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### RESEARCH ARTICLE

#### IDIOPATHIC INTRACRANIAL HYPERTENSION IN UNIVERSITY HOSPITAL IN SAUDI ARABIA, RETROSPECTIVE STUDY

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#### Abstract

**Background:** Idiopathic intracranial hypertension (IIH) is one of headache syndromes that is female predominate and associated with increase intracranial pressure without obvious etiology, it has variable clinical presentation, and it needs high index of suspicion to reach diagnosis even with presence of well-established diagnostic criteria. Visual symptoms, which range from visual obscuration to blindness significantly, affect the outcome of this disease. Unfortunately, there is limited literature about IHH in Middle East and in Saudi Arabia in particular. In this retrospective study, we try to shed the light on pseudo-tumor cerebri in university hospital in Saudi Arabia.

**Methodology:** This is a retrospective study conducted among 105 patients with IHH admitted to the university hospital in Saudi Arabia. Data on age, gender, as well as about symptoms, obesity, medication and surgeries, and CT/MRI results was collected.

**Results:** The mean age of patients was 37.72 years old with standard deviation of 13.48 where 96.2 % of patients were females. Headache is the more common symptom presented by 96.2 % of patients followed with blurred vision and papilledema (85.7 %) and over weight (77.1 %). Considering medications taken by patients because of IHH, we found that main medications was Diamox which prescribed to 96.2 % with mean dose of 942.3 mg. Regarding surgical intervention, 4.8 % had a surgery of VP-shunt and 1.9 % had optic nerve fenestration

**Conclusion:** We concluded that IHH incidence is higher among young women with higher body weight and associated with the use of hormonal contraceptives. The main symptoms of IHH are headache with papilledema and visual disturbances. Acetazolamide is the most common prescribed medication for IHH patients while 6.6 % of patients need surgical procedures.

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**Introduction:-**

Idiopathic intracranial hypertension is one of headache syndromes that is more prevalent in obese women during childbearing age. Initially, it was referred as Pseudo-tumor Cerebri (1904) and it was not well understood until 1940, when understanding of this condition was started [1]. It is diagnosed by exclusion of other etiologies that can increase intracranial pressure with the guidance of Dandy criteria which consists of 5 parameters: (1) awake and alert patient; (2) symptoms and signs of increased intracranial pressure; (3) absence of focal signs on neurologic examination (although sixth and seventh nerve palsies are permitted); (4) normal diagnostic studies (i.e., neuroimaging and CSF evaluation), except for evidence of increased intracranial pressure (i.e., a CSF opening pressure greater than 20 cm H<sub>2</sub>O with (5) no other etiology for increased intracranial pressure identified [2].

Epidemiologically, female predominant disease especially obese women in childbearing age, the incidence in this group around 12–20 per 100 000 people per year worldwide but only 0.5–2 per 100 000 people per year in the general population [3–5]. In children and males, there are few data about the incidence in these two groups. The annual incidence of IIH in children and adolescents (aged 1 to 16 years) was 0.71 per 100,000, this increased to 4.18 per 100,000 in obese males aged 12 to 15 years [6].

There are several theories behind the pathogenesis of IIH and no single mechanism can solely explain its pathogenesis. These mechanisms are related to CSF dynamics and venous sinus pressure, with contribution of other factors such as weight and hormonal factors. In CSF dynamics, it is either hypersecretion or decrease absorption due to outflow obstruction. The first theory was not supported by the advanced neuroimaging modalities such as MRI [7, 8]. CSF drainage and absorption is through arachnoid granulation and lymphatic system in mammals [9, 10]. The theory of reduced CSF absorption is supported by findings from isotope infusion studies showing a delay in clearance in patients with idiopathic intracranial hypertension [8, 11]. Venous sinus pressure increases in case of stenosis that is more common in transverse sinus. (12) In one study, the degree of stenosis was not related to clinical outcome or to CSF pressure in patients with venous sinus stenosis [12].

The most common presenting symptoms are headache transient visual obscurations, and pulsatile tinnitus. 84% of patients reported headache that is associated with neck pain or radicular pain. This headache can have the features of migraine or tension headache [13–15]. Visual obscurations (TVOs) occur in about 68% of patients with IIH [13,16]. These obscurations a partial or complete loss of vision that lasts for several seconds, followed by a rapid recovery of vision back to baseline precipitated by postural changes or Valsalva-like maneuvers.

