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M MED RESEARCH REPORT

IDIOPATHIC INTRACRANIAL HYPERTENSION: DEMOGRAPHIC PROFILE, CLINICAL FEATURES, ASSOCIATIONS AND CLINICAL AND VISUAL OUTCOMES IN BLACK AFRICAN PATIENTS PRESENTING TO ST JOHN EYE HOSPITAL

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IDIOPATHIC INTRACRANIAL HYPERTENSION: DEMOGRAPHIC PROFILE, CLINICAL FEATURES, ASSOCIATIONS AND CLINICAL AND VISUAL OUTCOMES IN BLACK AFRICAN PATIENTS PRESENTING TO ST JOHN EYE HOSPITAL

Hassan Dawood Alli

A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Masters of Medicine in Ophthalmology .

Johannesburg, 2010

Declaration

I declare that this research report is my own unaided work. It is being submitted for the degree of Master of Medicine in Ophthalmology at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other university.

_____ _____ day of _____ 2010

Hassan Dawood Alli

The work reported in this research report was carried out in the Department of Ophthalmology, St John Eye Hospital/Chris Hani Baragwanath Hospital, Johannesburg, South Africa.

Dedication

This research report is dedicated to my late mother, my family and my friends.

Abstract

Aim

To determine and document the demographic profile, clinical features, associations and clinical and visual outcomes in black African patients with idiopathic intracranial hypertension (IIH) attending St John Eye Hospital during 2006 and 2007.

Method

A retrospective descriptive study was conducted on black African IIH patients. Patient files and data of 21 of 32 IIH patients, seen in the Neuro-ophthalmology clinic at St John Eye Hospital over a two year period (2006 and 2007), were available and this study is based on these 21 patients.

All 21 patients fulfilled the modified Dandy criteria for the diagnosis of IIH.

Information obtained from files of the 21 patients were recorded on a data capture sheet. The demographics, initial (presenting) and final visual acuities and visual fields, initial and final clinical symptoms and signs, associations and treatment modalities were recorded on the data capture sheet. Visual and clinical outcomes were determined by comparing the final with the initial (presenting) symptoms and signs. The minimum follow-up period between the initial and the final visit was two months. Patients were regarded as legally blind if they had severe to profound visual acuity and/or visual field loss.

Results

All 21 patients were female and black African. Mean age was 31.2 ± 8.9 years (range 16 – 50 years). Mean period of follow up was 19.9 ± 20.1 months (range 2 – 77 months). 71.4% were obese. All patients presented with symptoms. The commonest presenting symptom was headache (90%) followed by visual loss (67%), transient visual obscurations (38%) and diplopia (29%). The results of the presenting signs were as follows: Seven eyes (17%) had visual acuity loss (most of which were mild [9.5%]), seven patients (33%) had abduction deficits, four patients (9.5%) had unilateral abnormal pupil reactions and all patients had papilloedema. Of the recorded associations seven patients (33%) were hypertensive, six (29%) were on contraception (two [9.5%] were on oral contraception) and two (9.5%) were taking prednisone prior to presentation. After the initial visit, all 21

IIH patients were treated with acetazolamide (Diamox) and weight loss was recorded in three patients (14%). Two patients (9.5%) had optic nerve sheath fenestrations (ONSF), two (9.5%) had lumbar-peritoneal shunts (LPS) and six (28.6%) had multiple lumbar punctures (LP's). The outcome analysis was as follows: Symptoms in 19 patients (90%) improved but 16 patients (76%) still had papilloedema. Two patients (9.5%) had abduction deficits at the final visit. Visual acuity loss occurred in five eyes (12%) at the final visit compared to seven eyes (17%) at the initial visit (presentation). From the initial visit (presentation) to the final visit, visual acuity in seven eyes (16%) improved, 31 eyes (74%) remained stable and four eyes (10%) worsened. Although visual fields in 33 eyes (79%) improved from the initial to the final visit, 36 eyes (86%) still had visual field loss at the final visit. 26% of eyes had severe to profound visual impairment i.e. were legally blind, at the final visit.

Conclusion

The results of 21 black African IIH patients reported in this study were similar to some other studies with regards to demographics, clinical features and clinical and visual outcomes. An association between IIH and oral contraceptives, steroids and hypertension could not be established. Although symptoms resolved in most patients, a significant number of patients still had papilloedema and visual field loss following treatment. Despite treatment, a quarter of the patients were legally blind at the final visit, indicating that this condition is not benign.

Presentations Arising From This Study

1. Presented at the University of the Witwatersrand Neurosciences meeting on the 5th August 2009.
2. Presented at the Ophthalmological Society of South Africa (OSSA) Congress on 13 February 2010.

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Nomenclature

APD	afferent pupil defect
BMI	body mass index
CEO	Chief Executive Officer
CF	counting fingers
C. H. Baragwanath Hospital	Chris Hani Baragwanath Hospital
cm H20	centimetre of water
CSF	cerebrospinal fluid
CT scan	computer tomography scan
HM	hand movements
IIH	idiopathic intracranial hypertension
IIHWOP	idiopathic intracranial hypertension without pressure
LP	lumbar puncture
LPOP	lumbar puncture opening pressure
LPS	lumbar-peritoneal shunt
MRI	magnetic resonance imaging
NR	no record
ONSF	optic nerve sheath fenestration
OSSA	Ophthalmological Society of South Africa
RAPD	relative afferent pupil defect
SJEH	St John Eye Hospital
SOL	space occupying lesion
USA	United States of America
VA	visual acuity
VF	visual field

CHAPTER 1

1.0 INTRODUCTION

1.1 Background

Idiopathic Intracranial Hypertension (IIH), also known as pseudotumor cerebri and benign intracranial hypertension, is a condition characterized by an increase in intracranial pressure and no hydrocephalus or space occupying lesion (SOL) on brain imaging [computed tomography (CT) or magnetic resonance imaging (MRI)]; cerebrospinal fluid (CSF) composition is normal.[1] Except for papilloedema (bilateral swelling of optic discs due to raised intracranial pressure) and abducens nerve paresis, neurologic examination is normal. Significant morbidity can occur because of loss of visual function and headache. The visual and other ophthalmological outcomes of IIH are highly variable.

IIH is rare in hospital-based studies.[2, 3]

IIH is strongly associated with obese, young women. It may be seen in association with hypertension, endocrine abnormalities, pregnancy and certain drugs and medications.[4-6]

A Pubmed search revealed only a few published studies on IIH from Africa. These included studies from Libya by Radhakrishnan et al. and a case series (6 patients) from Kenya.[7, 8] There are no published studies from Southern Africa, evaluating the demographic profile, clinical features, associations and clinical and visual outcomes in black patients with IIH.

1.2 Research objective

To determine and to document the demographic profile, clinical features, frequency of associations and clinical and visual outcomes in a study group of black African patients attending St. John Eye Hospital (SJEH) during the period 2006 and 2007.

1.3 Epidemiology

The annual incidence of IIH varies according to different population-based epidemiological studies.[1, 7, 9] In all these studies, the incidence is higher in young, obese females.

