Hypertension (PIH) encompasses a spectrum of disorders characterized by high maternal and fetal morbidity and mortality both in developed and developing countries[1].The disorders are multi-systemic and the ocular system is not spared. Various structures in the visual pathway can be affected. Due to the effect of hypertension on all vessels of the human body, examination and assessment of changes in the retinal vasculature of pregnant women can provide valuable information about the status of placental circulation as well as well-being of the fetus[2]. Retinal changes due to PIH are associated with low fetal birth weight as well as low Apgar scores[3,4].

Although most of the retinal changes in PIH resolve after delivery without sequelae, some of its ocular complications, in particular chorioretinopathy and serous retinal detachment, are sight-threatening and can cause blindness[5].

Results from studies done in Asia on the prevalence of retinopathy inpatients with PIH ranged from 12 to 59%[2,3,6–9]. There is paucity of data on the burden of this condition in Southern Africa. The available data in published literature, concerning the prevalence of hypertensive retinopathy in patients with PIH in Zimbabwe, is currently insufficient.

1.2 BACKGROUND

1.2.1 PREGNANCY-INDUCED HYPERTENSION (PIH)

Pregnancy-induced hypertension is hypertension which arises for the first time from 20 weeks of gestation in the absence of other causes of elevated blood pressure. The diagnosis is made when systolic blood pressure is ≥140mmHg and/or diastolic blood pressure of ≥90mmHg. An increase of 30mmHg or more of systolic pressure or a rise of 15mmHg diastolic pressure from baseline is also diagnostic. The blood pressure is recorded on two occasions after rest. This is then combined with generalized tissue swelling and/or protein in urine (300mg or more of protein in a 24-hour urine sample or 100mg/dl in at least two or more random urine samples collected six or more hours apart)[4].

The spectrum of PIH include; gestational hypertension, pre-eclampsia and eclampsia[10,11]. Gestational hypertension is high blood pressure without the presence of proteinuria and edema.

Pre-eclampsiais characterized by high blood pressure, protein in urine and generalized edema[10]. Pre-eclampsia is further divided into mild and severe pre-eclampsia. Mild pre-eclampsia is characterized by blood pressure ≥140/90mmHg with 1+ of protein in urine with or without mild pedal edema. Severe pre-eclampsia is characterized by blood pressure≥160/100mmHg, ≥ 2+ protein in urine, associated cerebral or visual disturbances, pain in the epigastric area, abnormal liver function tests and a raised creatinine concentration in serum. Table 1 shows conversion of urine dipstick protein into gm/l.

Eclampsia is pre-eclampsia with associated tonic-clonic convulsions or decreased level of consciousness[2,10,12].

Table 1: Grading of proteinuria

Urine dipstick	gm/l
+	0.3
++	1
+++	3
++++	10

The pathophysiology of PIH remains unclear but many theories implicate problems with placental implantation and trophoblastic invasion of the endometrium as possible causes. This will cause intense systemic vasospasm which results in reduced perfusion in almost all organs. There is an exaggerated inflammatory response in the body, endothelial dysfunction and activation of the coagulation cascade further compromising blood flow to the organs[12].

Risk factors for developing PIH include race (more common in blacks than whites), genetics (positive family history increases the risk), nulliparity, smoking, multiple pregnancy, diabetes, pre-existing high blood pressure and hyperlipidemia among other factors[10].

1.2.2 STRUCTURE OF THE NORMAL RETINA

The retina, or nervous coat, is a thin layer of neural tissue that lines the inside of the eye. At the centre of the retina lie the optic disc from which major blood vessels of the retina radiate. The optic nerve leaves the eye at the optic disc. About 4.5-5mm temporal to the retina, a blood vessel free reddish spot called the fovea can be seen. The fovea is the centre of the macula, which is the area for the most distinct vision.

The outer layer of the retina is in contact with the choroid which is well vascularised and nourishes the outer retinal layers[13]. The normal structure of the retina is illustrated in figure 1 below.

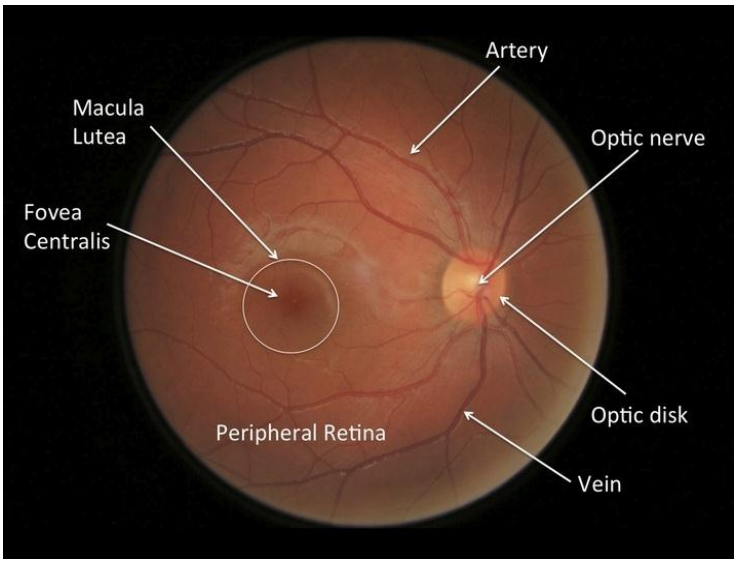


Figure 1: Normal retina

(Image courtesy of imagebank.asrs.com)

1.2.3 HYPERTENSIVE RETINOPATHY

Hypertensive retinopathy occurs when the retina and its vasculature are damaged by hypertension. There are several classifications of grading hypertensive retinopathy.

1. Keith-Wagener-Barker Hypertensive Retinopathy Classification[14]

Grade 1: Includes mild retinal vascular changes (generalized arteriolar narrowing).

Grade 2: Moderate to severe retinal vascular changes (AV crossing changes). These changes are due to decreased lumen size and hyalinization of arterial walls (Figure 2 below).

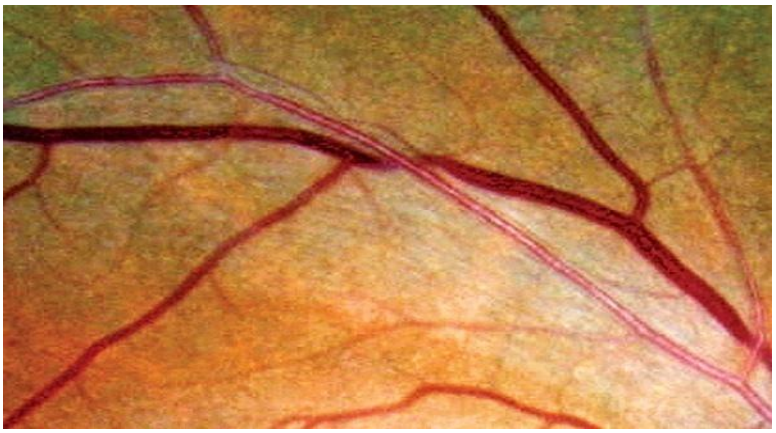


Figure 2: Grade 2 hypertensive retinopathy with A-V crossing changes

(Image courtesy of imagebank.asrs.org)

Grade 3: Includes grade 2 features plus cotton-wool spots, retinal hemorrhages and exudates. These features are the result of breakdown in the blood retinal barrier due to an acute rise in blood pressure (Figure 3 below).

Figure 3: Grade 3 hypertensive retinopathy

(Image courtesy of opusg.webs.com)

Grade 4: Grade 3, plus associated optic nerve head swelling and macular star formation. Patients in stage 4 often have reduced vision, headaches, monocular diplopia, scotomas and/or photopsias (Figure 4 below).

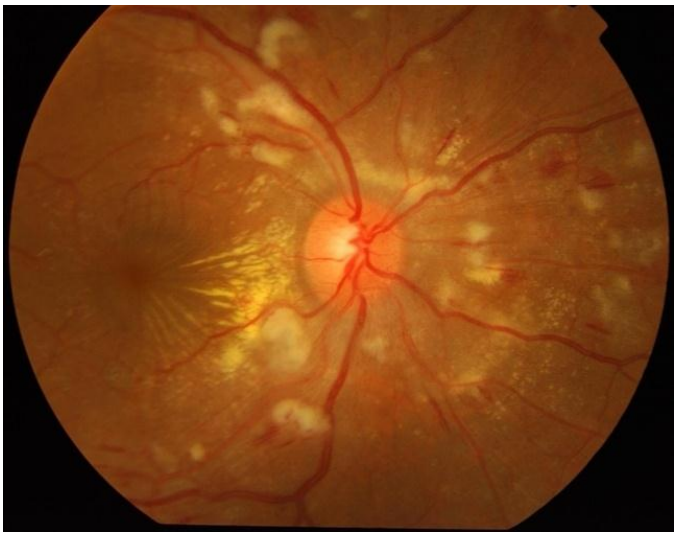


Figure 4: Grade 4 hypertensive retinopathy

(Image courtesy of imagebank.asrs.org)

2. Wong and Mitchell Hypertensive Retinopathy Classification[15]

This is a simplified version of the Keith-Wagener-Barker classification proposed by Wong and Mitchell in 2004.

Table 2: Wong and Mitchell classification of hypertensive retinopathy

Grade	Stage	Ophthalmoscopic signs	Systemic association
1	Mild retinopathy	One or more of the following arteriolar signs: -generalized narrowing -focal arteriolar narrowing -AV nicking -arteriolar wall opacity (silver wiring)	Modest association (risk and odds ratio of >1 but <2) with risk of clinical stroke, coronary heart disease and mortality.
2	Moderate retinopathy	One or more of the following arteriolar signs: -hemorrhage (blot, dot or flame-shaped) -microaneurysms -cotton wool spots -hard exudates	Strong association (risk and odds ratio of >2) with risk of clinical stroke, cognitive and cardiovascular mortality
3	Malignant retinopathy	Moderate retinopathy plus optic disc swelling + macula star	Strong association with mortality

3. Modified Scheie Classification[16]

Grade 0: No changes

Grade 1: Barely detectable arteriolar narrowing

Grade 2: Arteriolar narrowing which is obvious plus focal irregularities

Grade 3: Grade 2 plus retinal hemorrhages, exudates, cotton wool spots or retinal edema

Grade 4: Grade 3 plus papilloedema

In this study, the Keith-Wagener-Barker classification will be used to grade the hypertensive retinopathy as it is more popular and has been used in many studies. This will allow for comparison between studies.

1.3 LITERATURE REVIEW

1.3.1 OCULAR MANIFESTATIONS OF PREGNANCY-INDUCED HYPERTENSION

The visual system can be affected along its course by pregnancy-induced hypertension.

1.3.1.1 ADNEXAL AND ANTERIOR SEGMENT MANIFESTATIONS OF PIH

Drooping (ptosis) of the upper eyelids can be found in patients with severe pre-eclampsia. It is due to disinsertion of the levator palpabrae superioris muscle as a result of interstitial swelling[17]. Conjunctival vessels can develop spasms and constrict in some patients. This constriction can be mild or severe enough to cause localized ischaemia. Blood clots in the conjunctival vessels can be seen occasionally as well as petechial hemorrhages[18]. Pupil dilatation has also been reported in some patients with PIH[19].

