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Idiopathic Intracranial Hypertension—Clinical Characteristics, Neuroimaging and Outcome of Patients from Pretoria, South Africa

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ABSTRACT

Background: Idiopathic intracranial hypertension is a syndrome characterized by symptoms and signs of raised intracranial pressure without a secondary cause. It primarily affects young obese women who present with headache and papilledema. We report the clinical presentation, brain imaging findings and outcomes of patients with IIH from two large tertiary hospitals in Pretoria, South Africa.

Methods: All patients with confirmed IIH attending Steve Biko Academic Hospital and Kalafong Provincial Tertiary Hospital between July 2019 and June 2024 were included. Demographic data, presenting symptoms and signs, visual assessment, neuroimaging, management and outcomes were analyzed.

Results: Forty-seven patients were included (45 females; 96%). Mean age was 34 years and mean BMI was 38.2 kg/m^2. The most common presenting symptoms were headache (97.9%), visual abnormalities (blurred vision 55%, transient visual obscurations 42%) and pulsatile tinnitus (40.5%). Papilledema occurred in 46 patients (97.9%); the mean opening pressure was 32 cm H_2O. MRI had a higher sensitivity in detecting IIH-related features compared to CT (79% versus 63%). Tortuosity of the optic nerves was most common in 79% of the MRIs, followed by enlarged optic nerve sheaths in 68.4%. Four eyes were blind at presentation and remained blind. While most patients reported improvement on acetazolamide and/or topiramate, at discharge, 21.3% remained symptomatic.

Conclusion: Demographics and clinical presentation were comparable to international studies, showing that IIH is a disorder prevalent in young obese females. It is disconcerting that patients still lose vision due to a treatable condition and awareness of IIH should be raised.

1 | Introduction

Idiopathic intracranial hypertension (IIH), previously termed pseudotumor cerebri or benign intracranial hypertension, is a neuro-ophthalmological disorder characterized by raised intracranial pressure in the absence of an intracranial space-occupying lesion, infection, or venous obstruction. Specific causes and pathogenic mechanisms of IIH are still largely unknown, but the condition occurs most commonly in obese women of childbearing age [1].

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Different clinical criteria were developed and are used to diagnose IIH. The Modified Dandy Criteria [1], ICHD-III criteria [2], and revised Friedman criteria [3] are well accepted in clinical practice and research.

Globally, the prevalence of IIH appears to be on the rise, concurrent with the rise in obesity rates, especially among females [4].

There is a paucity of data regarding the prevalence and presentation of this condition from the African perspective and from South Africa. Only one small study reported outcomes in South African patients with IIH from an ophthalmologist's perspective [5]. The current expectation is that the prevalence of IIH will rise in the future. A recent epidemiological study from South Africa showed an alarming number of women of childbearing age to be either overweight (60%) or obese (35%) [6]. As a result of these trends, South African women may have a high risk of developing IIH. We have noted a rising number of young, mostly female, patients with this condition over the last few years with often delayed diagnosis and unfavorable outcomes. The lack of data from South Africa regarding IIH prompted us to investigate this disease in our population, and this study describes the demographics, clinical presentation, and outcomes of patients with IIH seen at two large tertiary referral hospitals in Pretoria.

2 | Methods

A descriptive cross-sectional retrospective study, identifying all adult patients diagnosed with IIH in two tertiary neurological centres affiliated with the University of Pretoria (Kalafong Provincial Tertiary Hospital and Steve Biko Academic Hospital) from July 2019 to June 2024 was conducted.

Patients had to meet the Friedman criteria [3] for IIH to be included. In Table 1 the criteria for IIH with and without papilledema are listed.

Demographic data, symptoms at presentation, ophthalmological findings, body mass index (BMI), comorbid conditions, CSF opening pressure, and radiological findings were collected and entered into Microsoft Excel spreadsheets. Descriptive statistics were utilized to analyze the data.

3 | Results

We identified 52 patients with suspected IIH; 47 patients fulfilled the Friedman Criteria and were included in the study. Five patients had alternative neurological diseases and comorbid conditions that could be identified as secondary causes (such as previous Arnold Chiari malformation, hydrocephalus, and use of methotrexate). Demographic findings are shown in Table 2.