Durcan et al. reported an annual incidence of 0.9 per 100 000 persons in the general population of Iowa.[1] When obesity and gender were considered, this incidence increased to 19.3 per 100 000 persons in overweight females between 20 and 44 years of age. The female to male ratio was 8:1.

Radhakrishnan et al. reported an annual incidence of 2.2 per 100 000 persons in the general population of Benghazi, northeastern Libya.[7] This incidence increased to 21.4 per 100 000 persons in obese females between 15 and 44 years of age.

A more recent study in Israel reported an annual incidence of 0.57 to 0.9 per 100 000 persons in the general population. This incidence increased to 4.02 per 100 000 females aged 15 to 45 years.[9]

Studies based on hospital experience also indicate that IIH is rare. Between 1939 and 1975, Corbett et al. treated 57 IIH patients at the University of Iowa in the United States of America.[2] Craig et al. reported 42 patients over a 5 year period from 1991 until 1995 at the Royal Victoria Hospital (RVH) in Belfast, Northern Ireland.[3]

1.4 Clinical features

The most common presenting symptom in IIH is headache, either intermittent or permanent, usually worse in the morning and with recumbent position.[2, 5, 10]

Monocular or binocular transient visual obscurations (TVO) may accompany the headache or occur independently.[1, 6] Lasting only a few seconds, they vary from slight blurring of vision to light perception and they may be provoked or exacerbated by changes in posture from supine to upright, physical exertion or valsalva manoeuvres.

Sustained visual loss can occur as a presenting feature. 26% of patient's in Wall and George's study presented with sustained visual loss.[5]

Intermittent or constant horizontal binocular diplopia usually indicates a sixth cranial nerve palsy which is the only cranial nerve palsy to occur commonly in IIH.[2, 5]
Other presenting symptoms include tinnitus, nausea and vomiting.

Significant morbidity associated with IIH are loss of visual function and headaches.
Celebisoy et al. reported an abnormal visual acuity in 27% and an abnormal visual field in 71% of patients at the initial visit.[10] The degree of visual field changes worsened in 22% of patients; in 51% it improved and in 27% it was stationary. Similar results were found in Wall and George's study.[5]
Although rare, IIH can potentially result in blindness. In Wall and George's study 4% of patients became blind in both eyes.[5] In the series of Corbett et al., 12% of patients became blind in one or both eyes.[2]
A recent study by Bruce et al.,from Atlanta, USA, concluded that black patients were 3.5 times more likely to develop severe visual loss than non-black patients and nearly five times as likely to be legally blind.[11] They suggested that race may be an independent risk factor for severe visual loss. No such racial differences were found in Wall and George's study.[5]

1.5 Diagnosis

There is no specific diagnostic test for IIH. Together with the clinical symptoms and signs, a combination of tests are used to make the diagnosis. These include neuroimaging (CT scan or MRI), lumbar puncture opening pressure (LPOP) and CSF composition.
To establish a diagnosis of IIH, the following modified Dandy criteria are used: i) normal neuroimaging (CT or MRI) i.e. no space occupying lesion (SOL) and no ventriculomegaly, ii) elevation of lumbar puncture opening pressure (LPOP) > 20 cm H_2O, iii) normal CSF composition and iv) normal neurologic examination except for papilloedema and abducens nerve paresis.[12] Exceptions to the diagnostic criteria can occur. IIH without papilloedema (IIHWOP) has been reported.[13, 14] Normal-pressure IIH has also been reported.[15]

1.6 Pathogenesis

The pathogenesis of IIH is poorly understood. Though many case reports and uncontrolled studies have reported associations between IIH and obesity, pregnancy, intracranial venous sinus thrombosis, certain medical conditions (anaemia, hypertension, hyperthyroidism, Addison's disease etc.) and certain medications (tetracycline, nalidixic acid, indocid, corticosteroid, vitamin A, oral contraceptive etc.), the strongest risk factors for IIH are obesity and female gender, especially amongst those in the reproductive age group.[4, 6]

Several hypotheses regarding the aetiology of IIH have been suggested, but no one hypothesis has been able to account for all the manifestations of the disease.

Metabolic and endocrine

Dysregulation of insulin, glucose metabolism, sex hormones, adipokines (leptin and ghrelin) , glucocorticosteroids, lipids and free fatty acids in obesity could predispose to IIH.[16] The exact mechanism is unknown. The possible link between metabolic disorders and the pathogenesis of IIH is a thrombotic tendency due to dysregulation of haemostatic risk factors.[16] This could result in cerebral sinus thrombosis or parasagittal venous lacunae thrombosis, with subsequent impaired resorption of cerebrospinal fluid and venous hypertension.

Vitamin A toxicity

For a long time, vitamin A excess has been implicated in the pathogenesis of IIH. The finding of increased levels of free retinol and decreased levels of retinol binding protein (RBP) supports this hypothesis.[17] Free retinol is thought to be toxic to the arachnoid villi. This toxicity is postulated to decrease CSF re-absorption by the arachnoid villi leading to IIH.

Intracranial venous hypertension

Karahalios et al. suggested that increase in intracranial venous pressure, which leads to an increase in CSF and intracranial pressure by resisting CSF absorption, may be a universal mechanism in IIH of different aetiologies.[18]

Sugarman et al. postulated that obesity leads to IIH via elevated intra-abdominal pressure, which impedes venous return from the brain to the heart, resulting in increased intracranial venous pressure and increased intracranial pressure.[19]

1.7 Management

Interventions and treatments of IIH target: (1) resolving the condition, (2) preventing visual loss, (3) treating headaches, and (4) improving quality of life. Weight loss in obese patients can result in resolution of the condition.[20, 21] Medical therapies to treat symptoms and to prevent visual loss are mainly diuretics aimed at lowering CSF pressure. Surgical therapies are used when medical therapy fails or when severe and rapid visual loss occurs at onset.

Weight loss

A retrospective series evaluating the effect of weight loss on visual function and papilloedema grade in 58 IIH patients showed more rapid improvement in papilloedema and visual fields in overweight women who lost weight than in those who did not lose weight.[22]

Medical management

Acetazolamide, which is a carbonic anhydrase inhibitor, is the most commonly used drug to treat IIH.[5, 23, 24] It decreases CSF production by the choroid plexus. Doses of 0.5-1 g/day are generally used and can be increased until clinical improvement is achieved or a dose of 3-4 g/day is reached. Side effects may include nausea and vomiting, peri-oral and distal limb paraesthesias, fatigue, depression and anorexia.

Topiramate, an anticonvulsant drug, is an attractive option for treating IIH.[25] It has multiple mechanisms of action including inhibition of CSF production and appetite suppression causing weight loss. It is also effective in resolving headaches. Side effects include acute angle-closure glaucoma, myopia and concentration difficulties.

Diuretics such as furosemide are also used to treat IIH, but are considered second-line treatment.[5] It is less potent than acetazolamide and it's mechanism of action in reducing increased intracranial pressure is not clear.

Panagopoulos has reported on somatostatin analogues as a useful alternative to existing treatments for IIH.[26] Further studies are needed to confirm this.