1.3.1.2 POSTERIOR SEGMENT MANIFESTATIONS OF PIH

The fundus changes which occur in PIH can be divided into 3 stages:

1. The stage of spasticity – characterized by spasm of the retinal arterioles[16,20].
2. The stage of sclerosis – characterized by changes superimposed on pre-existing sclerotic changes in the retinal vessels[16,20].
3. The stage of retinopathy- characterized by any one or more of the following; cotton wool spots, microaneurysms, flame-shaped and splinter hemorrhages, hard exudates, disc and macula edema[16,20].

SPASTIC STAGE

This is the first stage and is characterized by constriction of the vessel lumen. This can be localized at a single point or there can be a series of localized constrictions along the length of the arteriole. Patients who usually show generalized arteriolar attenuation may exhibit these localized constrictions and this indicates an active progressive disease[16,20]. Initially the constriction involves the superior nasal arterioles but may start at the periphery then progress towards the disc resulting in generalized attenuation. Short-lived spasmodic contractions of the arterioles result in obliteration of the lumen contributing to the symptoms of amarousis fugax[21]. Early detection of these angiospasmic changes and early management, may prevent the progression to more serious retinopathy as well as the PIH[16,20].

STAGE OF SCLEROSIS

There are three major signs associated with retinal evidence of vasosclerosis in PIH and these include; arterio-venous (A-V) changes, focal vascular narrowing and generalized attenuation associated with straightening of arterioles. A-V crossing changes include the Gunn's sign which is characterized by an apparent compression of a vein and Salus's sign which is a deflection in the course of the vein[16,20]. There is a significant relationship between narrowing of retinal arterioles and the value of the diastolic pressure[16,20].

STAGE OF RETINOPATHY

This stage reflects retinal ischaemia as a result of progressive narrowing of the retinal arterioles. It is characterized by the appearance of cotton wool spots, microaneurysms, hemorrhages, hard exudates and disc edema[16,18,20].

Chronic retinal edema may result in the deposition of hard exudates around the fovea in the layer of Henle with a macular star configuration[22].

RETINAL DETACHMENT

This is the most dramatic and potentially serious sight-threatening ocular complication of PIH[23]. Choriocapillaries ischaemia as a result of choroidal dysfunction, leads to breakdown in the blood retinal barrier so that fluid accumulates between retinal pigment epithelium (RPE) and the neurosensory retina. This causes subsequent serous neurosensory retinal detachment[23,24]. The development of serous retinal detachments can be an indication for termination of pregnancy[25]. The condition can resolve spontaneously within a few weeks after delivery.

CHOROIDOPATHY

The accelerated hypertension in PIH causes fibrinoid necrosis in arteries and arterioles of the choroid. This results in patchy areas of choriocapillaries non-perfusion (hypertensive choroidopathy)[24]. Choroidopathy is characterized by the presence of Elschnig spots which are small black spots surrounded by yellow halos. These represent areas of focal choroidal infarcts. Siegrist streaks are flecks which can be seen arranged linearly along choroidal vessels and are also an indication of fibrinoid necrosis[22].

PROLIFERATIVE RETINOPATHY

Peripheral retinal neovascularisation can occur in patients with severe PIH. This can be a potentially blinding complication if not recognized and managed promptly[26].

1.3.2 PREVALENCE OF HYPERTENSIVE RETINOPATHY IN PIH

Many studies on the prevalence of hypertensive retinopathy in PIH and its associations have been done in Asia.

Shah et al in their study in Maharashtra, India, reviewed 150 patients for retinal changes in pregnancy induced hypertension. They found a prevalence of 12% and a statistically significant positive association of retinal changes with blood pressure, proteinuria and severity of PIH[2].

In a similar study in India by Kaur et al, reviewed 50 patients and found a prevalence of hypertensive retinopathy in PIH of 26% and a positive correlation between grade of PIH and retinal changes[6].

Karki et al in 2010 published in the Nepalese Journal of Ophthalmology a study looking at associations between PIH fundus changes and fetal outcomes in 153 patients. In this study fundus changes were found in 13.7% of the patients who had PIH.A statistically significant positive association was found between retinal and optic nerve head changes and low birth weight. Choroidal and optic nerve head changes were also associated with babies with low Apgar scores[3].

Bhandari and collegues in their study in 2014, India, found retinal changes in 44% of the 100 patients they investigated. This study however looked at patients with severe PIH (pre-eclampsia and eclampsia). The results showed that the severity of the proteinuria and blood pressure was directly proportional to the severity of the retinal changes[5,8].

Reddy et al in Malaysia found retinal changes in 59% in a study of 78 patients. All the patients who had retinal changes had either Grade 1 or 2 according to the Keith-Wagener-Barker classification[14]. None had Grade 3 or 4 changes. A positive association which was statistically significant was found between retinal changes and blood pressure (p=0.001), proteinuria (p=0.018) and severity of PIH (p=0.024)[9].

Rasdi et al in Malaysia found a 32.5% prevalence of hypertensive retinopathy in a study of 154 subjects with hypertensive disorders of pregnancy. No statistically significant correlation was found between retinopathy and patient's age, presenting visual acuity, systolic and diastolic blood pressure[27].

In Croatia, Tadin et al found a prevalence of hypertensive retinopathy of 45% in their study of 40 patients with pre-eclampsia. There was a statistically significant association between severity of retinopathy and patients' age, Apgar score, proteinuria, systolic and diastolic blood pressure p=<0.001)[4].

In Africa, there was a study done by Mushumbusi et al in Tanzania (2016) looking at the magnitude and presentations of ocular manifestations in patients with only pre-eclampsia and eclampsia. One hundred and thirteen patients were enrolled and the overall prevalence of ocular pathology was 45.1%. The findings on fundoscopy included disc swelling, retinal edema, cotton-wool spots, arteriolar narrowing, haemorrhages and macula edema[28].

1.4 STUDY JUSTIFICATION

Hypertensive retinopathy and its sequelae in patients with PIH has not been investigated in Zimbabwe. The presence of hypertensive retinopathy in PIH has been associated with poor fetal outcomes as well as an increased risk of cerebrovascular and cardiovascular complications[3,29]. Complications of hypertensive exudative retinopathy such as retinal detachment and macula edema are sight-threatening.

Anecdotal data from SKH eye unit has shown that some women who had PIH during pregnancy present with visual loss as a result of optic atrophy and retinal detachment during the post-partum period.

Recognizing the prevalence of hypertensive retinopathy as well as sight-threatening complications in our patients with PIH might provide information which is important in advocating for institution of interventional methods.

1.5 RESEARCH QUESTION AND HYPOTHESIS

1.5.1 RESEARCH QUESTION

What is the prevalence of hypertensive retinopathy in patients with pregnancy-induced hypertension (PIH) at Parirenyatwa Group of Hospitals and what factors are associated with its severity?

1.5.2 STUDY HYPOTHESIS

In a population of pregnant women presenting with PIH at Parirenyatwa Group of Hospitals, the prevalence of hypertensive retinopathy is 12%. The assumed prevalence is based on a study by done by Shah et al.

1.6 OBJECTIVES

PRIMARY OBJECTIVE

- To determine the prevalence of hypertensive retinopathy in patients with PIH at Parirenyatwa Group of Hospitals.

SECONDARY OBJECTIVES

- To establish the severity of the hypertensive retinopathy in the study population.
- To identify associations between hypertensive retinopathy in PIH with age, parity, gestation, previous history of PIH, blood pressure (both systolic and diastolic), degree of proteinuria, visual acuity and HIV status in the study population.
- To identify sight-threatening complications associated with hypertensive retinopathy in the study population.

CHAPTER 2: MATERIALS AND METHODS

2.1 STUDY DESIGN

This was a hospital based cross-sectional study.

2.2 STUDY SETTING

The study was performed at Mbuya Nehanda Maternity Hospital which is a tertiary maternity centre that is part of Parirenyatwa Group of Hospitals. The study was carried out from the 8th of September 2016 to the 31st of March 2017.

2.3 SAMPLING

Convenience sampling was used to select participants for this study.

The minimum sample size was calculated to be 163 patients.

Sample size calculation was performed using the Dobson formula shown below.

$$SS = \frac{P(1-P)Z2}{d2}$$

SS = sample size, z = 1.96 (confidence interval at 95%), p = 0.12 (population proportion),

d = 0.05 (precision/level of significance)

Prevalence of hypertensive retinopathy in patients with PIH was assumed to be 12%. The assumed prevalence was based on a study done by Shah et al where they examined retinal changes in pregnancy-induced hypertension presenting at an Indian hospital. They found an overall prevalence of 12%[2].

The study factors were similar to our study and it looked at the whole spectrum of PIH in contrast to other studies which looked at different aspects of the spectrum. It was also a hospital based study.

The confidence level for this study was set at 95% with a precision of 5%.

2.4 SELECTION CRITERIA

2.4.1 INCLUSION CRITERIA

The participants were selected using the following inclusion criteria:

- All pregnant women with a diagnosis of PIH from 24 weeks gestation who are of consenting age
- All patients that gave informed consent

2.4.2 EXCLUSION CRITERIA

The exclusion criteria for the study participants were as follows:

- Patients with pre-existing hypertension
- Patient with diabetes mellitus, severe anaemia or other diseases which cause retinal pathology similar to hypertension
- Media opacities (cornea, lens, vitreous) that preclude good fundal view
- Patients not willing to participate in the study

2.5 STUDY TOOLS

- Data collection sheets
- Snellen visual acuity chart
- Pinhole occluder
- Penlight torch
- Indirect ophthalmoscope and a +20D(dioptre) lens
- Direct ophthalmoscope
- Welch Allyn retinal panfundoscope
- Topical anaesthetic drops (Amethocaine)
- Dilating drops (Mydriacyl)

2.6 VALIDITY OF DATA COLLECTION TOOLS AND GRADING OF HYPERTENSIVE RETINOPATHY

Pre-tests of the data collection tools were conducted using a small pilot study comprising of 20 patients. Retinal photographs of all patients were taken with a panfundoscope and 4 masked observers (consultant ophthalmologists and senior registrars) were asked to grade the hypertensive retinopathy.

2.7 METHOD OF DATA COLLECTION

All study participants had history taken and clinical examination on a single day by the investigator. No follow up examination was done except for patients with severe hypertensive retinopathy (Grade 3 and 4) who needed referral to SKH for close monitoring.

Patients with eclampsia were enrolled soon after delivery because most of them were too ill to give informed consent as well as to be examined adequately.

Clinical examination consisted of measuring visual acuity, examination of the anterior segment and dilated fundus examination.

Visual acuity (distance) was measured using a Snellen acuity chart. The ocular adnexa and anterior segment was examined for obvious abnormalities.

Ocular fundus examination was carried out first by instilling a drop of the local anaesthetic Amethocaine into each eye for patient's comfort. Another drop of a dilating agent Mydriacyl was instilled to dilate the pupils and allow detailed fundus examination.

The fundus examination was done using an indirect ophthalmoscope together with a +20D lens. Close assessment of the retinal vessels was done with a direct opthalmoscope. Fundus photographs were taken whenever possible.

Hypertensive retinopathy was graded using the Keith-Wagener-Barker classification[14] of hypertensive retinopathy (see above). Each eye was examined individually and an overall grade was assigned to the eye with the most severe changes.

The history and examination findings were captured on a data collecting sheet.

2.8 DATA MANAGEMENT AND ANALYSIS

DATA ENTRY

The software used for data entry was EpiData Entry (version 3.1, EpiData Association, Odense, Denmark). The data was exported to STATA Version 13 (STATA Cooperation, College Station, TX, USA) for analysis.