During the examination of these patient papilledema is the most common and important sign in IIH, bilateral and symmetric, although occasional patients have highly asymmetric papilledema [17,18]. The severity of papilledema can be graded based on the appearance of the optic disc using the modified Frisén scale. On the other hand, there is controversial entity is known as IIH without papilledema [19,20]. Where the anatomic compartmentalization of the subarachnoid space around the optic nerve stopping the CSF pressure gradient from reaching the retrolaminar portion of the optic nerve [21]. In this condition, opening pressure will be the gold standard of diagnosis. To confirm diagnosis of IIH, Brain images such as CT and MRI to rule out secondary causes of increase intracranial pressure, and there are couple of signs that indicate increase intracranial pressure such as an empty Sella turcica. Dilation and increased tortuosity of the optic nerve sheaths may be seen as well as posterior globe flattening [22]. Due to the significant overlap between IIH and cerebral venous sinus thrombosis (CVST) and a sinus stenosis was assumed to a factor in IIH pathology, MRV or CTV is part of the work up of these patients. The second step is CSF studies via lumbar puncture that has diagnostic and therapeutic role in IIH. Opening pressure is of great value in IIH without papilledema. Other diagnostic modalities include OCT (optical coherence tomography) to measure retinal nerve fiber layer thickness that must be interpreted with caution especially if edema is present [23].

The pillar of IIH management, is to preserve visual function and alleviate symptoms especially headache. Weight reduction is one of first initial steps in management of IIH (reduce 6-10%) of weight is adequate to induce remission in most patients with IIH symptoms [24]. In 2014, Idiopathic Intracranial Hypertension Treatment Trial was a double-blinded randomized controlled trial of diet plus placebo versus diet plus maximally tolerated acetazolamide. In acetazolamide group, there was statistically significant improvements in mean deviation, papilledema grade, symptoms, and quality of life [25].

Acetazolamide is well-tolerated medication with few side effects, the commonest among them are, paresthesia, dyspepsia, nausea, vomiting, and diarrhea [26]. However, there are several risk factors for treatment failure that

include, male sex, higher papilledema grade (ie, grades III–V), decreased visual acuity at presentation, greater than 30 transient visual obscurations per month, and peri-papillary retinal nerve fiber layer hemorrhages at presentation. Unfortunately, there is limited literature about IHH in Middle East and in Saudi Arabia in particular. In this retrospective study, we try to shed the light on pseudo-tumor cerebri in university hospital in Saudi Arabia.

### Methodology:-

This is a retrospective study, which was conducted among patients with IHH admitted to general university hospital in Saudi Arabia in the period between 2013 and 2018. Sample size of the study is 105. We collected data about age, gender, as well as about symptoms, obesity, medication and surgeries, and CT/MRI results. Inclusion criteria include patients with IHH and has completing profile, both gender and any age. After collecting the data, MS Excel was used for data entry while SPSS V 23 was used for data analysis. Frequency and percent were used for describing categorical variables while mean and standard deviation were used to describe ongoing variables. T-test and chi-test were used for determine difference and association between variables. P value lower than 0.05 was used to indicate the significance of relation or difference. The study had been conducted after having ethical approval from the hospital. No name of patients had been collected, and all data was used for the purpose of this study and will not be published as raw material.

**Table 1:-** Distribution of patients over age and gender categories.

Age	Mean	37.72	
	Standard deviation	13.48	
	Min.	5	
	Max.	71	
Gender	Male	4	3.8
	Female	101	96.2

### Results:-

In this study, we collected data related with 105 patients with IHH. The mean age of patients was 37.72 years old with standard deviation of 13.48 where 96.2 % of patients were females (Table 1).

Moreover, we found that headache is the more common symptom presented by 96.2 % of patients followed with blurred vision and papilledema (85.7 %) and over weight (77.1 %). Diplopia and tinnitus were presented in 44.8 % and 36.2 % of patients respectively (Figure 1).

**Table 2:-** The results of CT-CTV/MRI-MRV finding .

	Yes	No	NA
	Count	Count	Count
Slit Ventricles	16 (15.23%)	83 (79.07%)	6 (5.7 %)
Empty Sella	61 (58.1%)	38 (36.2 %)	6 (5.7 %)
Tortuous optic nerves	53 (50.4%)	46 (43.9 %)	6 (5.7 %)

**Table 3:-** Medication and doses taken be patients .

		Count	Column N %	Mean dose	Standard deviation
Diamox	Yes	101	96.2%	942.3	457.4
	No	4	3.8%		
Amitriptyline	Yes	26	24.8%	19.42	11.6
	No	79	75.2%		
Topamax	Yes	21	20.0%	57.62	44.23
	No	84	80.0%		

Moreover, we found that 5.7 % of patients did not have data about having CT-CTV/MRI-MRV. Slit ventricles were found in 15.23 % of patients while empty Sella was found in 58.1 % of them and tortuous optic nerves were presented in 50.4 % of patients (Table 2).