Corticosteroids are useful in treating IIH patients with rapid visual loss while waiting for a surgical procedure such as an optic nerve sheath fenestration (ONSF).[27] It is not recommended for routine and long-term management of IIH.

Surgical management

Surgical therapies are usually indicated when there is progressive loss of vision and persistent headache despite maximum medical therapy or when there is severe or rapid loss of vision at onset.[28, 29] Surgical options include optic nerve sheath fenestration (ONSF) and CSF diversion procedures. There is no strong evidence to suggest that one procedure is superior to the other. Often the decision to use either one of these procedures depends on the available resources and expertise.

Optic nerve sheath fenestration is usually the first-line procedure when loss of vision is the primary problem.[29] In one study, 88% of IIH patients had stabilization or improvement in visual fields after ONSF.[30] The procedure involves creating a defect in the dural sheath of the optic nerve behind the eye. The exact mechanism of action is uncertain but it is thought that ONSF functions through CSF filtration. Although complications may occur, most are transient and self-limiting. Complications may include diplopia, pupillary abnormalities and visual loss.

CSF diversion procedures include ventriculoperitoneal and lumbar-peritoneal shunting. These procedures are indicated in patients with visual loss associated with severe headache.[29] Widespread use is limited by infections, the need for repeated revisions and a high overall failure rate. Burgett et al., in their study, showed lumbar-peritoneal shunting to be effective in reducing CSF pressure, relieving headaches and improving visual function in patients with IIH.[31]

Other surgical therapies that are rarely considered in IIH are 1) venous sinus stenting for patients with CSF outflow obstruction secondary to fixed venous sinus stenosis and 2) gastric weight reduction surgery for morbidly obese patients.[14, 32]

CHAPTER 2

2.0 METHODS AND MATERIALS

A retrospective, descriptive study of patients with the diagnosis of Idiopathic Intracranial Hypertension (IIH) was conducted at St John Eye Hospital (SJEH). 32 IIH patients attended the Neuro-ophthalmology clinic over a 2 year period (1 January 2006 to 31 December 2007). Files of only 21 patients were available, and therefore the following analysis are of these 21 patients. Permission to review files was obtained from the Chief Executive Officer (CEO) of SJEH / C.H. Baragwanath Hospital. The Human Research Ethics Committee of the University of the Witwatersrand approved the study (Clearance certificate number M070907). The protocol for the study was approved by the Postgraduate Committee of the Department of Neurosciences, Faculty of Health Sciences, University of the Witwatersrand.

All patients fulfilled the following criteria for IIH: Modified Dandy criteria [12]

1) Elevation of cerebrospinal fluid opening pressure (> 20 cm H_2O).
2) Normal CSF composition.
3) Normal neuroimaging [computed tomography (CT) or magnetic resonance imaging (MRI)] i.e. absence of space occupying lesion (SOL) and no ventriculomegaly.
4) Normal neurologic examination, except for papilloedema and abducens nerve paresis.

The following information was obtained from patients files and captured on the data capture sheet (Appendix A):

1) Demographics: Age, gender, and race.
2) History: Symptoms (headaches, visual loss, transient visual obscurations, double vision, and nausea and vomiting), duration of symptoms, obesity or recent weight gain, pregnancy, medical conditions, and concomitant medication use.
3) Examination: Visual acuity, ocular motility, pupil reactions, and fundus examination (especially the optic discs) of both eyes at the initial and last/final visit.

4) Investigations: Neuroimaging (CT scan or MRI), lumbar puncture (CSF opening pressure and CSF composition), visual fields of both eyes (initial and last/final visit).
5) Management: Weight loss, medical treatment (acetazolamide, steroids), and surgical therapies (optic nerve sheath fenestration [ONSF], lumbar-peritoneal shunt [LPS] and multiple lumbar punctures [LP's]).

These data were entered into a Microsoft Excel spreadsheet.

The mean age of presentation, mean follow-up period (period between initial visit [presentation] and last/final visit) and mean lumbar puncture opening pressure (LPOP) were determined.

Percentages were calculated for the following parameters:
(1) Obesity which was assessed according to personal impression and not body mass index.
(2) Presenting clinical symptoms such as headaches, loss of vision, transient visual obscurations, double vision, nausea and vomiting and other symptoms.
(3) presenting clinical signs such as visual acuity loss, abduction deficit, abnormal pupil reactions and papilloedema.
(4) associations such as hypertension, diabetes mellitus, steroids (prednisone) and contraception.
(5) treatment modalities such as weight loss, acetazolamide, optic nerve sheath fenestration, lumbar-peritoneal shunt and multiple lumbar punctures.
(6) outcome measures of symptoms, abduction deficit, papilloedema, visual acuity and visual field.

Papilloedema was classified as follows: (1) early (2) acute/established (3) chronic (4) vintage (5) atrophic.[33]

The visual acuity was measured using a Snellen chart. The reason for using Snellen visual acuity as opposed to logMAR is that most of the journals referenced here used Snellen visual acuity and therefore it was easier to make comparisons. The visual acuity loss classification was based on the classifications used in a few studies including the Framingham, Baltimore, and Salisbury Eye studies and classified as follows:[34-37]
(1) Normal vision = $\geq$ 6/6 (i.e. 6/6 or better).
(2) Adequate vision for driving = $<$6/6 $\geq$6/12.

(3) Mild visual acuity loss = <6/12 ≥6/18.

(4) Moderate visual acuity loss = <6/18 ≥6/60.

(5) Severe visual acuity loss = <6/60 ≥CF (counting fingers).

(6) Profound visual acuity loss = <CF (worse than counting fingers).

The visual acuity at the last/final visit was compared to that of the first visit and graded into improved, stable or worse. If the visual acuity between the first and last visit changed from one group to the other in the above visual acuity loss classification, than it was graded as improved or worse.

The visual fields (central 30°) were generated by the Oculus automated perimeter. The visual field loss classification was based on the classifications used in Radhakrishnan's and VanNewkirk's studies.[7, 37] It was classified as follows:

(1) Normal = No visual field defect i.e. full field.

(2) Mild loss = presence of at least 20^0 radius field (≥ 20° radius field).

(3) Moderate loss = $<20^0 \geq 10^0$ radius field.

(4) Severe loss = $<10^0 \geq 5^0$ radius field.

(5) Profound loss = $<5^0$ radius field.

The visual field at the last visit was compared to that of the first visit and graded into improved, stable or worse. If the visual field between the first and last visit changed from one group to the other in the above visual field loss classification, than it was graded as improved or worse. In addition, the encroachment of the enlarged blind spot into the central 10° of the visual field equalled visual field loss and this was taken into consideration when grading the visual field into improved, stable or worse.

Patients were regarded as legally blind if the VA was < 6/60 (worse than 6/60) and/or the VF was <10° radius field (worse than 10° radius field) i.e. severe to profound VA and/or VF loss.

The minimum follow up period between the first and last visit was 2 months.

Statistics were performed using the statistical software SAS 9.1 (SAS Institute Inc., Cary, NC, USA). The graphs and pie charts were generated by this statistical programme. Calculations of the mean and range of the age of presentation, follow-up period and LPOP were performed by this programme. In addition, percentages were also calculated.