The mean age was 34 years (SD 10.4) with a range of 18 to 54 years. The age distribution is shown in Figure 1. Thirteen patients (27.6%) were 40 years or older at the time of diagnosis.

The mean BMI was 38.2 kg/m^2 (SD 6.8). BMI categories showed that one patient had a normal weight, one was overweight, and 44 patients (95.6%) were obese. The height and weight were not documented for one patient. Ethnicity distribution showed that 68% of the patients were black, 4% were of mixed ancestry, and 28% were white. Forty-five patients (96%) were female. More than 90% of patients had completed 12 years of school education, with 42.5% having earned an additional degree or diploma.

Seven patients (14.9%) had no other diseases at presentation, 13 (27.6%) had arterial hypertension, and anemia was noted in eight patients (17%). Regarding the HIV status, 36 patients (76.6%) were HIV-negative, eight patients (17%) were HIV-positive and in three patients, the status was unknown. All patients with HIV infection were on antiretroviral treatment. Other co-morbidities included obstructive sleep apnoea in two patients, and other medical conditions such as diabetes mellitus, hypothyroidism, pancreatic insufficiency, epilepsy,

TABLE 1 | Diagnostic criteria for Idiopathic intracranial hypertension modified from Friedman et al. [3].

Required for diagnosis of IIH

A. Papilledema
B. Normal neurologic examination except for cranial nerve abnormalities
C. Neuroimaging: normal brain parenchyma
D. Normal CSF composition
E. Elevated lumbar puncture opening pressure (≥ 25 cm CSF in adults) in a properly performed lumbar puncture

Diagnosis of IIH without papilledema

In the absence of papilledema, a diagnosis can be made if B-E from above are satisfied, and addition the patient has a unilateral or bilateral abducens nerve palsy

In the absence of papilledema or sixth nerve palsy, a diagnosis can be suggested but not made if B-E from above are satisfied, and in addition at least 3 of the following neuroimaging criteria are satisfied:

i. Empty sella
ii. Flattening of the posterior aspect of the globe
iii. Distension of the peri-optic subarachnoid space with or without a tortuous optic nerve
iv. Transverse venous sinus stenosis

Note: The diagnosis of IIH is definite if the patient fulfills criteria A–E. The diagnosis is considered probable if criteria A–D are met but the measured CSF pressure is lower than specified for a definite diagnosis.

TABLE 2 | Demographic characteristics of patients with IIH.

	Number of patients	Mean/(SD) or %
Age (years)	47	34 (10.4)
BMI (kg/m^2)	46	38.2 (6.8)
Ethnicity		
Black	32	68.1%
Mixed ancestry	2	4.3%
White	13	27.6%
Sex		
Female	45	95.7%
Male	2	4.3%
Highest level of education		
Primary level	3	6.4%
Matric (grade 12)	24	51.1%
Degree/diploma	20	42.5%
Socioeconomic background		
Unemployed	16	34%
Student	7	14.9%
Employed	22	46.8%
Self-employed	1	2.1%
Disabled medically boarded	1	2.1%

previous retinal detachment, systemic lupus erythematosus, major depressive disorder, and peptic ulcer disease occurred in single patients.

Figure 2 illustrates the symptoms at the time of presentation. All but one patient (97.9%) reported headaches as the main complaint. The headache was described as dull, aching, holocephalic in 12 (26.1%) patients, as a headache consistent with features of increased intracranial pressure in 13 (28.3%), as migraine-like in 11 (23.9%), and five patients (10.9%) described features of tension-type headaches. The headache was not specified in the remaining five patients.

Following headaches, visual symptoms were prevalent. Blurring of vision was noted by 26 (55.3%) patients, and transient visual obscurations occurred in 20 (42.6%), central vision loss in nine (19.1%), with two patients (4.3%) presenting with complete visual loss. Tinnitus and diplopia were reported in 40.4% and 17% respectively. Two patients had a cranial nerve six palsy, one patient reported rhinorrhoea.

