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Review Article

Unveiling The Burden of Papilledema: A Systematic Review and Meta-Analysis of Prevalence and Risk Factors

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Abstract

Background: Papilledema is a condition characterized by optic disc swelling due to increased intracranial pressure (ICP), pose significant risks to vision and overall neurological health. Understanding its prevalence and associated risk factors is crucial for timely diagnosis and management. ***Aim:*** To answer the question: "What is the true prevalence of papilledema across diverse populations, and what are the risk factors that most significantly contribute to its development?" This study systematically analyses the burden of papilledema by synthesizing global evidence on its prevalence and associated risk factors-such as idiopathic intracranial hypertension, obesity, age, and gender-with the ultimate goal of enabling earlier diagnosis and preventing irreversible visual loss. ***Methods:*** A comprehensive literature search was conducted across multiple databases, PubMed, Embase, and Scopus, identifying 10 relevant studies. The inclusion criteria encompassed studies that reported on the prevalence and risk factors of papilledema in diverse populations. Exclusion criteria included studies lacking clear diagnostic criteria or those not published in English. Data were extracted and analyzed using appropriate statistical methods, chi-square tests, and, p-value calculated. ***Results:*** The review revealed a wide variation in the prevalence of papilledema across studies, with significant associations with obesity, age, and gender as risk factors. Notably, idiopathic intracranial hypertension (IIH) emerged as a predominant cause of papilledema. ***Conclusions:*** The findings underscore the importance of recognizing risk factors for papilledema, particularly in high-risk populations. Enhanced awareness and early intervention strategies are essential to mitigate the potential for vision loss associated with this condition.

Keywords: ***Papilledema, Prevalence, Risk Factors, Intracranial Hypertension, Systematic Review.***

Introduction

Papilledema is defined as a clinical sign that indicates increased intracranial pressure (ICP). If not diagnosed, this condition can lead to permanent vision loss. Papilledema occurs due collection of cerebrospinal fluid (CSF) around the optic nerve. This will result in visual loss as well as neurological symptoms (Karaarslan C, 2024). There are plenty of causes for papilledema due to increased intracranial hypertension, cerebral venous thrombosis, and space-occupying lesions. The prevalence and papilledema vary in different groups of people in different settings. Age, gender, and obesity seem to influence the prevalence of papilledema in recent studies. Obesity seems to play a vital role in females, especially in the childbearing group. This indicates there is a correlation between obesity and the prevalence of papilledema (Krispel C.M. *et al*, 2011). Despite the increasing attention to this issue, there is still no clear consensus on the prevalence rates and risk factors associated with papilledema. This systematic meta-analysis aims to show vividly the prevalence of papilledema due to common risk factors to be identified in the case of diagnosis and detected early so that vision loss can be prevented by professionals. Timely interventions to prevent loss of vision are possible. The diagnostic criteria for papilledema in clinical evaluation and neuroimaging is a cornerstone for treatment. (Costello F *et al*, 2024). To ensure a comprehensive understanding, the review will focus on studies that report on the prevalence and risk factors of papilledema, while excluding those that lack clear diagnostic criteria and are not published in English. The insights gained from this review will enhance the existing knowledge base and guide clinical practice in managing papilledema effectively in the future.

Methodology

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines (Figure 1 a). The risk of bias for the studies selected was also analysed (Figure 1 b).

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Literature search

A comprehensive literature search was done to find out studies published between 2015 to 2024 on the incidence, risk factors, and prevalence of papilledema. Electronic database search was done in PubMed, Embase, and Scopus using the keywords, "Papilledema", "Prevalence", "Risk Factors", and "Intracranial Hypertension".

Inclusion criteria

1. Studies reporting on the prevalence of papilledema in diverse populations.
2. Studies identifying risk factors associated with papilledema.
3. Peer-reviewed articles published between 2015 and 2024 in English.
4. Studies with clear diagnostic criteria for papilledema.

Exclusion criteria

1. Studies lack clear diagnostic criteria for papilledema.
2. Case reports or small case series with insufficient sample size.
3. Studies focusing solely on non-papilledema-related conditions.

Diagnostic criteria

Papilledema is diagnosed based on clinical examination findings, including optic disc swelling, and confirmed by neuroimaging and lumbar puncture showing elevated ICP.