CHAPTER 3

3.0 RESULTS

3.1 DESCRIPTIVE ANALYSIS

3.1.1 Demographic analysis

There were 21 patients. All the patients were female and black.

Age of presentation of patients ranged from 16 years to 50 years and the mean age was 31.2 ± 8.9 years (Figure 3.1).

The follow-up period (period between first and last/final visit) ranged from two to 77 months and the mean follow-up period was 19.9 ± 20.1 months (Figure 3.2).

Of the 21 patients, 71.4% were obese, 4.8% were not obese and in the remaining 23.8% obesity was not recorded [NR] (Figure 3.3).

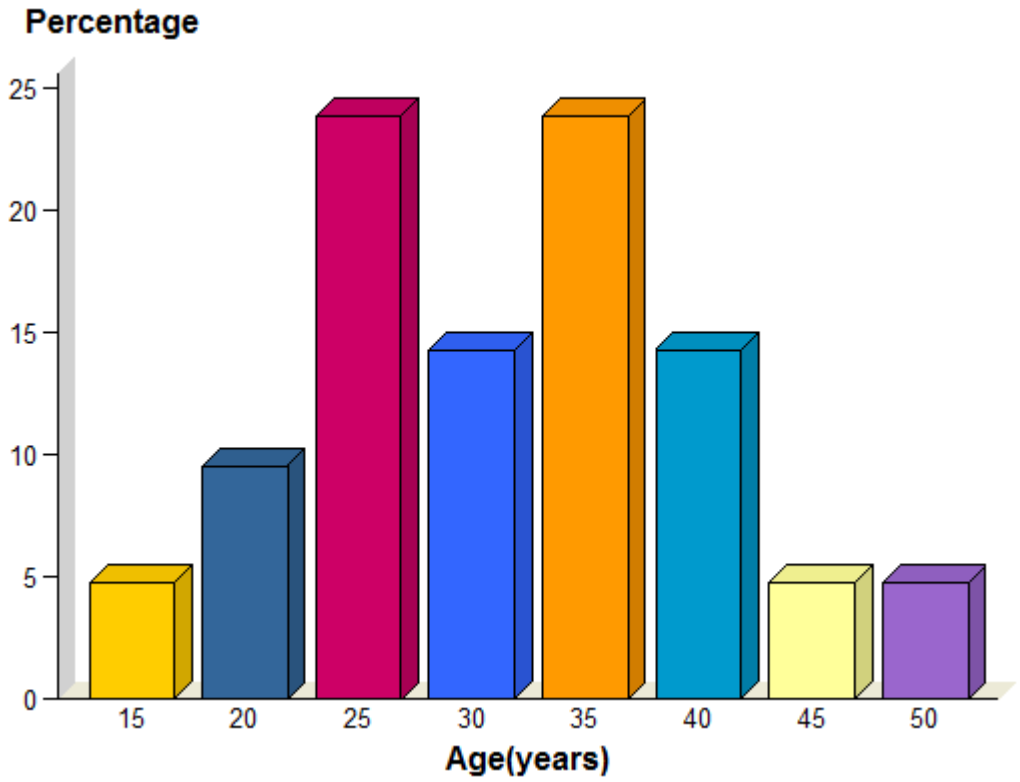


Figure 3.1 Age distribution of patients presenting with IIH.

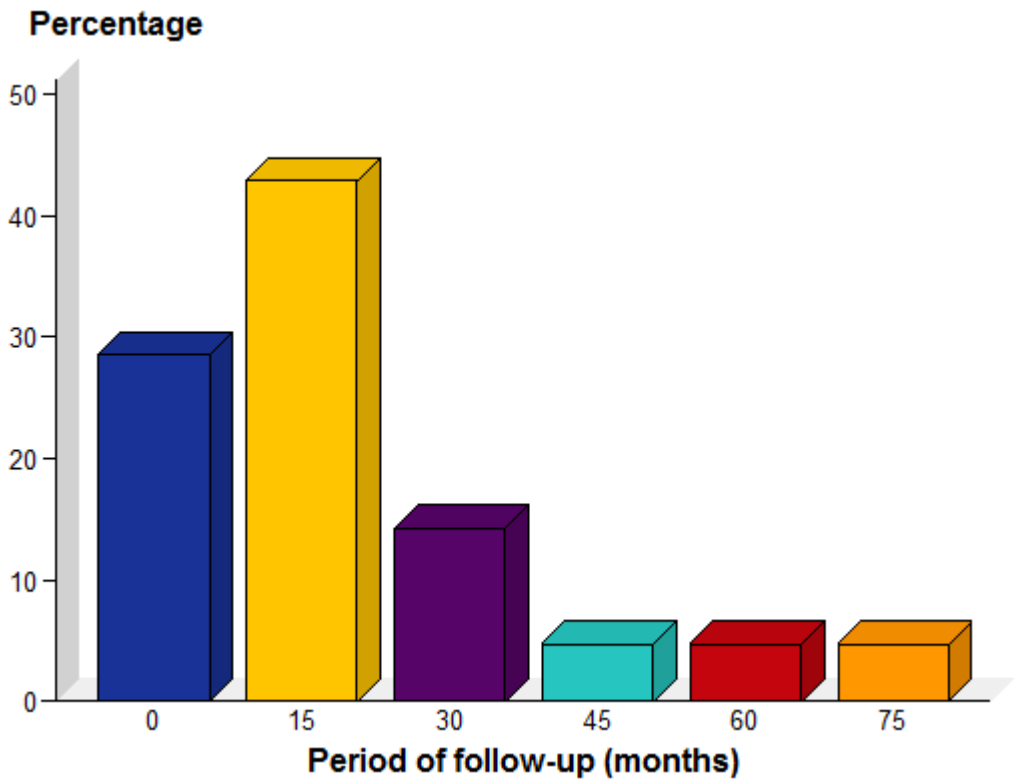


Figure 3.2 Distribution of follow-up period of IIH patients.

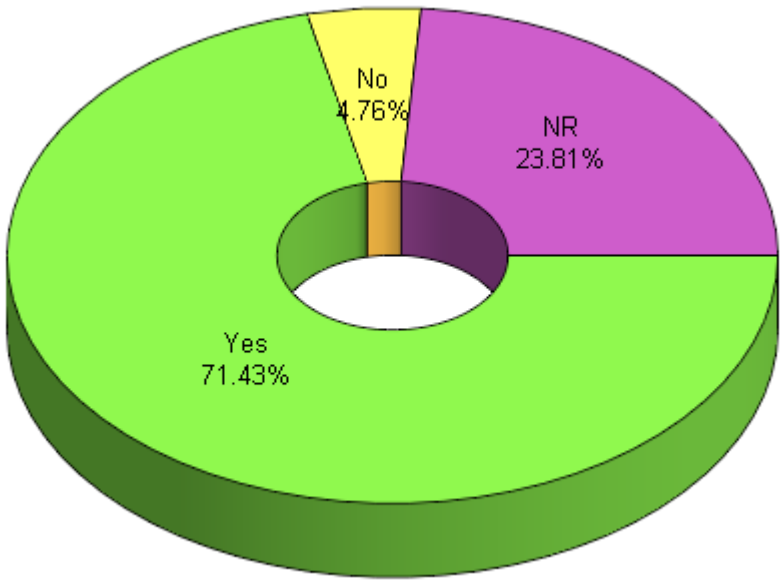


Figure 3.3 Pie chart of analysis of obesity. (NR = not recorded)

3.1.2 Clinical features

The following results are summarized in Table 3.1

All 21 IIH patients presented with symptoms.
19 patients (90%) presented with headaches alone or in association with other symptoms.
14 patients (67%) presented with visual loss alone or in association with other symptoms.
13 patients (61.9%) presented with both headaches and visual loss.