DATA ANALYSIS

Categorical data was reported using tables and graphs and interpreted using Chi-square tests as well as proportions. Continuous variables were interpreted by use of means, standard deviations and 95% confidence intervals. T-test was used to test for differences between continuous variables which are normally distributed. Regression analysis was employed to assess the significance of risk factors. In these tests a p-value less than 0.05 was regarded as statistically significant.

2.9 STUDY PERMISSION

Approval to carry out the study was granted from the Clinical director of Parirenyatwa group of Hospitals, the Joint Parirenyatwa Hospital and College of Health Sciences Research Ethics Committee (JREC), the head of department Sekuru Kaguvi Eye Hospital and the head of department in Obstetrics and Gynaecology.

2.10 ETHICAL CONSIDERATIONS

Written informed consent in either English or Shona was obtained from all study participants by the researcher. Interviews and clinical examinations were carried out in consultation rooms and the participants were identified using a research number.

CHAPTER 3: RESULTS

3.1 PREVALENCE OF HYPERTENSIVE RETINOPATHY

One hundred and sixty-three patients were enrolled in this study. All the participants were black Africans. One hundred and eleven of the total recruited (68.1%) had clinically evident hypertensive retinopathy. Fifty-two (31.9%) had no hypertensive retinopathy. Table 3 gives a summary of hypertensive retinopathy according to severity.

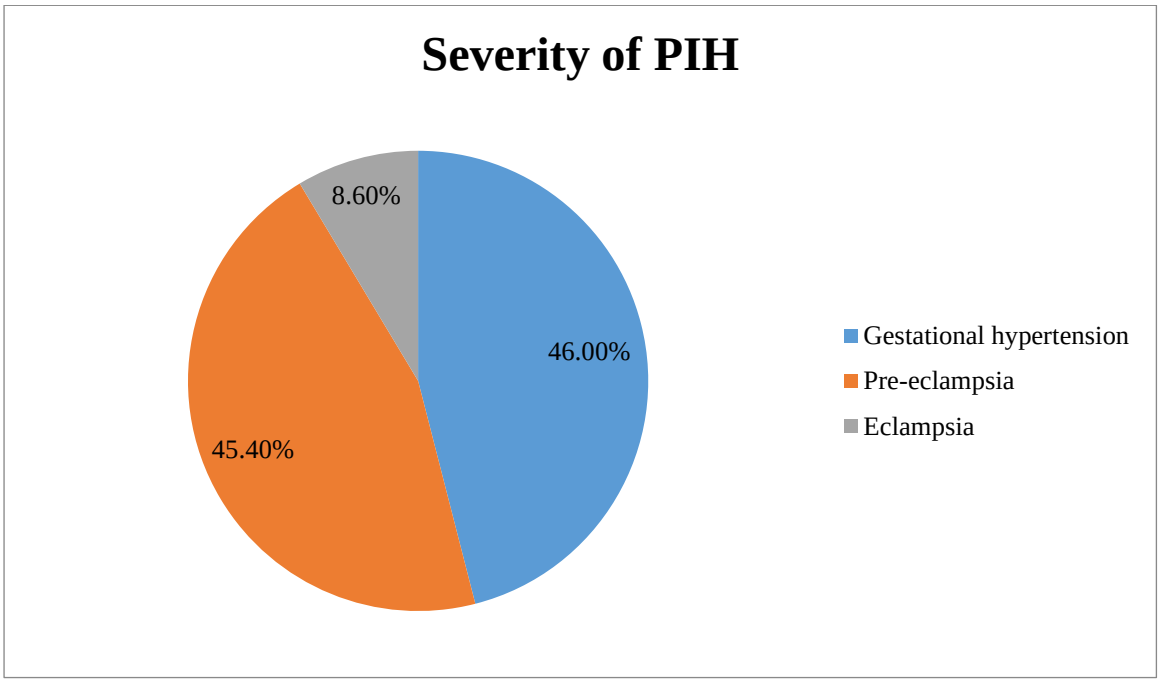
Table 3: Distribution of hypertensive retinopathy according to severity

Characteristic	Number of patients (n)	Percentage (%)
No hypertensive retinopathy	52	31.9
With hypertensive retinopathy	111	68.1
Grade 1	58	52.3
Grade 2	32	28.8
Grade 3	17	15.3
Grade 4	4	3.6
Total	163	100

3.2 HYPERTENSIVE RETINOPATHY AND SEVERITY OF PIH

Seventy-five patients (46%) had gestational hypertension, 74 (45.4%) had pre-eclampsia and 14 (8.6%) had eclampsia (Figure 5). Of those with gestational hypertension 40 (53.3%) had hypertensive retinopathy and 35 (46.7%) had no retinopathy. Fifty-eight participants (78.4%) with pre-eclampsia had hypertensive retinopathy and 16 (21.6%) had no retinopathy. Of those with eclampsia 13 (92.9%) had hypertensive retinopathy and 1 (7.1%) had no retinopathy. Table 4 and 5 gives a summary of severity of PIH and hypertensive retinopathy.

There was a statistically significant positive association between severity of PIH and severity of hypertensive retinopathy (Chi test p=0.000).



N=163

Figure 5: Severity of PIH

Table 4: Hypertensive retinopathy and severity of PIH

Severity of PIH	With retinopathy	Without retinopathy
Gestational hypertension	40 (53.3%)	35 (46.7%)
Pre-eclampsia	58 (78.4%)	16 (21.6%)
Eclampsia	13 (92.9%)	1 (7.1%)

N=163 with retinopathy n=111 without retinopathy n=52

Table 5: Grades of hypertensive retinopathy and severity of PIH

Severity of PIH	Without retinopathy	Grade 1 retinopathy	Grade 2 retinopathy	Grade 3 retinopathy	Grade 4 retinopathy
Gestational hypertension	35 (46.7%)	32 (42.7%)	5 (6.7%)	0 (0%)	3 (4.0%)
Pre-eclampsia	16 (21.6%)	24 (32.4%)	23 (31.1%)	11 (14.9%)	0 (0%)
Eclampsia	1 (7.1%)	2 (14.3%)	4 (28.6%)	6 (42.9%)	1 (7.1%)

N=163

3.3 HYPERTENSIVE RETINOPATHY AND BLOOD PRESSURE

Seventy-one subjects (45.6%) had a systolic blood pressure less than 160mmHg and 92 (56.4%) had a systolic blood pressure greater than 160mmHg. The average systolic blood pressure was 167.2 mmHg and the median was 162mmHg.

One hundred and seventeen participants (71.8%) had a diastolic blood pressure less than 110mmHg and 46 (28.2%) had a diastolic blood pressure greater than 110mmHg. The average diastolic blood pressure in the study population was 104.5mmHg and the median diastolic blood pressure was 102mmHg. Table 6 shows the distribution of hypertensive retinopathy changes and blood pressure. There was a statistically significant association between severity of blood pressure (both systolic and diastolic) and severity of hypertensive retinopathy, (Chi test p=0.000).

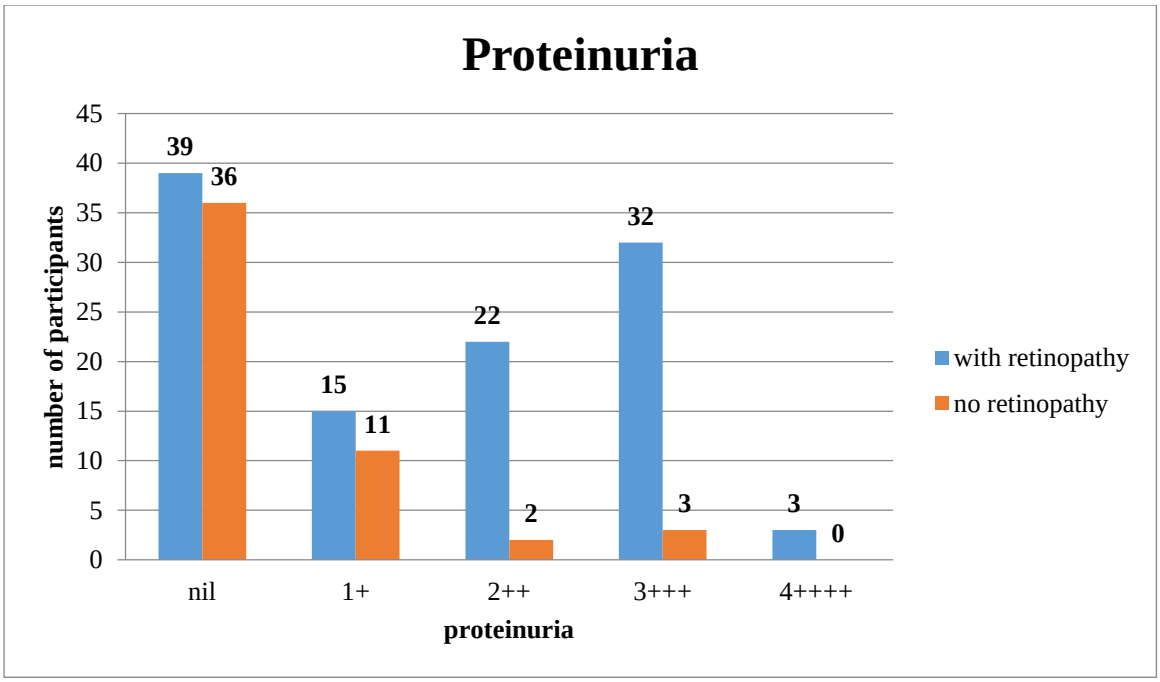
Table 6: Distribution of hypertensive retinopathy and blood pressure

Blood pressure groups	No retinopathy	Grade 1 retinopathy	Grade 2 retinopathy	Grade 3 retinopathy	Grade 4 retinopathy
<160mmHg systolic	39 (54.9%)	24 (33.8%)	7 (9.9%)	1 (1.4%)	0 (0%)
>160mmHg systolic	13 (14.1%)	34 (37.0%)	25 (27.2%)	16 (17.4%)	4 (4.4%)
<110mmHg diastolic	49 (41.9%)	44 (37.6%)	19 (16.2%)	5 (4.3%)	0 (0%)
>110mmHg diastolic	3 (6.5%)	14 (30.4%)	13 (28.3%)	12 (26.1%)	4 (8.7%)

N=163

3.4 HYPERTENSIVE RETINOPATHY AND PROTEINURIA

There was a statistically significant association between severity of hypertensive retinopathy and proteinuria, p= 0.000. Figure 6 shows a summary of hypertensive retinopathy and degree of proteinuria.