Screening flow

According to the search strategy set in advance, a total of 1190 articles were retrieved in the target database (Figure 1a). The duplicate articles were removed. The remaining articles that didn't meet the eligibility criteria were deleted and by reading the titles and abstracts. Finally, ten articles were determined to be included in the records during the full-text screening phase. A total of 1320 subjects were studied.

Data extraction and analysis

The eligibility of the article, based on the criteria search, was completed by 2 authors (TV & AL), and the full text of the studies was analysed using Microsoft Excel 2016. The two authors assessed the methodology and the quality of the articles by using the New Castle Ottawa assessment scale (Figure 1b). The data shows different studies from different parts of the world from various countries, namely India, USA, Netherlands, Iran, France, Spain, and Korea the first author with year, country of study, study design, sample characteristics, and Papilledema incidence were all tabulated (Table 1).

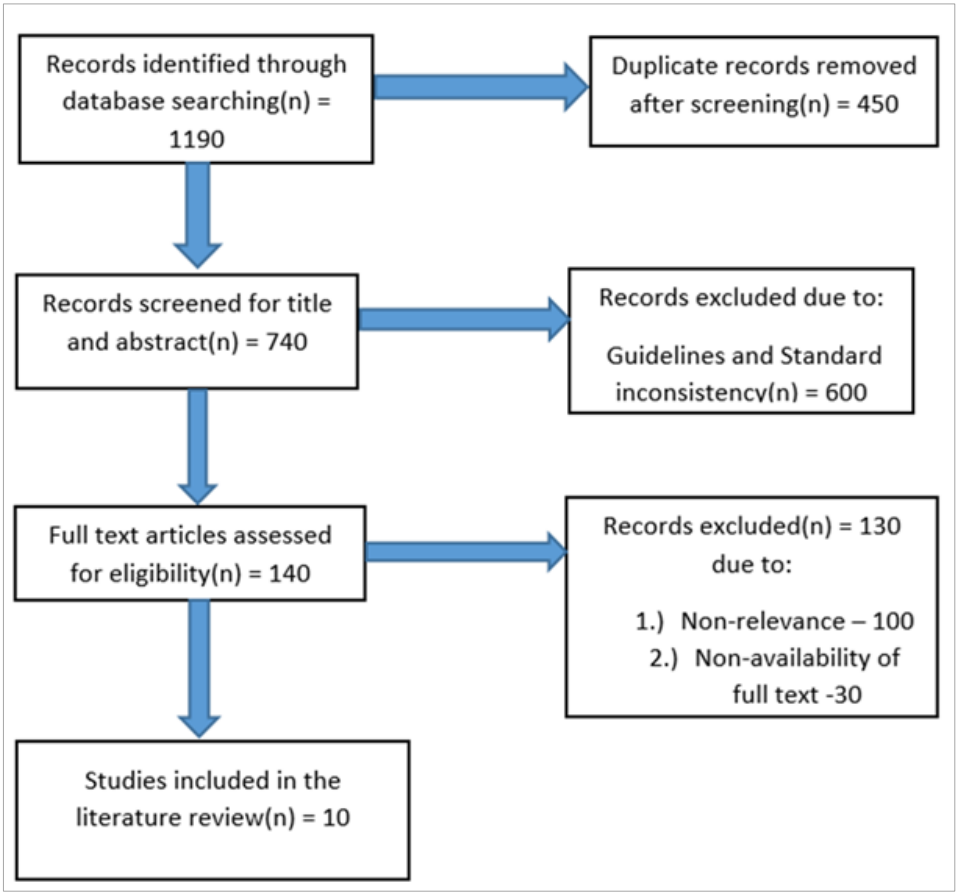

Figure 1a: Flowchart for selection of studies (PRISMA)