Eight out of the 21 patients (38%) had transient visual obscurations (TVO's). All eight patients had concomitant headaches and six of the eight patients had concomitant visual loss i.e. none of these patients presented with TVO's alone.

Six patients (29%) had double vision.

Four patients (19%) had associated nausea and vomiting, ten (48%) had no associated nausea and vomiting and in seven patients (33%), nausea and vomiting (NR) was not recorded.

Two patients (9.5%) presented with other ocular symptoms in addition to headache; one patient presented with a right conjunctival 'growth' and the other presented with itchy eyes.

The duration of symptoms before presentation ranged from two weeks to more than one year.

Table 3.1 Presenting features

Symptoms	Number of patients n = 21 (%)
Headaches	19 (90%)
Loss of vision	14 (67%)
Transient visual obscurations	8 (38%)
Double vision	6 (29%)
Nausea and vomiting	4 (19%)
Other	2 (9.5%)

3.1.3 Clinical signs on presentation

The following results are summarized in Table 3.2

Initial Snellen visual acuity of 19 of 42 eyes (45%) were normal (≥6/6). 16 eyes (38%) had adequate vision for driving (<6/6 ≥6/12) and seven eyes (17%) had visual acuity loss [four (10%) had mild visual acuity loss (<6/12 ≥6/18), one (2%) had severe visual acuity loss (<6/60 ≥CF) and two (5%) had profound visual acuity loss (<CF)]. None of the patients had moderate visual acuity loss (<6/18 ≥6/60).

Seven of the 21 patients (33%), on presentation, had abduction deficits i.e. abducens (sixth cranial nerve) paresis/palsies. Because two patients had unilateral abduction deficits, the number of eyes with abduction deficits was 12 (29%).

Pupil reactions were abnormal in four of the 42 eyes (9.5%) i.e. four of the 21 patients (19%) had unilateral abnormal pupil reactions. Three patients had a relative afferent pupil defect (RAPD) and one had an afferent pupil defect (APD).

All 21 IIH patients had papilloedema (bilateral swollen discs). The stage of papilloedema was documented in eight patients (38%): two had early papilloedema, three established papilloedema, one chronic papilloedema and two atrophic papilloedema. The stage of papilloedema was not documented in 13 patients.

All 21 patients had normal neurological examinations.

Table 3.2 Clinical presentations

	Number of eyes n = 42 (%)
Visual acuity loss	7 (17%)
Abduction deficit	12 (29%)
Abnormal pupil reaction	4 (9.5%)
Papilloedema	42 (100%)

3.1.4 Associations

Medical Conditions

Of the 21 patients, eight (38%) had systemic illnesses. The remaining 13 patients (62%) had no systemic illnesses. Seven out of the 21 patients (33%) had hypertension and the remaining one patient (5%) had diabetes.

Pregnancy

None of the 21 patients was pregnant.

Medications / Drugs

Six of the 21 patients (29%) were taking contraception. Two were taking oral contraception and four were taking injectables.

Two of the 21 patients (9.5%) took oral prednisone prior to presentation; one patient was being treated for uveitis and the other was being treated for pulmonary disease.

Table 3.3 Associations

	Number of patients n=21 (%)
Medical conditions	
Hypertension	7 (33%)
Diabetes Mellitus	1 (5%)
Medication/Drug history	
Prednisone	2 (9.5%)
Contraceptives	6 (29%)

3.1.5 Investigations

All of the 21 IIH patients met the modified Dandy criteria with normal CT scans (no SOL and no ventriculomegaly) and normal CSF compositions. Four patients had additional MRI scans which showed no SOL and no ventriculomegaly.

The mean lumbar puncture opening pressure (LPOP) in centimetres of water (cm H_20) was 34.67 ± 10.53 (range 20-55) [Figure 3.4].

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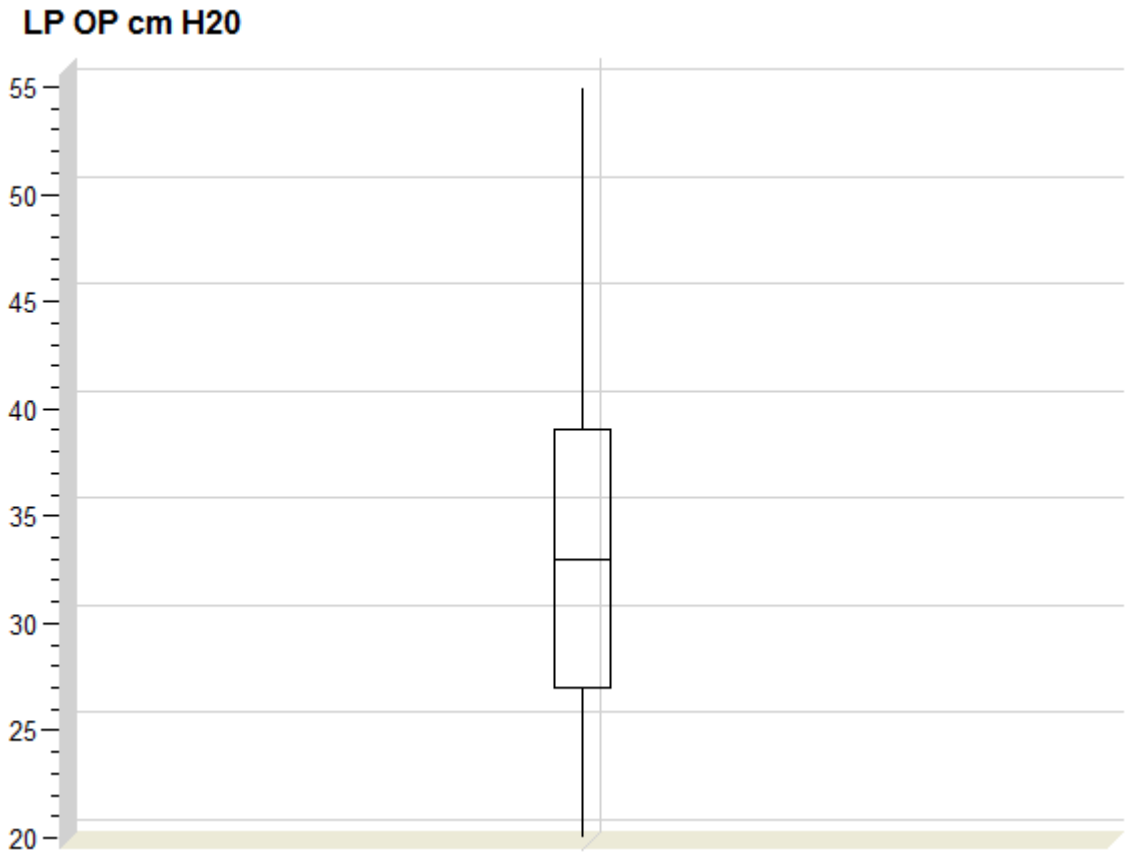


Figure 3.4 Box and Whisker plot of lumbar puncture opening pressure (LPOP).