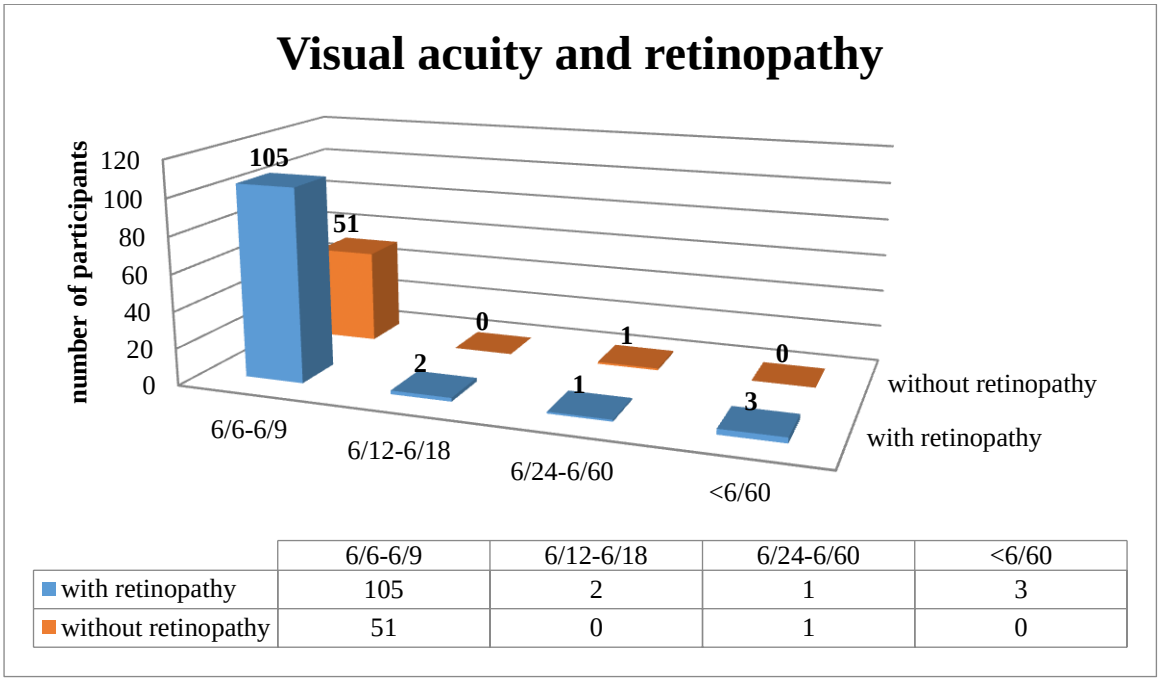
N=163 with retinopathy n=111 without retinopathy n=52

Figure 6: Hypertensive retinopathy and degree of proteinuria

3.5 HYPERTENSIVE RETINOPATHY AND VISUAL ACUITY

One hundred and fifty-six participants (95.7%) had a visual acuity of 6/9 or better. Two patients (1.2%) had visual acuity from6/12 to 6/18.Two participants (1.2%) had visual acuity from 6/24 to 6/60. Three patients (1.8%) had visual acuity worse than 6/60.

There was no statistically significant association between visual acuity and hypertensive retinopathy, p= 0.442. Figure 7 summarises visual acuity and the presence of hypertensive retinopathy.



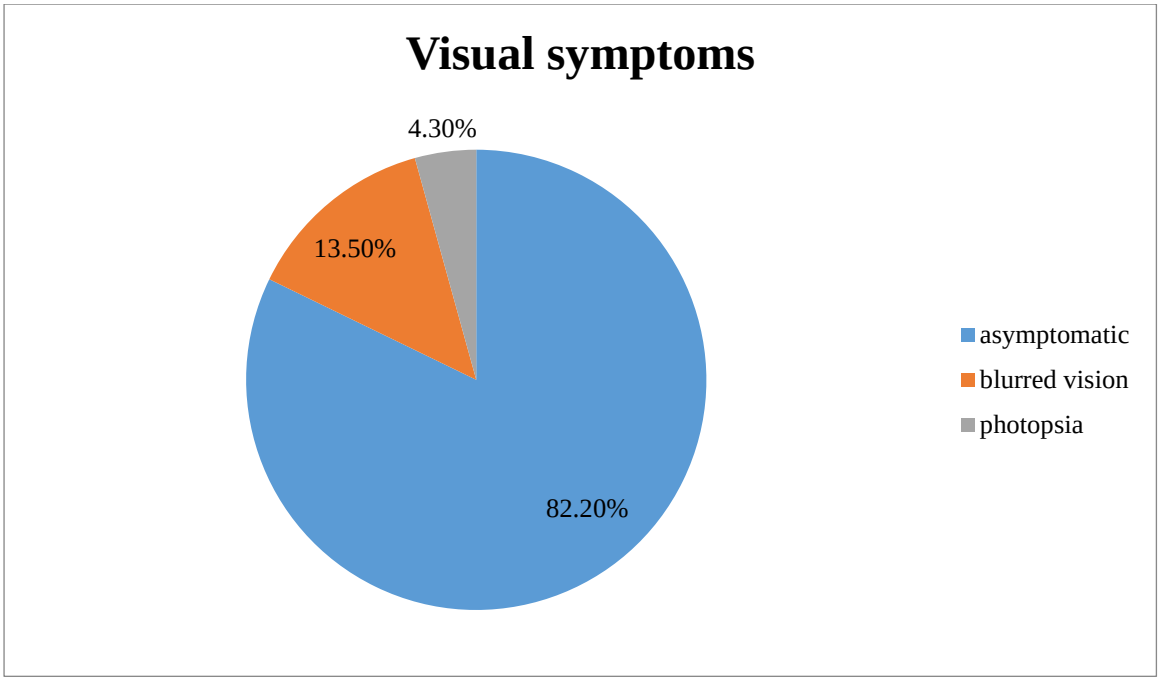
	6/6-6/9	6/12-6/18	6/24-6/60	<6/60
with retinopathy	105	2	1	3
without retinopathy	51	0	1	0

N=163 with retinopathy n=111 without retinopathy n=52 p=0.442

Figure 7: Summary of visual acuity and presence of hypertensive retinopathy

3.6 HYPERTENSIVE RETINOPATHY AND VISUAL SYMPTOMS

One hundred and thirty-four study participants (82.2%) had no visual symptoms. Twenty-two (13.5%) had blurred vision and 7 (4.3%) had photopsia. None of the patients had scotomas or diplopia. The visual symptoms are summarized in figure 8.

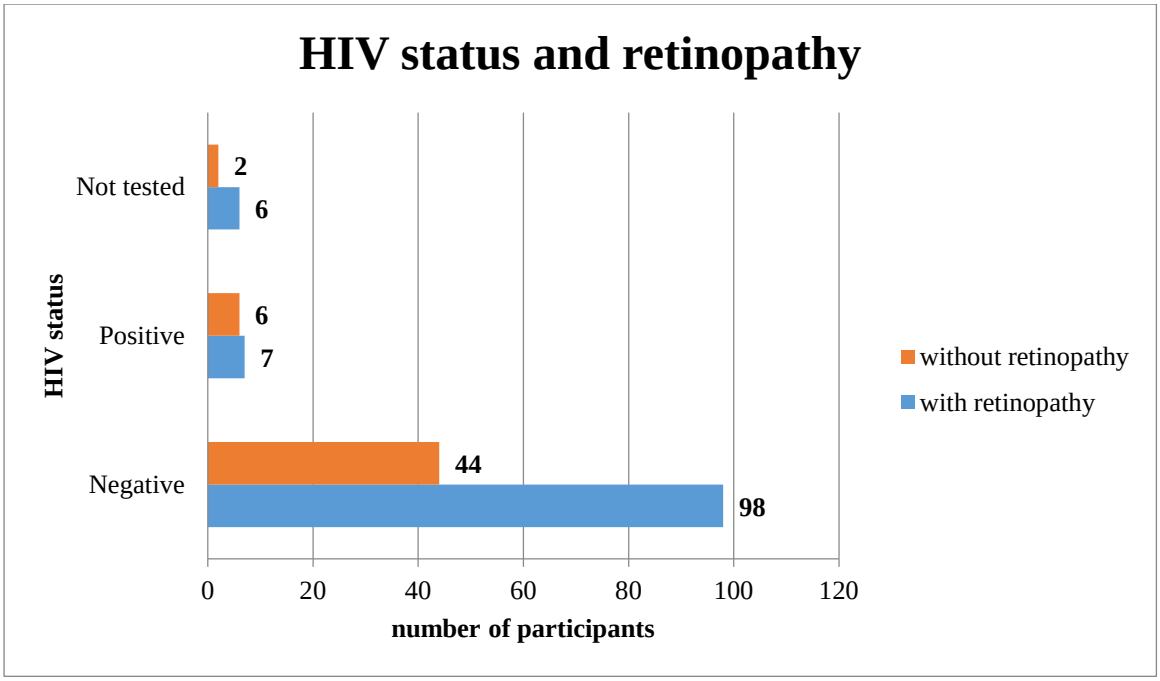


N=163

Figure 8: Visual symptoms of the study participants

3.7 HYPERTENSIVE RETINOPATHY AND HIV STATUS

One hundred and forty-two participants were HIV negative (87.1%), thirteen were HIV positive (8%) and eight participants had not been tested for HIV (4.9%). There was no statistically significant association between HIV status and hypertensive retinopathy, p= 0.485. Figure 9 shows the distribution of the presence of hypertensive retinopathy and HIV status.

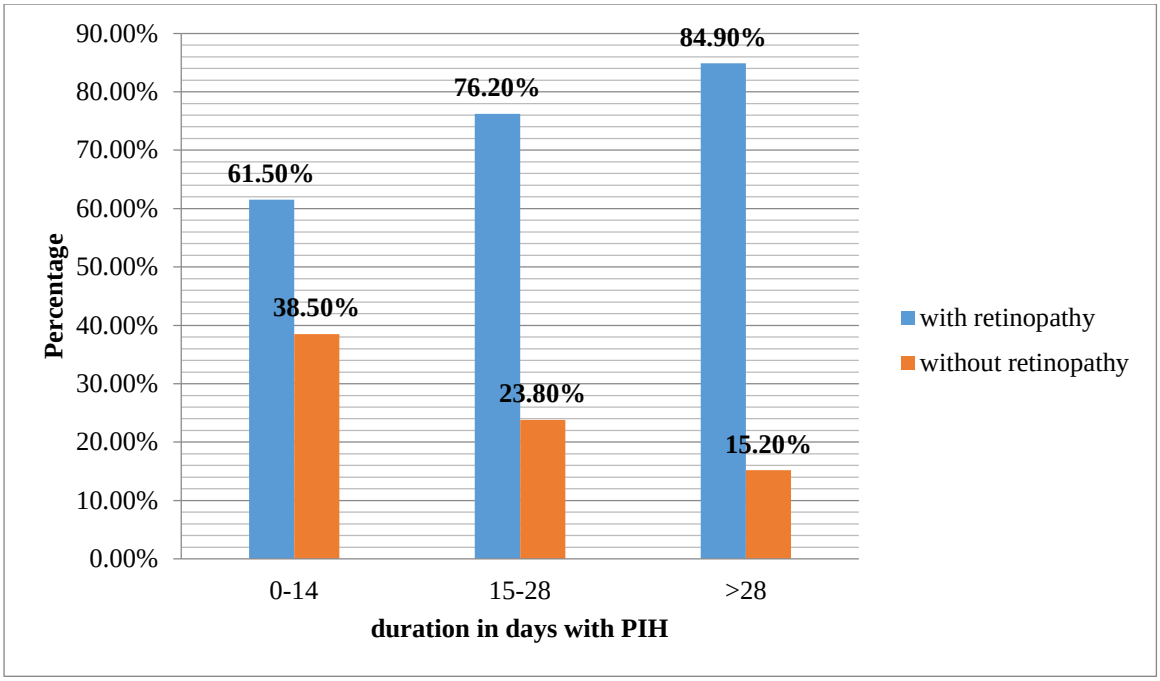


N= 163 Chi test p= 0.485

Figure 9: Distribution of hypertensive retinopathy and HIV status

3.8 DURATION WITH PIH AND HYPERTENSIVE RETINOPATHY

The duration (in days) with PIH since the diagnosis of PIH was made was assessed between the study participants. The duration ranged from 0 days to 56 days. There was a statistically positive association between duration with PIH and hypertensive retinopathy (figure 10), Chi test p=0.029.