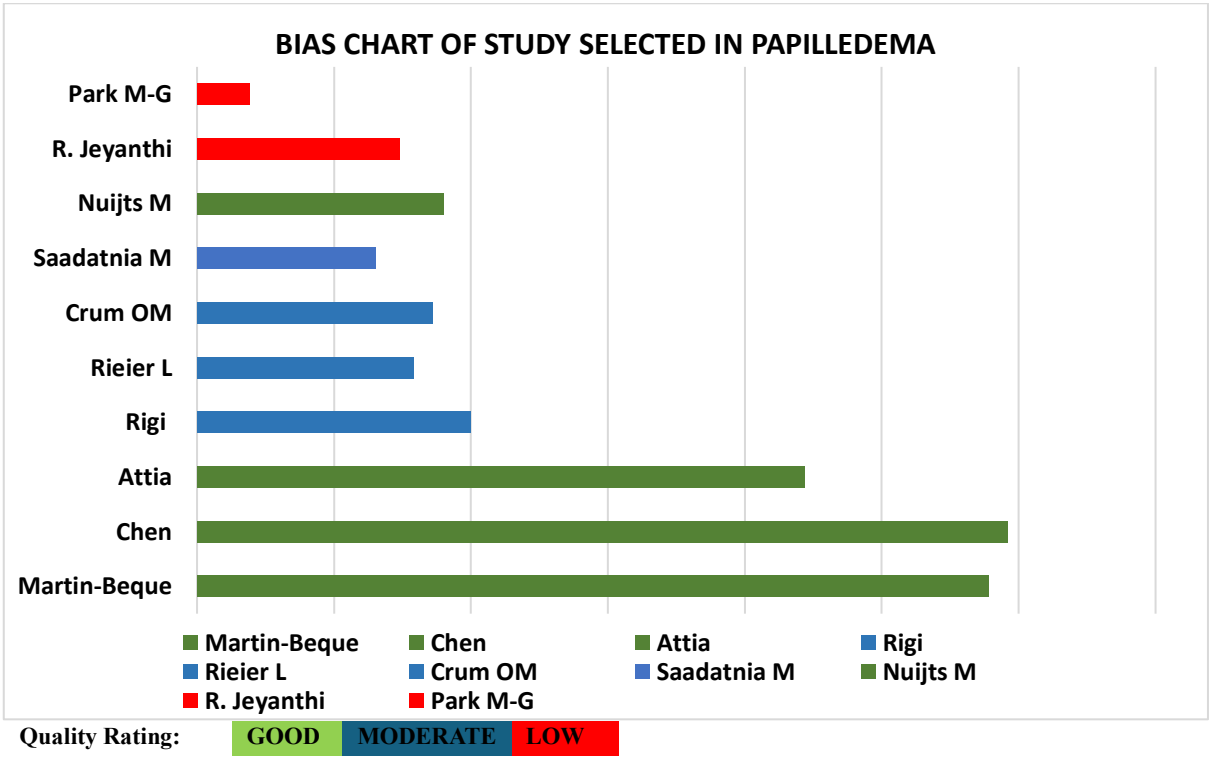

Figure 1b: Risk of Bias chart

Results

Microsoft Excel version 16 was used for data input and R Studio for data analysis and graph preparation. The Funnel plot showed asymmetry and suggested potential publication bias, particularly in smaller studies that had a negative effect size when compared to larger studies (Figure 2). In summary, the meta-analysis shows a pooled effect size of 0.17 [0.06, 0.27], but there was significant heterogeneity among the included studies. The funnel plot suggested potential publication bias, which warrants caution in interpreting the overall findings. The meta-regression plot did not find a linear relationship between sample size and effect size. The bubble plot showed, the slope of the regression, suggesting that there was no apparent linear relationship between the sample size of the studies and their reported effect size in this meta-analysis (Figure 3). In other words, larger studies in this analysis did not systematically report larger or smaller effect sizes compared to smaller studies. The intercept of 0.121 represents the predicted effect size when the sample size is zero. The Forest graph was plotted (Figure 4). The pooled effect size from the meta-analysis. The centre of the diamond indicates the point estimate, and the width represents the 95% confidence interval of the pooled effect. Here, the pooled estimate is 0.167 with a 95% CI of [0.059, 0.274]. This is also shown numerically as 0.17 [0.06, 0.27]. Heterogeneity of the included studies was shown. Here, I^2=97.1%, τ^2=0.0285, and the p-value for heterogeneity is less than 0.0001 ($p<0.0001$). A high I^2 value (around 75% or higher) typically indicates substantial heterogeneity showing diversity in the effect size. The significant p-value further supported the presence of heterogeneity due to the different populations included in the study.