3.1.6 Management

All 21 IIH patients were treated after the initial visit i.e. after presentation.

Weight loss was recorded in three of the 21 patients (14%).

All 21 patients were treated with acetazolamide (Diamox).

None of the 21 patients was treated with oral or intravenous steroids.

Two of the 21 patients (9.5%) had optic nerve sheath fenestrations (ONSFs); one presented with severe unilateral visual impairment (<6/60 ≥CF) and the other with profound unilateral visual impairment (< CF) which did not improve following the procedure. The VA's in the other eyes, on presentation, were 6/9 (adequate for driving) and 6/6 (normal) respectively.

Two of the 21 patients (9.5%) had lumbar-peritoneal shunts. One patient presented with 6/9 vision (adequate for driving) and the other patient presented with 6/18 vision (mild visual impairment) in the worse eye.

Of the 21 patients, six (28.6%) had multiple lumbar punctures (LPs).

Table 3.4 Management

	Number of patients n = 21 (%)
Weight loss (recorded)	3 (14%)
Acetazolamide (Diamox)	21 (100%)
Optic nerve sheath fenestration (ONSF)	2 (9.5%)
Lumbar-peritoneal shunt (LPS)	2 (9.5%)
Multiple lumbar punctures	6 (28.6%)

3.2 OUTCOME ANALYSIS

3.2.1 Clinical Outcomes

At the initial visit, all 21 IIH patients had symptoms and papilloedema. Seven patients (33%) had abduction deficits (abduction nerve paresis) i.e. 12 of the 42 eyes (29%) had abduction deficits.

At the final visit, 19 patients (90%) had symptoms that improved but 16 (76%) had persistent papilloedema. Two patients (9.5%) had unilateral abduction deficits i.e. two of the 42 eyes (5%) had abduction deficits.

Table 3.5 Clinical outcomes

	Initial	Final
	Number of eyes n = 42 (%)	Number of eyes n = 42 (%)
Abduction deficit	12 (29%)	2 (5%)
Abnormal pupil reaction	4 (9.5%)	3 (7%)
Papilloedema	42 (100%)	32 (76%)

3.2.2 Visual Outcomes

3.2.2.1 Visual acuity

The initial and final Snellen visual acuities of each of the 21 patients are shown in Appendix (B). In addition, the analysis of the initial and final visual acuities is shown in Table 3.6

The initial visual acuities of 19 of the 42 eyes (45%) were normal (≥6/6). 16 eyes (38%) had adequate vision for driving (<6/6 ≥6/12) and seven eyes (17%) had visual acuity loss. Four eyes (9.5%) had mild visual acuity loss (<6/12 ≥6/18), one eye (2.5%) had severe visual acuity loss (<6/60 ≥CF) and two eyes (5%) had profound visual acuity loss (<CF). None of the patients had moderate visual acuity loss (<6/18 ≥6/60).

The final visual acuities of 20 of the 42 eyes (48%) were normal. 17 eyes (40%) had adequate vision for driving (<6/6 ≥6/12) and five eyes (12%) had visual acuity loss. One eye (2.5%) had mild visual acuity loss (<6/12 ≥6/18), one eye (2.5%) had moderate visual acuity loss (<6/18 ≥6/60) and three eyes (7%) had profound visual acuity loss (<CF). None of the patients had severe visual acuity loss (<6/60 ≥CF).

From the initial to the final visit, visual acuities of 31 of the 42 eyes (74%) were stable; seven eyes (16%) improved and four eyes (10%) got worse (Table 3.7). The one patient that presented with severe visual acuity loss (<6/60 ≥CF) in one eye progressed to profound visual acuity loss (<CF). This patient, in addition to one of the patients that presented with unilateral profound visual acuity loss (<CF), had an optic nerve sheath fenestration (ONSF). None of the patients presented with bilateral severe (<6/60 ≥CF) or profound (<CF) visual acuity loss.

Table 3.6 Analysis of initial and final visual acuities (based on data in Appendix B).

Visual Acuity (VA)		Initial VA Number of eyes	Final VA Number of eyes
		n=42(100%)	n=42(100%)
Normal Vision	≥ 6/6	19(45%)	20(48%)
Adequate vision for driving	<6/6 ≥6/12	16(38%)	17(40%)
Mild visual acuity loss	<6/12 ≥6/18	4(9.5%)	1(2.5%)
Moderate visual acuity loss	<6/18 ≥6/60	0(0%)	1(2.5%)
Severe visual acuity loss	<6/60 ≥counting fingers(CF)	1(2.5%)	0(0%)
Profound visual acuity loss	< counting fingers(CF)	2(5%)	3(7%)
	Total number of eyes	42(100%)	42(100%)

Table 3.7 Analysis of visual acuity grading (based on data in Appendix B).

Visual acuity Grading	Number of eyes n=42(100%)
Improved	7(16%)
Stable	31(74%)
Worse	4(10%)
Total number of eyes	42(100%)

3.2.2.2 Visual field

The following results are summarized in Table 3.8 and Table 3.9. The analysis of visual field classification and blind spot size is shown in Table 3.8. The analysis of visual field grading is shown in Table 3.9

Initial visual field loss occurred in 39 of the 42 eyes (93%). Initial visual field loss in nine of the 42 eyes (21%) was moderate (<20° ≥10° radius field), in 26 of 42 eyes (62%) was severe (<10° ≥5° radius field) and in four of 42 eyes (10%) was profound (<5° radius field). None of the patients had a normal visual field or mild visual field loss (≥20° radius field). 26 of 42 eyes (62%) had enlarged blind spots, two (5%) had normal blind spots and blind spots of 11 eyes (26%) could not be determined because of severe or profound visual field loss. Visual field testing of three of the 42 eyes (7%) was not done because of severe or profound visual acuity loss

Final visual field loss occurred in 36 eyes of the 42 eyes (86%). Final visual field loss in three of the 42 eyes (7%) was mild (≥20° radius field), in 25 of the 42 eyes (60%) was moderate (<20° ≥ 10°), in seven of the 42 eyes (17%) was severe (<10° ≥5° radius field) and in one of 42 eyes (2%) was profound (<5° radius field). Three of the 42 eyes (7%) had normal visual fields. 21 of 42 eyes (50%) had enlarged blind spots, 13 (31%) had normal blind spots and blind spots of five eyes (12%) could not be determined because of severe or profound visual field loss. Visual field testing of three of the 42 eyes (7%) was not done because of severe or profound visual acuity loss.