N= 163 Chi test p=0.029 with retinopathy n= 111, without retinopathy n= 52

Figure 10: Duration with PIH and hypertensive retinopathy

3.9 COMPLICATIONS OF HYPERTENSIVE RETINOPATHY

None of the participants had clinically evident retinal detachment or choroidopathy.

3.10 HYPERTENSIVE RETINOPATHY AND DEMOGRAPHIC PARAMETERS

3.10.1 AGE DISTRIBUTION

The median age of the participants was 31 years (range 16 years to 41 years). There was no statistically significant association between extremes of age and hypertensive retinopathy changes (p=0.871). Table 7 summarizes hypertensive retinopathy changes and age.

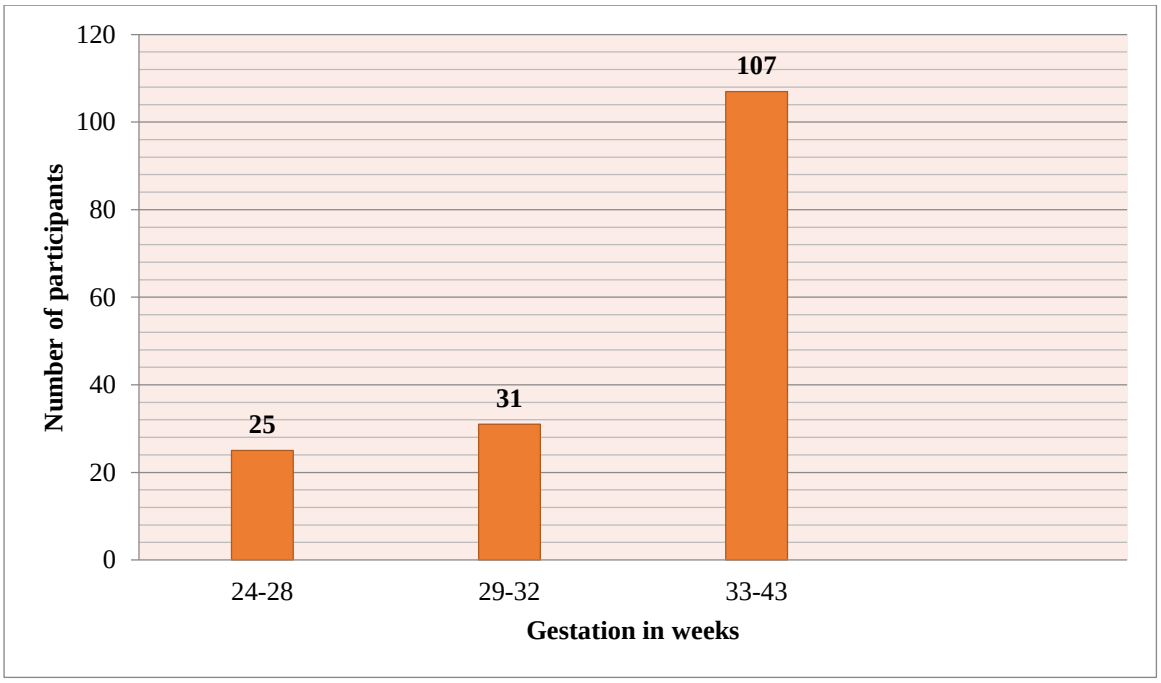
Table 7: Age and hypertensive retinopathy changes

Age Groups (number)	With retinopathy (%)	Without retinopathy (%)
<20 years (10)	7 (70.0)	3 (30.0)
21-30 years (58)	38 (65.5)	20 (34.5)
>30 years (95)	66 (69.5)	29 (30.5)

N=163

3.10.2 GESTATION

The average gestation was 34.2 weeks and the median was 36 weeks (range 24 weeks to 43 weeks). The gestation of the study participants is summarized in figure 11 below.

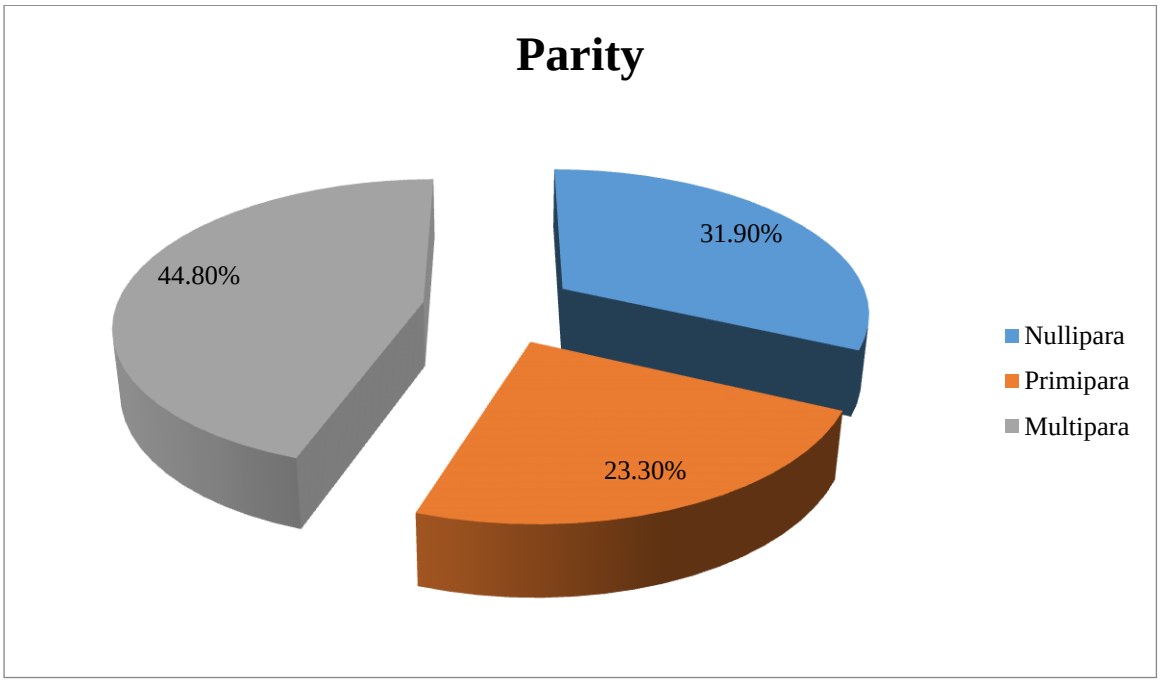


N=163

Figure 11: Gestational age of the study participants

3.10.3 PARITY OF PARTICIPANTS

Fifty-two (31.9%) were nullipara; thirty-eight (23.3%) were primipara and 73 (44.8%) were multipara (figure 12).



N=163

Figure 12: Parity of the study participants

There was significant association between parity and hypertensive retinopathy (Chi test p=0.048). Table 8 shows association between parity and retinopathy changes.

Table 8: Parity and hypertensive retinopathy changes in the study population

Parity (Number)	With retinopathy (%)	Without retinopathy (%)
Nullipara (52)	31 (59.6)	21 (40.4)
Primipara (38)	23 (60.5)	15 (39.5)
Multipara (73)	57 (78.1)	16 (21.9)

N= 163 with retinopathy=111 without retinopathy=52

CHAPTER 4: DISCUSSION

4.1 PREVALENCE OF HYPERTENSIVE RETINOPATHY

The prevalence of hypertensive retinopathy in our study population was 68.1% which was quite high compared to other studies. This is greater than 12 to 59% found in the various studies[2-4,6,8,9,27]. The reason for our high prevalence might be due to racial factors. All our study patients were black Africans. The black race has been implicated as a risk factor for the development of pregnancy-induced hypertension[30-32]. Most of the documented studies were done in Asians. In an African study done in Tanzania by Mushumbusi et al[28], they found a prevalence of 45.1% which was still lower than that found in our study. They only studied participants with pre-eclampsia and eclampsia excluding those with gestational hypertension. This might explain their low prevalence compared to our study. A high prevalence in our study might also be due to late antenatal booking in our patients, due to socio-economic factors, thus delaying diagnosis and treatment of PIH. Another possibility for the high prevalence might be due to previously undiagnosed essential hypertension. Anecdotal data has shown that a lot of women in our population do not go for routine blood pressure checks unless they are ill or pregnant.

Our study was also conducted at a tertiary hospital where complicated cases are referred. This also could have accounted for the high prevalence of hypertensive retinopathy. The study only looked at admitted patients who probably had more severe pathology.

The majority of patients had less severe retinal changes, 52.3% had grade 1 hypertensive retinopathy and 28.8% had grade 2 changes. The minority had more severe retinal changes with 15.3% and 3.6% having grade 3 and 4 changes respectively. This is in agreement with other studies which found a greater proportion having grade1 and 2 changes and a lesser proportion with grades 3 and 4 changes.

Reddy et al[9] found 52.6% with grade 1 changes and 6.4% with grade 2 changes. No one had either grade 3 or 4 changes in his study. Bhandari et al[8] found 34% with grade 1 changes, 5% with grade 2 changes, 2% with grade 3 changes and 2% with grade 4 changes.

The study disproved the hypothesis which postulated that the prevalence of hypertensive retinopathy in our population is 12%. We found a prevalence which is five times more than the postulated prevalence.

4.2 HYPERTENSIVE RETINOPATHY AND SEVERITY OF PIH

In this study there was a statistically significant association between severity of PIH and severity of hypertensive retinopathy, p=0.000. This is in keeping with other studies which also found a statistically significant association[2–6,9]. Nearly 93% of participants with eclampsia in our study had hypertensive retinopathy.

In contrast, Karki et al in their study found 33.33% of eclamptic patients with hypertensive retinopathy[3]. Bhandari et al found 61% of eclamptic patients with hypertensive retinopathy[5].

4.3 HYPERTENSIVE RETINOPATHY AND BLOOD PRESSURE

In our study, the mean systolic blood pressure was 167.2mmHg (range 140-243) and mean diastolic blood pressure was 104.5mmHg (range 78-150). This is comparable to a mean systolic of 168.48mmHg and a mean diastolic of 104.32mmHg found by Bharathi et al in their study[7]. Of those with systolic blood pressure <160mmHg, 54.9% had no hypertensive retinopathy and 45.1% had retinopathy. Those with systolic blood pressures >160mmHg, only 14.1% had no evidence of hypertensive retinopathy and 85.9% had retinopathy.

Those with a diastolic blood pressure <110mmHg, 41.9% had no hypertensive retinopathy and 58.1% had hypertensive retinopathy. Those with a diastolic blood pressure >110mmHg, 93.5% had hypertensive retinopathy and 6.5% did not have hypertensive retinopathy.

There was a statistically significant association between severity of blood pressure (both systolic and diastolic) and severity of hypertensive retinopathy, p=0.000. This is in keeping with other studies which also found a statistically significant association between hypertensive retinopathy and blood pressure[2–4,7,9].

In our study, systolic blood pressures >160mmHg and diastolic blood pressures >110mmHg were associated with more severe grades of hypertensive retinopathy. None of the patients with systolic blood pressure < 160mmHg or diastolic < 110mmHg had grade 4 hypertensive retinopathy.

4.4 HYPERTENSIVE RETINOPATHY AND PROTEINURIA

In this study, there was a statistically significant correlation between hypertensive retinopathy and severity of proteinuria (p= 0.000). Seventy-five study participants (46.0%), had no proteinuria and of these subjects only 39 (52%) had retinopathy. Twenty-six patients (16.0%) had 1+ of proteinuria and 57.7% of them had retinopathy. Twenty-four participants (14.7%) had 2+ of proteinuria and 91.7% of them had hypertensive retinopathy.