Forty-six patients (97.9%) had papilledema on examination; only one patient had a normal fundoscopy. The severity of papilledema was recorded using the modified Frisen scale and is shown in Table 3. Low degree to moderate papilledema, grades II and III, was seen in 72.3% of the patients.

Visual acuity was tested in all patients. Table 4 summarizes the findings. As the eyes in some patients were differently affected, we present eyes (not patients). One eye was blind from another cause (previous retinal detachment). Ten eyes (10.6%) were either completely blind or so severely affected (only light perception) that they fit the definition of legal blindness. Another eight eyes (8.5%) showed moderate to low vision. The majority (76 eyes/80.8%) had normal, near normal or mildly impaired vision.

In forty-five patients, perimetric studies were attempted. In some patients only one eye was assessed due to the loss of vision in the other eye (Table 5). Scotomas were the most common finding on perimetry.

All patients underwent a lumbar puncture to measure the opening pressure and confirm the diagnosis. The mean opening pressure was 32 cm H_2O (SD 5.6) ranging from 25 to 47 cm H_2O. Except for three patients with mildly raised CSF protein levels (all with traumatic lumbar punctures of whom one was HIV positive), all CSF parameters (including cell count, protein, glucose, gram stain and cultures) were normal or negative in all patients.

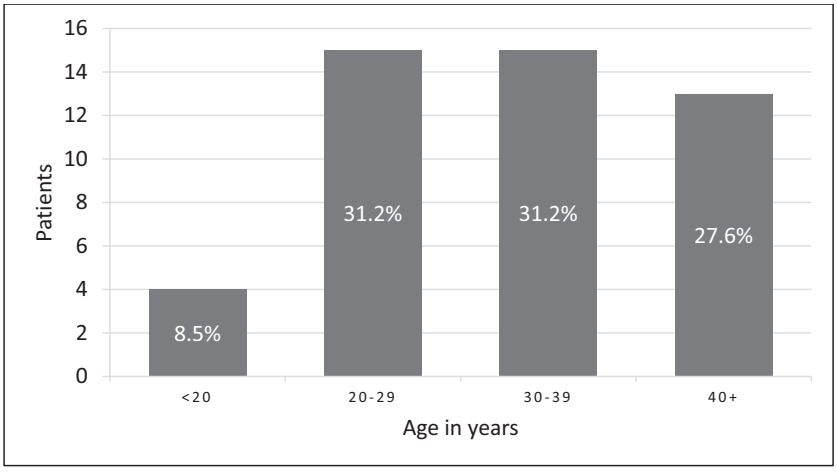

FIGURE 1 | Age distribution in cohort of patients with IIH.

Neuroimaging was available in all patients, with 43 having had a CT of the brain and 19 an MRI. Thirteen patients had both an MRI and a CT of the brain. Figure 3 illustrates the findings and compares the two imaging modalities.

The MRI had a higher sensitivity of 79% in detecting IIH-related features compared to the CT with 63%. The most common finding on both modalities was tortuosity of the optic nerves. This was found in 79% of the MRIs, and together with enlarged optic nerve sheaths, present in 68.4%, these were the two most important abnormalities. An empty, or partially, empty sella turcica was also common in 27.9% of CTs and 63.2% of MRIs.

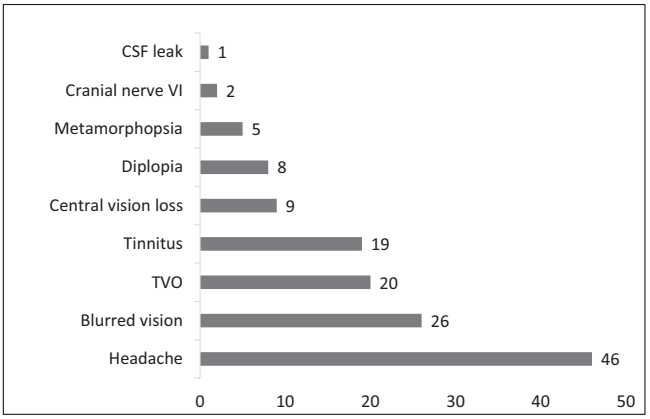

FIGURE 2 | Clinical presentation of patients with IIH (TVO transient visual obscurations).