From the initial to the final visit, visual fields of 33 of the 42 eyes (79%) improved and six of the 42 eyes (14%) remained stable (Table 3.9).

None of the visual fields worsened. As mentioned above, visual field testing of three of the 42 eyes (7%) was not done.

26% of eyes had severe to profound visual impairment (i.e. visual acuity loss and/or visual field loss) at the final visit.

Table 3.8 Analysis of visual field classification and blind spot size (based on data in Appendix C).

Visual Field (VF) Classification:	Initial VF (on presentation) Number of eyes	Final VF (last visit) Number of eyes
No VF loss	0 (0%)	3 (7%)
Mild VF loss ≥20˚ radius field	0 (0%)	3 (7%)
Moderate VF loss <20˚≥10˚radius field	9 (21%)	25 (60%)
Severe VF loss <10˚≥ 5˚ radius field	26 (62%)	7 (17%)
Profound VF loss <5˚ radius field	4 (10%)	1 (2%)
VF not done	3 (7%)	3 (7%)
Total number of eyes	42 (100%)	42 (100%)

Blind Spot:		
Enlarged	26 (62%)	21 (50%)
Normal	2 (5%)	13 (31%)
Unable to determine from VF	11 (26%)	5 (12%)
VF not done	3 (7%)	3 (7%)
Total number of eyes	42 (100%)	42 (100%)

Table 3.9 Analysis of visual field grading (based on data in Appendix C).

Visual field grading	Number of eyes n=42(100%)
Improved	33(79%)
Stable	6(14%)
Worse	0(0%)
VF not done	3(7%)
Total number of eyes	42(100%)

CHAPTER 4

4.0 DISCUSSION

Patient data of 21 of 32 IIH patients seen in the Neuro-ophthalmology clinic at St John Eye Hospital over a two year period (2006 and 2007) were available and this study is based on these 21 patients. All 21 patients were black African female. The preponderance of females and the high percentage of obesity (71.4%) reported in this study are shown in other studies.[1, 5-7, 9] In one study, obesity occurred less frequently.[10] The mean age at diagnosis, in this study, was 31.2 ± 8.9 years which was similar to other studies.[3, 9] The range of follow-up (2-77 months) in this study was similar to another study.[7]

The most common presenting symptom in IIH are usually headaches followed by transient visual obscurations (TVOs).[3, 5, 6, 10] In this study, headache was the commonest symptom (90%) but sustained loss of vision was the second most common symptom (67%) with transient visual obscurations (TVOs) being the third most common symptom (38%). The possible reason for sustained loss of vision but not TVOs being the second most common symptom is that our patients may be presenting later. The other possible reason was the vision loss wrongfully recorded as sustained whereas it was transient.

At presentation (initial visit), visual acuity loss was found in 17% of eyes. This figure was higher than that found in Wall and George's study.[5] Seven patients (33%) had abduction deficits (abduction nerve paresis/paralysis) at presentation. All patients that presented with diplopia had abduction deficits. The abnormal pupil reactions reported in 19% of patients in this study was similar to that reported in Wall and George's study but lower than that reported in Corbett et al's study.[2, 5] In this study, three of the four patients that had unilateral abnormal pupil reactions (APD/RAPD) presented with unilateral severe to profound visual acuity loss. This was expected because these patients had atrophic papilloedema.

In this study, 33% of the patients had hypertension. This was higher than the 23% reported by Corbett et al. and equal to the 33% reported by Ireland et al.[2, 4] Two case-control studies reported a significant association between hypertension and IIH.[4, 6] This association was not observed by Radhakrishnan et al.[7] In Ireland et al's study, ten of the 13 hypertensive

patients (77%) were ≤ 25 years.[4] In this study, one of the seven hypertensive patients (14%) was ≤ 25 years of age; the other six patients were 35 years or older.

Though IIH has been anecdotally associated with oral contraceptives, pregnancy and menstrual irregularities, Ireland et al., in their case-control study, reported no differences in case and control subjects regarding prior oral contraceptive-use, pregnancy histories and menstrual irregularities.[4] In this study, two of the 21 patients were taking oral contraceptives at the time of diagnosis of IIH. Because one patient was taking prednisone and the other was obese, it was difficult to comment whether there was an association between oral contraceptive-use and IIH. None of the patients was pregnant at the time of diagnosis. Menstrual irregularities were not recorded.

Though corticosteroid-use has been associated with IIH, Ireland et.al did not find a causal relationship between corticosteroid-use and IIH.[4] In this study, two of the 21 IIH patients were taking prednisone prior to the diagnosis of IIH. It was difficult to determine whether there was an association between prednisone-use and IIH, because one patient was obese and the other was taking oral contraceptives.

The mean lumbar puncture opening pressure (LPOP) in this study was 34.67 ± 10.53 cm H_2O (range 20-55). Similar averages were found in other studies.[9, 10] Kesler et al. suggested that the high lumbar puncture opening pressure may be due to obesity.[9]

All 21 IIH patients were treated after the initial visit. Whether patients lost weight or not was recorded in only three of the 21 patients (14%). All patients were treated with acetazolamide (Diamox). Four of the 21 patients (19%) had surgery after failure of conservative management: two (9.5%) had optic nerve sheath fenestrations (ONSFs) for progressive visual loss and two (9.5%) had lumbar-peritoneal shunts for persistent headaches. Three of these four patients had multiple lumbar punctures while waiting for surgery. Although there is a lack of good randomized trials to guide management decisions, this sequence (i.e. from conservative to surgical treatment) in the management of IIH patients is widely accepted.[28]

In this study, all 21 patients had IIH symptoms and papilloedema at the initial visit (i.e. at presentation). At the initial visit seven patients (33%) had abduction deficits, seven eyes (17%) had visual acuity loss and 39 eyes (93%) had visual field loss. At the final visit, 19 patients (90%) had symptoms that improved but 16 (76%) had persistent papilloedema. Thus a significant number of patients had persistent papilloedema. However, a third of

patients with persistent papilloedema had a short follow–up period. If these patients were followed up for a longer period, the papilloedema in some of these patients may have resolved, resulting in a lower percentage of patients classified as having persistent papilloedema. Two patients (9.5%) had abduction deficits at the final visit. In Wall and George's study 64% of patients had papilloedema and none had abduction deficits at the final visit.[5]

13% of eyes at presentation and 10% of eyes at the final visit had visual acuity loss in Wall and George's study.[5] In this study, seven of the 42 eyes (17%) had visual acuity loss at presentation (initial visit) but at the final visit, five of the 42 eyes (12%) had visual acuity loss. There was no significant difference in visual acuity loss between the initial visit and the final visit. Comparing the visual acuity at the final visit to that of the initial visit, visual acuity in seven eyes (16%) improved, 31 (74%) remained stable and four (10%) worsened.