Thirty-five patients (21.5%) had 3+ of proteinuria and from these 91.4% had retinopathy. Only 3 patients (1.8%) had 4+ of proteinuria and all of them (100%) had hypertensive retinopathy.

This showed that the more severe the degree of proteinuria the greater the likelihood of developing hypertensive retinopathy. Previous studies also showed similar positive association between degree of proteinuria and hypertensive retinopathy[2,4,8,9,33,34].

Muhammad et al[34] in their study of 168 patients found 46.1% of patients with 1+ of proteinuria to have retinopathy, 75% with 2+ of proteinuria had retinopathy and 100% with 3+ of proteinuria had retinopathy. This is quite comparable to our study. They however had no patients with 4+ of proteinuria in their study. This shows that our study population had patients with more severe grades of proteinuria probably accounting for the high prevalence of hypertensive retinopathy.

4.5 HYPERTENSIVE RETINOPATHY AND VISUAL ACUITY

The majority of patients (95.7%) had visual acuity of 6/9 or better. Of those with visual acuity of 6/9 or better, 67.3% had hypertensive retinopathy. This showed that having good visual acuity did not rule out the presence of hypertensive retinopathy. This therefore means that clinicians should not use decreased visual acuity as a marker of severity of hypertensive retinopathy. Reduced vision has been used as a marker of severity of PIH, usually as a sign of imminent eclampsia. There was no statistically significant correlation between decreased visual acuity and severity of hypertensive retinopathy, p=0.442. Rasdi et al[27] in his study of 154 patients found similar results.

4.6 HYPERTENSIVE RETINOPATHY AND VISUAL SYMPTOMS

The majority of patients, 82.2% had no visual symptoms. Only 13.5% had blurred vision and 4.3% had photopsia. None of the patients had diplopia or scotomas which are some of the symptoms found in patients with grade 4 hypertensive retinopathy[14]. Of those patients with no visual symptoms, 64.2% had hypertensive retinopathy and 35.8% had no retinopathy. Those who had blurred vision, 86.4% had hypertensive retinopathy and 13.6% did not. Of those with photopsia, 85.7% had retinopathy and 14.3% did not.

Even though there was no statistically significant association between visual symptoms and hypertensive retinopathy (p=0.070), visual symptoms were a better indicator of severity of retinopathy than visual acuity (p=0.442).

All of the patients with Grade 4 hypertensive retinopathy had visual symptoms. Even though visual symptoms are an indication of severity of PIH, the absence symptoms did not rule out hypertensive retinopathy as evidenced by the 64.2% who had hypertensive retinopathy despite having no visual symptoms.

4.7 HYPERTENSIVE RETINOPATHY AND HIV STATUS

There was no statistically significant correlation between HIV status and presence of hypertensive retinopathy, p=0.485. Most of our study participants were HIV negative (87.1%) and of these, 69% had hypertensive retinopathy whilst 31% did not. Eight percent of the patients were HIV positive and of these, 53.8% had hypertensive retinopathy whilst 46.2% did not have retinopathy.

HIV can cause retinal changes similar to hypertensive retinopathy but the incidence has decreased due to the introduction of anti-retroviral drugs[35].

All of our patients who were HIV positive were on anti-retroviral drugs. No studies have been done to compare the severity of hypertensive retinopathy in patients who have PIH and are HIV positive.

4.8 HYPERTENSIVE RETINOPATHY AND DURATION WITH PIH

There was a statistically significant positive correlation between longer duration with PIH from diagnosis and hypertensive retinopathy, p=0.029. Those who had PIH for more than 28 days, 84.9% had hypertensive retinopathy and 15.2% did not have retinopathy.

This showed that the longer the patient stayed with PIH the greater the likelihood of developing hypertensive retinopathy. No other studies were done to compare the duration with PIH and hypertensive retinopathy.

4.9 COMPLICATIONS OF HYPERTENSIVE RETINOPATHY

None of the patients in this study had either retinal detachment or choroidopathy. This in keeping with other studies which found similar results[2,9]. However, other studies found the presence of retinal detachments, choroidopathy or both in their patients and it was associated with increased severity of PIH[5,7,23–25,28,33,36].

4.10 HYPERTENSIVE RETINOPATHY AND DEMOGRAPHIC PARAMETERS

4.10.1 AGE

The mean age of the study participants was 29.9 years (range 16-44). This was nearly similar to that found in other studies[4,9]. This was however more than 23.06[7], 25.1[2] and 27.66[34] years found in other studies.

There was no statistically significant association between severity of hypertensive retinopathy and extremes of age, p=0.871. This is in keeping with other studies in literature[2,7,27].

4.10.2 PARITY

In this study, there was a statistically significant positive correlation between increasing number of pregnancies and hypertensive retinopathy (p=0.048). Literature has long established nulliparity as a risk factor for the development of PIH[10]. Muhammad et al, in their study of 168 patients found a statistically significant correlation between severity of retinal changes and an increasing number of pregnancies (p=0.001)[34]. Other studies however did not find any significant association between hypertensive retinopathy and parity[2,9].

Shah et al found that retinopathy was 2.6 times more in multigravida than primigravida though the result was not significant[2].

4.10.3 GESTATION

The mean gestational age in our study population was 34.2 weeks (range 24-43 weeks). This is nearly similar to that found in other studies[2,9,34]. However, there was no statistically significant positive association between gestational age and hypertensive retinopathy (p=0.552).

4.11 STUDY LIMITATIONS

This was a hospital based study making the study biased as patients with more severe illness are referred to central hospitals.

There was also selection bias as the participants were chosen by convenience sampling and only those who were admitted were enrolled into the study. This excluded patients who were not admitted.

The study participants were examined using both the direct and indirect ophthalmoscope and some patients with small retinal detachments, mild disc swelling or subtle macular changes might have been missed. A slitlamp biomicroscope provides good stereoscopic assessment of macular and optic disc pathology.

The study was only a prevalence study. There was no follow up of patients to see if the hypertensive retinopathy resolved post-partum. Only those with severe hypertensive retinopathy (Grade 3 and 4) were referred to SKH for further follow up and management. Amongst those referred, only 2 patients turned up for further follow up.

CHAPTER 5: CONCLUSIONS AND RECOMMENDATIONS

5.1 CONCLUSIONS

This study has shown that the prevalence of hypertensive retinopathy in our patients with PIH admitted at Parirenyatwa Group of Hospitals is, in comparison to other developing countries, quite high. Whilst mild to moderate hypertensive retinopathy is common in our population, severe hypertensive retinopathy and its complications are not.

The positive risk factors found in the study for developing hypertensive retinopathy were an increase in blood pressure (both systolic and diastolic), severity of PIH, proteinuria, prolonged duration with PIH and increasing parity. Visual acuity, gestation, HIV status and maternal age were not associated with the development of hypertensive retinopathy.

5.2 RECOMMENDATIONS

Ophthalmologists and obstetricians should be aware that the majority of patients with PIH have hypertensive retinopathy. Obstetricians and midwives should screen patients who have the risk factors for developing hypertensive retinopathy and refer them to Ophthalmologists. Patients with severe hypertensive retinopathy (Grade 3 and 4), will also need long term follow up as there is a risk of developing cardiovascular and cerebrovascular complications.

Early antenatal bookings should be encouraged so that PIH is diagnosed and managed early thus delaying the progression to severe hypertensive retinopathy and its sequelae.

Practitioners should not use visual symptoms and acuity as the only markers for the presence of hypertensive retinopathy. The majority of patients with hypertensive retinopathy in this study had no visual symptoms and had normal visual acuity.

A follow up study is needed to see if the presence of hypertensive retinopathy has any effect on fetal outcomes. It would also be prudent to determine whether all hypertensive retinopathy resolves post-partum in all patients.

REFERENCES

1. Wolde Z, Segni H, Woldie M. Hypertensive Disorders of Pregnancy in Jimma University Specialized Hospital. Ethiop J Health Sci. 2011 Nov;21(3):147–54.

2. Shah A, Lune A, Magdum R, Deshpande H, Bhavsar D, Shah A. Retinal changes in pregnancy-induced hypertension. Med J Dr Patil Univ. 2015;8(3):304.

3. Karki P, Malla P, Das H, Uprety DK. Association between pregnancy-induced hypertensive fundus changes and fetal outcomes. Nepal J Ophthalmol Biannu Peer-Rev Acad J Nepal Ophthalmic Soc NEPJOPH. 2010 Jun;2(1):26–30.

4. Tadin I, Bojić L, Mimica M, Karelović D, Dogas Z. Hypertensive retinopathy and pre-eclampsia. Coll Antropol. 2001;25 Suppl:77–81.

5. Bhandari A, Bangal S, Gogri P. Ocular fundus changes in pre-eclampsia and eclampsia in a rural set-up. J ClinOphthalmol Res. 2015;3(3):139.

6. Kaur S, Chopra A, Gupta KB, Singh S. Prevalence of Ocular Changes in Pregnancy Induced Hypertension. Ann Health Health Sci. 2014;1(2):123.

7. Bharathi NR, Raju NSR, Prasad PK, Raju RSN, Premalatha P, Mayee K, et al. Fundus changes in pregnancy induced hypertension: a clinical study. J Evol Med Dent Sci. 2015 Jan 29;04(09):1552–62.

8. Bhandari A, Bangal S, Padghan D, Gogri P. Relation of ocular fundus changes with blood pressure and proteinuria in pregnancy induced hypertension. Egypt Retina J. 2014;2(3):97.

9. Reddy SC, Sivalingam N, Shiela Rani KG, Tham SW. Fundus changes in pregnancy induced hypertension. Int J Ophthalmol. 2012 Dec 18;5(6):694–7.

10. Jun Zhong, Jonathan Zeisler, Maureen C. Hatch, Gertrud Berkowtz. Epidermiology of Pregnancy-induced hypertension. Epidemiol Rev 1997. Vol 19(No. 2).

11. Sheth BP, Mieler WF. Ocular complications of pregnancy. Curr Opin Ophthalmol. 2001 Dec;12(6):455–63.

12. Wagner LK. Diagnosis and management of preeclampsia. Am Fam Physician. 2004 Dec 15;70(12):2317–24.

13. Snell RS, Lemp MA. Clinical Anatomy of the Eye. Wiley; 1997. 436 p.

14. Keith NM, Wagener HP, Barker NW. Some different types of essential hypertension: their course and prognosis. Am J Med Sci. 1974 Dec;268(6):336–45.

15. Wong TY, Mitchell P. Hypertensive Retinopathy. N Engl J Med. 2004 Nov 25;351(22):2310–7.

16. Scheie HG. Evaluation of ophthalmoscopic changes of hypertension and arteriolar sclerosis. AMA Arch Ophthalmol. 1953 Feb;49(2):117–38.

17. Sanke RF. Blepharoptosis as a complication of pregnancy. Ann Ophthalmol. 1984 Aug;16(8):720–2.

18. Bakhda RN. Ocular manifestations of Pregnancy Induced Hypertension. Delhi J Ophthalmol 2015;26(2),88-92.

19. Lowenstein O, Kawabata H, Loewenfeld IE. The pupil as an indicator of retinal activity. Am J Ophthalmol. 1964 Apr;57:569–96.