TABLE 3 | Fundoscopy at the time of diagnosis in patients with IIH.

Grade	0	I	II	III	IV	V
N	1	8	19	15	4	0
%	2.1	17	40.4	31.9	8.5	0

Note: Using modified Frisen Scale: 0 normal disc, I = minimal papilledema, II = low degree papilledema, III = moderate papilledema, IV = marked papilledema, V = severe papilledema.

Forty-six patients were treated with pharmacological treatment, and one was only on observation as she was in her 3rd trimester of pregnancy. Thirty-nine patients (83%) were started on acetazolamide monotherapy, two (4.3%) on topiramate monotherapy, and five (10.6%) were on combination therapy consisting of topiramate and acetazolamide. All patients received dietary counseling and attempted weight loss. One patient with vision loss received CSF shunting in another hospital and afterwards, again followed up with us.

At the time of discharge from hospital, four eyes remained blind, while 37 (78.7%) patients reported good clinical improvement, Brian and 10 (21.3%) still had some residual headaches or mild symptoms. Furthermore, most of our patients reported a good clinical outcome at follow-up visits, with only 13% of patients at 3 months, and 8% at 6 months complaining of residual headache.

4 | Discussion

Idiopathic intracranial hypertension is still viewed as a rare disease with an incidence of 1.0/100,000 per annum in the general population [7]. However, when obesity is considered, the incidence increases to 13–14/100,000 annually. A recent study from Wales showed that the incidence of IIH increased by a factor of three from 2003 to 2017 (2.3/100,000/year to 7.7/100,000/year) parallel to the increase of obesity in the general population [8]. Research from Kuwait estimated a crude annual incidence of IIH of 3.3/100,000 population, which is higher than the incidence in Western cohorts [9]. Although no data for the prevalence or incidence of IIH in South Africa exist, we have seen a rising number of patients with IIH in our academic hospitals in Pretoria, with the suspicion that the condition remains largely unrecognized in primary health care facilities.

IIH primarily affects women of childbearing age who are overweight or obese and our data confirms the strong association with the female sex [3, 10–11]. Only 4.3% of our patients were male compared to 2.4% in the large IIH treatment trial in 2014 (IIHTT) [11]. Interestingly, smaller cohort studies from developing countries showed a higher male representation with 10% in

TABLE 4 | Visual acuity at presentation.

Visual acuity (Snellen)	Classification	Grading	Right eye ($n = 47$)	Left eye ($n = 47$)
Normal (6/6)	Normal	Normal (80.8%)	19	21
Adequate for driving (< 6/6, > 6/12)	Near normal		14	10
Mild loss (< 6/12, > 6/18)	Mild visual impairment		5	7
Moderate loss (< 6/18, > 6/60)	Moderately visual impaired	Low vision (8.5%)	3	3
Severe loss (< 6/60 > counting fingers)	Severely visual impairment		1	1
Profound loss (light perception)	Legally blind	Blindness (10.6%)	3	3
Blind	Totally blind		2	2

Note: Visual acuity was measured at 6 m using a Snellen chart; classification is based on the Framingham, Baltimore, and Salisbury Eye Studies [7].

TABLE 5 | Perimetry at presentation in patients with IIH (84 eyes).

	Right eye ($n=17$)	Left eye ($n=17$)	Both eyes ($n=60$)	n/%
Normal visual fields	6	3	14	23/27.4
Central/ centrocecal scotoma	3	4	10	17/20.2
Arcuate scotoma	2	1	8	11/13.1
Temporal wedge scotoma	4	2	16	22/26.2
Hemianopic defects	2	1	8	11/13.1
Not done	0	6	4	10

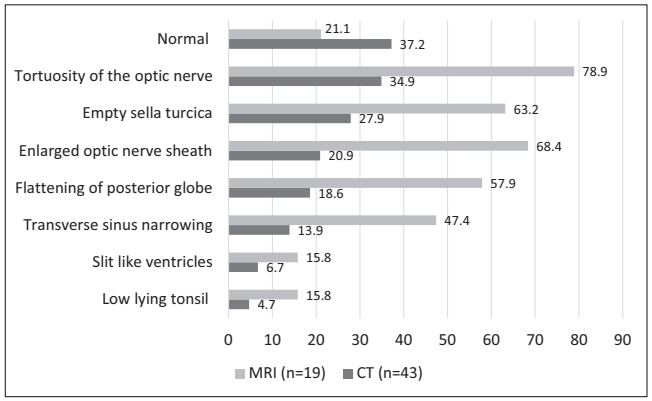

FIGURE 3 | Findings on brain imaging of patients with IIH.