In Wall and George's study, 88% of eyes had visual field (automated) loss on presentation and at the final visit, 71% of eyes had visual field loss.[5] In this study, 39 eyes (93%) had visual field (automated) loss at presentation (initial visit). At the final visit, 36 eyes (86%) had visual field loss. A much higher percentage of eyes had visual field loss than Snellen visual acuity loss indicating that visual fields are a much more sensitive measure of vision loss. Most of the eyes (62%) in the present study had severe ($<10° \geq 5°$ radius field) visual field loss at the initial visit. Most of the eyes (60%) had moderate ($<20° \geq 10°$ radius field) visual field loss at the final visit. Comparing the visual field loss at the final visit to that of the initial visit, visual fields in 33 eyes (79%) improved and in six eyes (14%) remained stable.

Bruce et al. concluded that IIH in blacks is more aggressive and that blacks are 3.5 times more likely to develop severe visual loss than non-blacks.[11] They reported severe visual loss in at least one eye in 23% of black patients and 7% of non-black patients at the final visit. In this study, 26% of patients had severe to profound visual impairment at the final visit i.e. 26% were legally blind at the final visit.

Limitations of the study: (1) This was a retrospective study; (2) Small sample size; (3) Short follow-up period in some of the patients; (4) Obesity was determined according to personal impression and not body mass index (BMI); (5) Other associations of IIH such as menstrual irregularities were not included in the questionnaire; (6) weight loss as part of a management strategy was not recorded in most patients

CHAPTER 5

5.0 CONCLUSION

The findings in a cohort of 21 black African female IIH patients are similar to some other studies with regards to demographics, clinical features and clinical and visual outcomes.

In this study, IIH occurred mainly in obese females in the reproductive age group.

Although a third of the IIH patients in this study had hypertension, an association between IIH and hypertension could not be established. An association between IIH and prednisone or oral contraceptives was also not established in this study.

Although 90% of patients reported improved symptoms following treatment, 76% of patients still had evidence of papilloedema at the final visit.

The percentage of eyes with visual impairment assessed by Snellen visual acuity was lower than that assessed by visual field at presentation (initial visit) and at the final visit. Therefore visual field was found to be more sensitive than visual acuity in detecting visual impairment.

Although 79% of eyes had visual fields which improved following treatment, 86% of eyes still had visual field loss at the final visit.

Finally, in this study, a quarter of the patients, despite treatment, were legally blind clearly indicating that this condition is not benign.

APPENDIX A: DATA CAPTURE SHEET

Patient Number:

Age: **Sex** **Race**:

HISTORY

Symptoms: **Headaches** ☐
Visual loss ☐
Transient visual obscurations ☐
Double vision ☐
Nausea & vomiting ☐
Nil ☐

Duration of symptoms

Associations: **Obesity or recent weight gain** ☐
Medical conditions ☐ List:
Pregnancy ☐
Medication or drug use ☐ List:

Examination:

Visual acuity: **Initial** **R** **L** **Last visit** **R** **L**
Ocular motility: **R** **L**
Pupil reactions: **R** **L**
Fundus examination:
Optic discs **R** **L**
Rest of fundus **R** **L**
Neurological examination:

Investigations:

Neuroimaging: **CT scan** **MRI**
Lumbar puncture: **Opening pressure** **CSF composition**
Visual field(Oculus): **Initial** **R** **L** **Last visit** **R** **L**
Grading: **Improved** ☐
Stable ☐
Worse ☐

Management:

Weight loss: ☐
Medical: **Diamox** ☐ **Steroids** ☐
Surgical: **ONSF** ☐ **Lumbar peritoneal shunt** ☐ **Multiple LP'S** ☐

APPENDIX B

Visual acuity classification and grading of all IIH patients.

Patient Number	Right eye			Left eye		
	VA Loss Classification		Grading	VA Loss Classification		Grading
	Initial	Final		Initial	Final	
1	Normal	Adequate	Worse	Adequate	Adequate	Stable
2	Normal	Normal	Stable	Normal	Normal	Stable
3	Adequate	Normal	Improved	Adequate	Normal	Improved
4	Normal	Normal	Stable	Normal	Normal	Stable
5	Adequate	Adequate	Stable	Profound	Profound	Stable
6	Normal	Adequate	Worse	Normal	Normal	Stable
7	Severe	Profound	Worse	Adequate	Adequate	Stable
8	Profound	Profound	Stable	Normal	Adequate	Worse
9	Normal	Normal	Stable	Mild	Adequate	Improved
10	Normal	Normal	Stable	Normal	Normal	Stable
11	Adequate	Adequate	Stable	Adequate	Adequate	Stable
12	Normal	Normal	Stable	Normal	Normal	Stable
13	Adequate	Adequate	Stable	Adequate	Adequate	Stable
14	Normal	Normal	Stable	Normal	Normal	Stable
15	Adequate	Normal	Improved	Adequate	Normal	Improved
16	Normal	Normal	Stable	Adequate	Adequate	Stable
17	Mild	Mild	Stable	Mild	Adequate	Improved
18	Adequate	Adequate	Stable	Normal	Normal	Stable
19	Normal	Normal	Stable	Mild	Moderate	Improved
20	Adequate	Adequate	Stable	Adequate	Adequate	Stable
21	Normal	Normal	Stable	Adequate	Adequate	Stable
	Number of right eyes		21	Number of left eyes		21
			↘		↙	
			Total number of eyes	42		

APPENDIX C

Visual field classification and grading of all IIH patients.

Patient no.	Right eye VF Loss Classification Initial	Right eye VF Loss Classification Final	Right eye Grading	Left eye VF Loss Classification Initial	Left eye VF Loss Classification Final	Left eye Grading
1	Moderate	Moderate	Stable	Moderate ↑ Blind spot- involving central 10˚	Moderate ↑Blind spot- not involving central 10˚	Improved
2	Moderate	Moderate	Stable	Severe	Moderate	Improved
3	Severe	Moderate	Improved	Severe	Moderate	Improved
4	Severe	Moderate	Improved	Severe	Moderate	Improved
5	Severe	Severe	Stable	NP	NP	NP
6	Moderate	Moderate	Stable	Severe	Moderate	Improved
7	NP	NP	NP	Profound	Severe	Improved
8	NP	NP	NP	Profound	Profound	Stable
9	Severe	Severe	Stable	Severe	Moderate	Improved
10	Moderate	Mild	Improved	Moderate	Mild	Improved
11	Profound	Severe	Improved	Profound	Severe	Improved
12	Severe	Moderate	Improved	Severe	Moderate	Improved
13	Severe	Moderate	Improved	Severe	Moderate	Improved
14	Severe	Moderate	Improved	Severe	Moderate	Improved
15	Severe	Moderate	Improved	Severe	Moderate	Improved
16	Severe	Moderate	Improved	Severe ↑Blind spot- involving central 10˚	Severe ↑Blind spot- not involving central 10˚	Improved
17	Severe	Moderate	Improved	Severe ↑ Blind spot- involving central 10˚	Severe ↑Blind spot- not involving central 10˚	Improved
18	Severe	Moderate	Improved	Severe	Moderate	Improved
19	Severe	Moderate	Improved	Severe	Moderate	Improved
20	Severe	Mild	Improved	Moderate	Normal	Improved
21	Moderate	Normal	Improved	Moderate	Normal	Improved
	NP= Not Possible					

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