20. Klein R, Klein BE, Moss SE, Wang Q. Hypertension and retinopathy, arteriolar narrowing, and arteriovenous nicking in a population. Arch Ophthalmol Chic Ill 1960. 1994 Jan;112(1):92–8.

21. Mathew M, Rajani CK, Gulati N. Amaurosis in toxaemia of pregnancy. Indian J Ophthalmol. 1975 Apr 1;23(1):25.

22. Kanski JJ, Bowling B. Clinical Ophthalmology: A Systematic Approach. 7th edition. Elsevier Health Sciences; 2011. 921 p.

23. Sathish S, Arnold JJ. Bilateral choroidal ischaemia and serous retinal detachment in pre-eclampsia. Clin Experiment Ophthalmol. 2000 Oct;28(5):387–90.

24. Fastenberg DM, Fetkenhour CL, Choromokos E. Choroidal vascular changes in toxemia of pregnancy. Am J Ophthalmol. 1980 Mar;89(3):362–8.

25. Bos AM, van Loon AJ, Ameln JG. [Serous retinal detachment in preeclampsia]. Ned Tijdschr Geneeskd. 1999 Nov 27;143(48):2430–2.

26. Brancato R, Menchini U, Bandello F. Proliferative retinopathy and toxemia of pregnancy. Ann Ophthalmol. 1987 May;19(5):182–3.

27. Rasdi AR, Nik-Ahmad-Zuky NL, Bakiah S, Shatriah I. Hypertensive retinopathy and visual outcome in hypertensive disorders in pregnancy. Med J Malaysia. 2011 Mar;66(1):42–7.

28. Mushumbusi EF, Mafwiri MM, Sanyiwa AJ, Kisimbi SJ, Mosenene S, Padhan DH, et al. Ocular manifestations among patients with pre-eclampsia and eclampsia at Muhimbili National Hospital; magnitude and presentations. J Ophthalmol East Cent Afr. 2016 Jul;20(1):2–7.

29. Ahmed R, Dunford J, Mehran R, Robson S, Kunadian V. Pre-Eclampsia and Future Cardiovascular Risk Among Women A Review. J Am Coll Cardiol. 2014 May 13;63(18):1815–22.

30. Lehrer S, Stone J, Lapinski R, Lockwood CJ, Schachter BS, Berkowitz R, et al. Association between pregnancy-induced hypertension and asthma during pregnancy. Am J Obstet Gynecol. 1993 May;168(5):1463-6.

31. Cande V. Ananth, Olga Basso. Impact of pregnancy-induced hypertension on stillbirth and neonatal mortality. Epidermiology2010;21:118-123.

32. Bryant AS, Seely EW, Cohen A, Lieberman E. Patterns of Pregnancy-Related Hypertension in Black and White Women. Hypertens Pregnancy. 2005 Jan 1;24(3):281–90.

33. Bakhda RN. Clinical study of fundus findings in pregnancy induced hypertension. J Fam Med Prim Care. 2016 Jun;5(2):424–9.

34. Muhammad Imran Janjua, SairaBano, Ali Raza. Retinopathy in Pregnancy Induced Hypertension. Pak J Ophthalmol. 2015;31(4).

35. Copeland Robert A. Ocular Manifestations of HIV Infection: Overview, Adnexal Manifestations, Anterior Segment Manifestations. Drugs & Diseases Ophthalmology. Dec 2015:1-12.

36. Dewilde E, Huygens M, Cools G, Van Calster J. Hypertensive choroidopathy in pre-eclampsia: two consecutive cases. Ophthalmic Surg Lasers Imaging Retina. 2014 Aug;45(4):343–6.

APPENDICES

APPENDIX A: STUDY QUESTIONNAIRE

SECTION A: DEMOGRAPHIC DATA

Initials: **Hospital Number:**

Age:

Gestation: **Parity:**

Occupation (indicate with a tick): Employed ( ) Unemployed ( ) Student ( )

Residence: Urban ( ) Rural ( )

Marital status: Married ( ) Single ( ) Widow ( )

SECTION B: CLINICAL DATA

BP: Systolic ☐ **Diastolic** ☐

Proteinuria: Nil ( ) + ( ) ++ ( ) +++ ( ) ++++ ( )

Type of PIH: Gestational hypertension ( ) Pre-eclampsia ( ) Eclampsia ( )

Duration with PIH since diagnosis (days) ☐

Treatment: Yes ( ) No ( ) Name(s) of medication .....

Previous PIH: Yes ( ) No ( )

HIV status: Negative ( ) Positive ( ) Not sure ( )

Visual symptoms: Blurred vision ( ) Photopsia ( ) Scotomas ( ) Diplopia ( )

Other ( )

SECTION C: OCULAR EXAMINATION

Visual acuity: RE ☐ **LE** ☐

ANTERIOR SEGMENT EXAMINATION

Normal ☐ **Abnormal** ☐

If abnormal, state abnormality .....

FUNDUS EXAMINATION

A. Grade of retinopathy	**Parameters**	**RE (Right eye)**	**LE (Left eye)**
1	Generalized arteriolar narrowing		
2	A-V crossing changes		
3	Cotton wool spots Retinal haemorrhages Exudates		
4	Macular star Optic nerve swelling		
0	No changes		
B. Complications of hypertension	Retinal detachment Choroidopathy		

Overall grade of hypertensive retinopathy:

COMMENTS:

APPENDIX B: INFORMED CONSENT IN ENGLISH

+ P. O Box A178
Avondale
HARARE, Zimbabwe

Telephone: 791631 ext. 2454
Fax: (263) (4) 791995
Telex: 26580 UNIVZ ZW
Email:ophthalmologysecretary@gmail.com

COLLEGE OF HEALTH SCIENCES **UNIVERSITY OF ZIMBABWE**
DEPARTMENT OF OPHTHALMOLOGY

PARTICIPANT INFORMED CONSENT

PROTOCOL TITLE: Prevalence of hypertensive retinopathy in patients with pregnancy-induced hypertension (PIH) at Parirenyatwa Group of Hospitals

NAME OF RESEARCHER:Dr Batsirai Lizzie Chimera Muchemwa

PHONE:0773818639

PROJECT DESCRIPTION:A study will be done on women who have been diagnosed with high blood pressure in pregnancy. These women are at risk of developing damage to the inner part of their eyes as a result of the high blood pressure and its complications.

YOUR RIGHTS

Before you decide whether or not to volunteer for this study, you must understand its purpose, how it may help you, the risks to you, and what is expected of you. This process is called informed consent.

PURPOSE OF THE RESEARCH STUDY

- To establish the proportion of pregnant women with high blood pressure who develop problems inside their eyes as a result of the high blood pressure.
- To determine if the age, blood pressure, type of high blood pressure in pregnancy etc, has an effect on the seriousness of the damage inside the eye.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

The study aims to enroll 163 patients with high blood pressure in pregnancy, who are either admitted at Mbuya neHanda Maternity Hospital, or being followed up at the Antenatal clinic.

HOW LONG WILL THE STUDY LAST?

The study is expected to last from 1st of October 2016 to 31st of May 2017.

PROCEDURES INVOLVED IN THE STUDY

If this study has been explained to you, and you decide to take part in this study you will be asked to sign this consent form.

An eye drop will be put in your eyes to reduce pain and improve comfort. Another eye drop will then be put in your eyes to enable the inside of the eye to be examined for signs of damage due to the high blood pressure. A photograph of the inside of your eye will be taken where possible.

DISCOMFORTS AND RISKS

The eye drops that are used to examine the inside of the eye can cause blurring of vision especially when reading. This is temporary and resolves within a few minutes. The eye drops that will be put in your eyes have no effect on the unborn baby.

POTENTIAL BENEFITS

If we see that the high blood pressure has affected the inside part of your eyes, you will be referred to an eye hospital for further management and follow up. This study will also benefit other patients in future.

STUDY WITHDRAWAL

You may choose not to enter the study or withdraw from the study at any time without loss of benefits entitled to you.

CONFIDENTIALITY OF RECORDS

All records from this study will be kept confidential. When you enter the study you will be given a study number.

PROBLEMS/QUESTIONS

Please ask questions about this research or consent now. If you have any questions in future you can phone and talk to Dr. Batsirai Chimera Muchemwa on 0773818639.

AUTHORIZATION

I have read this paper about this study or it was read to me. I understand the possible risks and benefits of this study. I know being in this study is voluntary. I choose to be in this study: I know I can stop being in the study and I will not lose any benefits entitled to me. I will get a copy of this consent form. (Initial all the previous pages of the consent form).

Client Signature Date

Client Name

Researcher Signature Date

Witness Signature Date

APPENDIX C: INFORMED CONSENT IN SHONA

P. O Box A178
Avondale
HARARE, Zimbabwe

Telephone: 791631 ext. 2454
Fax: (263) (4) 791995
Telex: 26580 UNIVZ ZW
Email:ophthalmologysecretary@gmail.com

COLLEGE OF HEALTH SCIENCES **UNIVERSITY OF ZIMBABWE**
DEPARTMENT OF OPHTHALMOLOGY

GWARO REMURWERE ROKUBVUMIDZA KUPINDA MUONGORORO

ZITA RETSVAKIRIDZO:Ongororo yekutarisa mukati memaziso evanhukadzi vakazvitakura vane chirwere cheBP inouya nepamuviri.

ZITA REMUONGORORI: Chimera Muchemwa Batsirai Lizzie (chiremba)

NHAMBA DZENHARE:0773818639

TSANANGUDZO YETSVAKIRIDZO: Chirwere cheBP yakakwira uine pamuviri (PIH) chinokwanisa kukanganisa mukati memaziso zvinogona kuita kuti kuona kudzikire.

KODZERO YEMURWERE

Musati mapinda mutsvakiridzo iyi munofanira kuziva chinangwa, betsero nezvisingabatsire kubvamutsvakiridzo. Iyi ndiyo inonzi mvumo yenyu yekuva mutsvakiridzo. Makasununguka kubvuma kana kuramba kupinda muongororo iyi. Munokwanisa kubuda muongororo iyi pamadira uyezve hamuna zvamunorasikirwanazvo kana mabuda muongororoiyi.

CHINANGWA CHETSVAKIRIDZO

Chinangwa chetsvakiridzo ino ndechekouna kuti vakadzi vangani vakazvitakura vane PIH vakanganiswa mukati memaziso avo nechirwere ichi. Tinenge tichida kuonakuti makore emurwere, makwiriro Ebp nezvimwewo, kuti zvine chekuita here nekukanganisika kwemukati memaziso.

VANHU VANGANI VARI MUTSVAKIRIDZO IYI?

Tinotarisira kuwana vanhu vanoita zana nemakumi matanhatu netatu (163) vachapinda mutsvakiridzo ino.

TSVAKIRIDZO ICHATORA NGUVA YAKADINI?

Tsvakiridzo inotarisirwa kutanga munaGumiguru 2016 ichizopera mumwedzi waChivabvu 2017.

ZVICHAITWA MUTSVAKIRIDZO IYI

Kana tsvakiridzo iyi yatsanangurwa kwamuri uyezve mabvumakupinda mairi muchakumbirwa kuti muise runyororwenyu pagwaro iri.

Mushonga wechiveve uchadonhedzerwa mumaziso enyu kuti musarwadziwe pakuongororwa. Muchadonhedzerwazve mushonga wekuti tikwanise kunyatsoongorora mukati memaziso nekuti ndimomunokanganiswa nechirwere ichi. Tinokwanisa kubva tatora mufananidzo wemukati memaziso enyu.