China and Morocco, 11% in India, 11.9% in Turkey and 13% in Kuwait [9, 12–15].

The mean age of our patients (34 years) was slightly higher than the age in the IIHTT (29 years) and notably, in our study 13 patients (27.6%) were above 40 years—a finding that is considered atypical [16]. Although the age at diagnosis is often higher in men [17], all our patients above 40 years were female, and our two male patients were both younger than 20 years. The BMI of these older patients was 40.7 kg/m^2 and thus higher than the average BMI of our cohort (38.2 kg/m^2); this also differs from the above-mentioned studies in which older patients with IIH had lower BMIs [16].

We found a high incidence of obesity (mean BMI 38.2 kg/m^2; 32% severely obese with BMIs over 40 kg/m^2), strongly supporting the correlation between obesity and IIH. Of concern is the recent rise in overweight and obesity in young female South Africans, with rates of 60% for overweight and 35.2% for obesity in non-pregnant women of childbearing age [6]. Higher educational levels, urban residence, and a wealthier socioeconomic background were significantly associated with being overweight and obese [6]. In our cohort, 90% of patients had either the highest school exit exam or a higher educational level, supporting this observation. In addition, 63.8% were either employed or studying, likewise a high proportion in the South African context.

Anemia and HIV infection were each noted in 17% of our patients. Anemia is common in South Africa, with a 22% prevalence of anemia in adult females and 12.2% in adult males [18, 19]. Recently, an association of IIH and iron deficiency anemia has been reported, with faster response and better prognosis if the anemia is treated simultaneously [20, 21]. HIV infection was another common comorbidity with eight affected patients in our cohort. All of those were on antiretroviral treatment and mimics of IIH in these patients were carefully excluded.

Headache, reported in 84%–90% of patients, is the most common symptom encountered in IIH, and the main reason why patients seek medical attention [11, 22]. In our cohort, 97.9% described headache as the initial and main symptom. Headache features may vary in IIH, and headaches suggestive of increased intracranial pressure occurred in 28.3% of our patients, a dull aching holo-cephalic pain in 26.1%, and 23.9% described migraine-like features.

Visual symptoms were the second most common complaints of our patients with blurring of vision in 55.3%, followed by TVOs in 42.6%. Although TVOs were the leading visual complaint (68%) in the IIHTT, other studies found blurring of vision to be more common than TVOs [5, 9]. Blurring of vision is believed to result from a hyperopic shift due to the shortening of the globe, while TVOs may occur because of transient ischemia of the oedematous optic nerve head [23, 24]. The greatest danger of IIH is central vision loss and blindness which are signs of fulminant IIH. In our study, 19.1% had central vision loss (blind patients included). We also found diplopia, which can result from latent unilateral or bilateral sixth-nerve palsy, in 17% and an additional two patients had overt abducens nerve palsy, similar to the 18% reported in the IIHTT [11].

Tinnitus, an often-overlooked symptom in IIH, is pulsatile, can be uni-or bilateral, intermittent or continuous [24]. It was the third most common symptom in 40.4% of our patients and lower than the 52% reported in the IIHTT [11].