Considering medications taken by patients because of IIH, we found that main medications was Diamox which prescribed to 96.2 % with mean dose of 942.3 mg. moreover, amitriptyline was prescribed to 24.8 % of patients with mean dose of 19.42 mg while Topamax was taken by 20 % of patients with mean dose of 57.62 mg (Table 3)

Considering OP, 63.8 % of patients had been tested for OP with mean OP of  $95.3 \pm 148$  cm/h25. Moreover, DSA was done in 6.7 % of patients and was not remarkable in all patients. Autoimmune tests was negative in 19 % of patients and 17.1 % were positive who all were positive with ANA, 17.6 % of positive patients had RF and 5.9 % were positive with AntiTG. Regarding surgical intervention, 4.8 % had a surgery of VP-shunt and 1.9 % had optic nerve fenestration (Table 4).

**Table 4:-** The results of some conducted tests.

		Count	Column N %
OP	Not done	38	36.2%
	Conducted	67	63.8 %
DSA	Not done	98	93.3%
	Unremarkable	7	6.7%
Auto-immune work up	Not conducted	67	63.8%
	Negative	20	19.0%
	Positive	18	17.1%
VP-shunt	Yes	5	4.8%
	No	100	95.2%
optic nerve fenestration	Yes	2	1.9%
	No	103	98.1%

### Discussion:-

The distribution of IIH seems to be widespread with an approximate incidence of 1 to 3/100000 person/years [27]. In this study, we included 105 patients with IIH with mean age of 37.7 years old ranged between 5 and 71 years. Our mean of age was higher than that reported by Merle H who reported mean age of  $30.5 \pm 6.3$  years (range, 20 to 42 years) [28], study of Chagot C who reported mean age of  $33 \pm 12$  years old [29], study of Ma Z, who reported mean age of 36 years old [30] and study of Martin Y who reported a mean age of IIH of 35.38 years old [31]. It is known that IIH is more prevalent among women than males [32] which is consist with our results where 96.2 % of IIH patients were females and this was in agreement with previous studies [28–31].

Considering symptoms of IIH represented in patients in our study, headache was the main symptom occurred in 96.2 % of patients followed with blurred vision and papilledema (85.7 %) and over weight (77.1 %). Headache is main symptom of IIH which is reported in different studies [33,34]. The high prevalent of obesity among IIH patients was reported by other studies including study of Merle H [28] demonstrating the relationship between IIH and obesity. High incidence rates of IIH in Saudi Arabia [4] are probably related to a high prevalence of obesity in these countries. In the United States (Iowa), the incidence of IIH increases with obesity and is consistently higher in obese women aged 20 to 44 years (19.3 per 100,000) than in the general population (0.9 per 100,000) [5]. Improvement of IIH by eating a low-calorie diet alone is a striking finding of a positive association between the disease and obesity [35]. Moreover, in study of Chagot C, papilledema and headache were the main symptoms related to IIH [29], and similar results found in the study of Merle H [28]. Papilledema is the most specific sign of intracranial hypertension and it can be observed during the evaluation of the fundus oculi. It is an optic disc swollen due to the raised pressure exerted on the optic nerves, causing an impaired axoplasmic flow [36]. However, we have to keep in mind that there are cases of IIH patients with no papilledema in the literature [37,38]

Patients suffering from chronic headache and not presenting papilledema at the evaluation of the fundus oculi are more likely to be misdiagnosed, since the absence of the typical sign could lead not to consider the possibility of IIH. Neuroradiological signs assume a major significance in these cases, since they may suggest, but not define, the diagnosis of IIH if papilledema or the sixth nerve palsy are absent, according to Friedman criteria [39]. In our study, neurodiology was conducted in most patients with IIH. An empty Sella, best observed in T1 sagittal magnetic resonance (MR) sequences, can be a suggestive sign of IIH, with a sensitivity of 65% and a specificity of 95.3% according to Maralani and coworkers [40]. In our study, empty Sella was observed in 58.1 % of patients.

The most common and rapidly effective treatment option is acetazolamide. In our study, Diamox (Acetazolamide) is the most common medications taken by almost all patients (96.2 %) with doses of 942 mg daily. In study of Martin Y, 90 % of patients had been treated with acetazolamide with dose between 750 and 1500 mg daily [31] and similar results were reported by Killer H [41] and Corbett J [42].

Among the 105 patients admitted with signs of IIH, 7 (6.6%) needed more aggressive treatments where 4.8 % of patients needed VP-Shunt and 1.9 % needed optic nerve fenestration. This is similar to results of Martin Y [31].

Our study included some limitations. The main one is due to its retrospective nature and the amount of missing data. Moreover, some data was missed including success rate of both medical and surgical procedures as well as affected eye. Therefore, our findings will need to be confirmed in multi-centric prospective studies

We concluded that IIH incidence is higher among young women with higher body weight and associated with the use of hormonal contraceptives. The main symptoms of IIH are headache with papilledema and visual disturbances. Acetazolamide is the most common prescribed medication for IIH patients while 6.6 % of patients need surgical procedures.

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