ZVINGAKANGANISIKA MUTSVAKIRIDZO IYI

Mushonga uno donhedzerwa muziso kuti tikwanise kuona mukati meziso zvakanaka unokwanisa kuita kuti kuona zvinhu zviri pedyo kudzikire. Izvi zvinopfuura nekukurumidza. Mishonga ichadonhedzerwa mumaziso haikanganise mwana ari mudumbu.

ZVINGABATSIRA MUTSVAKIRIDZO IYI

Kana tikaona kuti mukati memaziso enyu makanganiswa nechirwere chePIH, tinokasira kukutumirai kuchipatara chamaziso kwamunonobatsirwa nevana mazvikokotavemaziso. Tsvakiridzo iyi inokwanisa kuzobatsirawo mamwe madzimai akazvitakura mumakore anotevera.

KUBUDA MUTSVAKIRIDZO

Munobvumidzwa kubuda mutsvakiridzo iyi pamunodira asi muchibvumidzwa kuwana betsero sevamwe vari mutsvakiridzo iyi.

KUCHENGETEDZWA KWEZVINYORWA

Zvese zvemutsvakiridzo iyi zvichachengetedzwa zvakanaka nemuwongorori pasina kufumuka. Muongorori achashandisa manhamba kwete mazita pamapepa ezvinyorwa zvemutsvakiridzo iyi.

MIBVUNZO

Munobvumirwa kubvunza mibvunzo yese yamungada pamusoro petsvakiridzo iyi chero nguva zvayo. Makasununguka kuchaya runhare kunachiremba Chimera Muchemwa Batsirai panhamba dzinoti 0773818639 kana mune mibvunzo yamuchawana pamberi panotevera.

MVUMO YEMURWERE

Ndaverenga bepa iri ndikanzwisisa zvinodiwa pamwe nebetsero yetsvakiridzo iyi. Ndinoziva kuti kuva mutsvakiridzo iyi kuzvidira. Ndasarudza kuva mutsvakiridzo. Ndinogona kusarudza kusava mutsvakiridzo iyi asi ndichiwana betsero sevamwe vari mutsvakiridzo. Ndichavawo nerimwe gwaro rakafanana nerandaverenga iri.

Runyoro rwemurwere Zuva

Zita remurwere

Runyoro rwemuwongorori Zuva

Runyoro rwechapupu Zuva

APPENDIX D: REFERRAL FORM FOR THOSE WITH SEVERE RETINOPATHY AND COMPLICATIONS

Private and confidential

Referral form

Referring site:

Receiving site:

Date:

Name: **Age:** **Sex:**

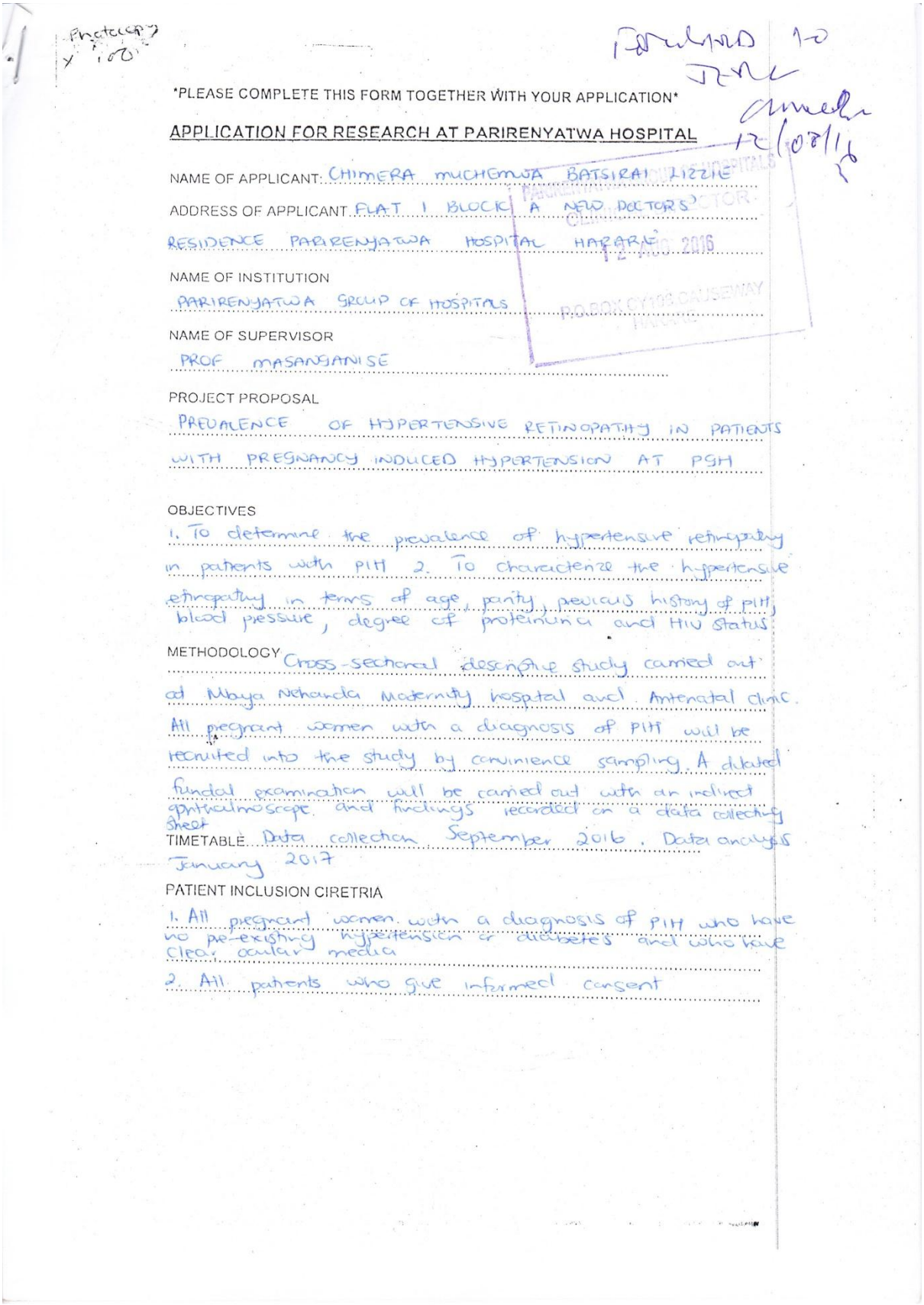
The above named participated in a study that involved fundal examination for presence of hypertensive retinopathy and its complications. The patient has complications of hypertensive retinopathy as a result of PIH, and has been referred to you for further management and follow up.

Referred by: .....

Your assistance will be greatly appreciated. If you have any questions and require further information and clarification please contact:

Dr Batsirai Lizzie Chimera Muchemwa-Chinembiri at the University of Zimbabwe Department of Ophthalmology; Cell phone number 0773818639.

APPENDIX E: PARIRENYATWA HOSPITAL APPROVAL



PLEASE COMPLETE THIS FORM TOGETHER WITH YOUR APPLICATION

APPLICATION FOR RESEARCH AT PARIRENYATWA HOSPITAL

NAME OF APPLICANT: CHIMERA MUCHEMWA BATSIRAI LIZZIE

ADDRESS OF APPLICANT FLAT 1 BLOCK A NEW DOCTORS RESIDENCE PARIRENYATWA HOSPITAL HARARE

NAME OF INSTITUTION

PARIRENYATWA GROUP OF HOSPITALS

NAME OF SUPERVISOR

PROF MASANGANISE

PROJECT PROPOSAL

PREVALENCE OF HYPERTENSIVE RETINOPATHY IN PATIENTS WITH PREGNANCY INDUCED HYPERTENSION AT PGH

OBJECTIVES

1. To determine the prevalence of hypertensive retinopathy in patients with PIH 2. To characterize the hypertensive retinopathy in terms of age, parity, previous history of PIH, blood pressure, degree of proteinuria and HIV status

METHODOLOGY Cross-sectional descriptive study carried out at Mbare Nehanda Maternity hospital and Antenatal clinic. All pregnant women with a diagnosis of PIH will be recruited into the study by convinience sampling. A dilated fundal examination will be carried out with an indirect ophthalmoscope and findings recorded on a data collecting sheet

TIMETABLE Data collection September 2016. Data analysis January 2017

PATIENT INCLUSION CIRETRIA

1. All pregnant women with a diagnosis of PIH who have no pre-existing hypertension or diabetes and who have clear ocular media
2. All patients who give informed consent

USE OF RESULTS

Will help to assess the magnitude of the problem facilitating institution of interventional methods

REFERENCES

1. Shah A, Lure A, Magdum R, Deshpande H, Bavsar D, Shah A. Retinal changes in pregnancy induced hypertension. Med J Dr Patil Univ 2015; 8(3)
2. Karki P, Malla P, Das H, Uprety D. Association between pregnancy induced hypertensive fundus changes and fetal outcomes. Nepal J. Ophthalmol

I promise to forward the Conclusions of the study to the CLINICAL DIRECTOR

NAME DR. B.L Chimera Muchemwa SIGNATURE

STATION PERMISSION

1. CONSULTANT

   NAME:

   Agree/Do ~~not Agree~~

2. WARD MANAGER

   NAME: F. Dzvaku

   Agree/~~Do not Agree~~

APPENDIX F: JREC APPROVAL LETTER

Parirenyatwa Group of Hospitals

Joint Research Ethics Committee For The University of Zimbabwe, College of Health Sciences and Parirenyatwa Group of Hospitals

JREC Office No. 4, 5th Floor College of Health Sciences Building
Telephone: +263 4 708140/ 791631 Exts 2241/2242
Email:jrec.office@gmail.com/jrec@medsch.uz.ac.zw, website:www.jrec.uz.ac.zw

University of Zimbabwe College of Health Sciences

APPROVAL LETTER

Date: 7th September 2016

JREC Ref: 228/16

Name of Researcher: **Dr Batsirai Lizzie Chimera Muchemwa**
Address: University of Zimbabwe, Department of Ophthalmology

RE: **PREVALENCE OF HYPERTENSIVE RETINOPATHY IN PATIENTS WITH PREGNANCY-INDUCED HYPERTENSION AT PARIRENYATWA GROUP OF HOSPITALS.**

Thank you for your application for ethical review of the above mentioned research to the Joint Research Ethics Committee. Please be advised that the Joint Research Ethics Committee has reviewed and approved your application to conduct the above named study. You are still required to obtain MRCZ approval and if required by the nature of your study, RCZ approval as well, before you commence the study.

- **APPROVAL NUMBER** JREC/228/16
- **APPROVAL DATE:** 7th September 2016
- **EXPIRY DATE:** 6th September 2017

This approval is based on the review and approval of the following documents that were submitted to the Joint Ethics Committee:

a) Completed application form
b) Full Study Protocol
c) Informed Consent in English and/or appropriate local language
d) Data Collection tool.

After this date the study may only continue upon renewal. For purposes of renewal please submit a completed renewal form (obtainable from the JREC office) and the following documents before the expiry date:

a. A Progress report
b. A Summary of adverse events.
c. A DSMB report

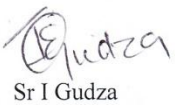
- **MODIFICATIONS:**

Prior approval is required before implementing any changes in the protocol including changes in the informed consent.

- **TERMINATION OF STUDY**

On termination of the study you are required to submit a completed request for termination form and a summary of the research findings/results.

Yours sincerely



Sr I Gudza
For JREC Chairman