Papilledema forms part of the diagnostic criteria for IIH and is the most reliable clinical sign for diagnosing IIH [25]. It predominantly occurs bilaterally and, with increasing severity of the papilledema, the odds ratio of poor visual outcomes rises [26]. All but one of our patients (97.9%) had papilledema which is higher than reported in a Turkish cohort (71%), but comparable to cohorts from Morocco (97%), Kuwait (99.3%) or India (100%) [9, 13–14]. Evaluation of the optic nerve function is best accomplished by combining the outcome of the best corrected visual acuity, visual field, contrast sensitivity testing and color vision [27]. Of these modalities, we were able to assess visual acuity and visual fields. Most eyes had normal to mildly impaired vision, but concerningly, 18 eyes (19.1%) had at least moderately impaired vision or worse, with 10 eyes showing either profound

vision loss or blindness. This is higher than in the IIHTT (9%) or some other, smaller cohorts and may reflect reduced awareness of this condition [11, 28]. Data from the United States have shown that black IIH patients are more likely to have severe visual loss [29], but this occurred equally in our patients irrespective of ethnicity. Most patients with IIH (> 90%) have defects in the visual field of at least one eye [30]. We identified temporal wedge scotomas in 22 eyes (26.2%) as the most common finding, similar to 23% in a study from the United States that looked particularly into peripheral defects [31]. In the IIHTT, partial arcuate defects and enlarged blind spots were seen in 31.5% of patients and we found central or centrocecal scotoma in 20.2% as the second and arcuate scotoma in 13.1% as the third most common pathology [32].

Imaging findings in IIH include tortuosity of the optic nerve, peri-optic subarachnoid space dilatation, flattening of the posterior globe, slit-like ventricles, empty or partial empty sella, posterior displacement of the pituitary stalk, and transverse sinus narrowing [33–35]. MRI studies are considered more accurate to identify these features, as was also seen in our patients, where almost 80% of MRIs demonstrated IIH-related findings compared to 63% of CT scans. On MRI, optic nerve abnormalities were the most common findings in our patients, with tortuosity of the optic nerve and dilated optic nerve sheath in 80% and 63% respectively, comparing well to a recent study from India [33]. Other studies have shown lower frequencies of this finding, ranging from 40% to 60% [34, 35]. In the study from India, posterior scleral flattening was the second most common finding (80%), which was reported in 58% of our patients. Partial empty sella is a well-known imaging feature of IIH, but was the least specific sign in the above-mentioned study (77%) and we observed this in 63% of the patients on MRI and 28% on CT [33]. The importance of transverse sinus narrowing in IIH (47% on MRI and 14% on CT in our patients) is currently still unclear, with some authors suggesting this as a causative or contributing factor to the development of the disorder. Follow-up MRI studies in our patients with this sign when symptoms have resolved, would thus be of value.

The main treatment goals are preservation of visual function and reduction of symptoms [11]. All patients received a combination of medical therapy and lifestyle intervention. Medical therapy with acetazolamide, topiramate or a combination was administered according to current guidelines [36, 37] without treatment-related complications.

At discharge, the majority of patients reported clear improvement of symptoms, while about one in five still had headache or other symptoms. Unfortunately, four eyes remained permanently blind. Although a continuous decline in the number of patients with persistent headache was noted at the three-month (13%) and six-month follow-up (8%), not all symptoms resolved. The persistence of headache in patients with IIH despite appropriate treatment and improvement of visual function and papilledema is well documented and may represent other headache disorders in these mostly young, female cohorts [38]. In a long-term follow-up study, chronic headache was still present in 67% of patients; this headache, however, was heterogenic and not related to relapses of the IIH [39].

The retrospective nature of our study, the relatively small number of patients and the missing data on neuroimaging and perimetry after the treatment, limit our findings and a prospective well-planned study, preferably including patients from all academic hospitals in South Africa, may contribute more data in the future.

In conclusion, the clinical presentation of our patients was comparable to other international studies, showing that IIH is a disorder prevalent in young obese females. We observed a higher proportion of older patients, but even in those IIH was related to severe obesity. Visual examinations and results of brain imaging in our patients are also similar to the findings of other research centres. IIH patients living with HIV did not differ in presentation, obesity rates or neuroimaging findings from non-HIV patients. In our setting, it is disconcerting that patients still lose vision due to a treatable condition and awareness of IIH should be raised.

Funding

The authors have nothing to report.

Ethics Statement

Ethical clearance from the University of Pretoria (Research Ethics Committee of Faculty of Health Science Number 73/2024) and from the National Health Research Database (GP-202410-012) was obtained.

Consent

The need for written consent was waived given the retrospective nature of our study. All data was obtained during routine clinical practice.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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