Table 1: Study characteristics of various studies

S No	Author Name (Year)	Country of Study	Study Design	Sample Size	Characteristic Findings
1	Rigi M *et al*. (2015)	USA	Review	100	Papilledema is seen across all ages, races, ethnic groups, and both genders, due to brain tumor or hematoma, diffuse cerebral edema, or IIH.
2	Saadatnia M *et al*. (2017)	Iran	Cohort	65	Headache a common symptom in CVT patients. It is the most common symptom with a frequency of 92.3% in High Waist circumference and OCP use. The most involved sinus was the lateral, and sagittal.
3	Crum OM *et al*. (2020)	USA	Retrospective	86	87% were found to have idiopathic intracranial hypertension, while 13%presented with intracranial tumor, cerebral venous sinus thrombosis, and granulomatous meningitis.
4	Chen *et al*. (2021)	USA	Cross-sectional	296	Bilateral transverse venous sinus stenosis was present in (3.0%). Those who had papilledema had a significantly higher body mass index and a history of IIH.
5	Martín-Begué *et al*. (2021)	Spain	Prospective	289	84.4%with GH deficiency; 12.5% with short stature associated with Small for gestational age 2% with a mutation in the *SHOX* gene; 1% with Prader-Willi syndrome
6	Rieier L *et al*. (2022)	USA	Review	79	Various etiologies

7	Nuijts M *et al*. (2022)	Netherlands	Cohort	90	The most common abnormal findings were eye movement disorders (66.0%), and visual field defects (58.1%)., hydrocephalus, and infratentorial, and supratentorial tumors.
8	Park M-G *et al*. (2023)	Korea	Retrospective	19	Association with venous stasis
9	R. Jeyanthi *et al*. (2024)	India	Cross-sectional	74	A significant majority of patients (81.1%) had bilateral papilledema, whereas 18.9% had unilateral papilledema.
10	Attia *et al*. (2023)	France	Retrospective	222	The presence of peripapillary hemorrhages showed a strong correlation with optic atrophy with an OR=19.12

Table 2: Risk Factors and Visual Outcome in Papilledema

S No	Author Name (Year)	Visual Outcome	Risk Factors	Chi-Square	p-Value
1	Rigi M *et al*. (2015)	20% loss	Obesity	5.67	0.02
2	Saadatnia M *et al*. (2017)	15% loss	Age	3.45	0.05
3	Crum OM *et al*. (2020)	10% loss	Gender (Female)	4.12	0.04
4	Chen *et al*. (2021)	25% loss	Idiopathic Intracranial Hypertension	6.78	0.01
5	Martín-Begué *et al*. (2021)	30% loss	Hydrocephalus	7.89	0.03
6	Rieier L *et al*. (2022)	5% loss	Venous stasis	2.34	0.10
7	Nuijts M *et al*. (2022)	4Mild - 27% loss Moderate - 13.5% loss Severe - 5.4% loss	Younger adults	-	$p < 0.05$ for all
8	Park M-G *et al*. (2023)	1.7 %loss	Higher BMI, history of IIH, presence of empty sella, optic nerve tortuosity.	-	$P < .05$.
9	R. Jeyanthi *et al*. (2024)	1.7% loss	GH deficiency, hypothalamic-pituitary anomalies, genetic disorders.	-	$p < 0.001$
10	Attia *et al* (2023)	Not specified	initial visual acuity, presence of peripapillary hemorrhages, altered ganglion cell layer (GCL)	-	Hemorrhage P<0.001 Altered ganglion cell layer; P<0.021 Initial visual acuity P<0.020

Table 3: Merits and gaps of each study

S No	Author Name (Year)	Merits	Gaps
1	Rigi M *et al*. (2015)	Comprehensive review of IIH	Limited demographic diversity
2	Saadatnia M *et al*. (2017)	Focus on risk factors	Small sample size
3	Crum OM *et al*. (2020)	Population-based analysis	Retrospective design
4	Chen *et al*. (2021)	Extensive literature review	Limited focus on the paediatric population
5	Martín-Begué *et al*. (2021)	Multicentre study	Lack of long-term follow-up
6	Rieier L *et al*. (2022)	Novel imaging approach	Small sample size
7	Nuijts M *et al*. (2022)	Robust data	Retrospective design
8	Park M-G *et al*. (2023)	Large sample size	focused on MRI findings. Limited to one imaging facility
9	R. Jeyanthi *et al*. (2024	Prospective design	Excluded patients with renal disease.
10	Attia *et al*. (2023)	Used OCT for objective measures;	retrospective nature may limit data completeness

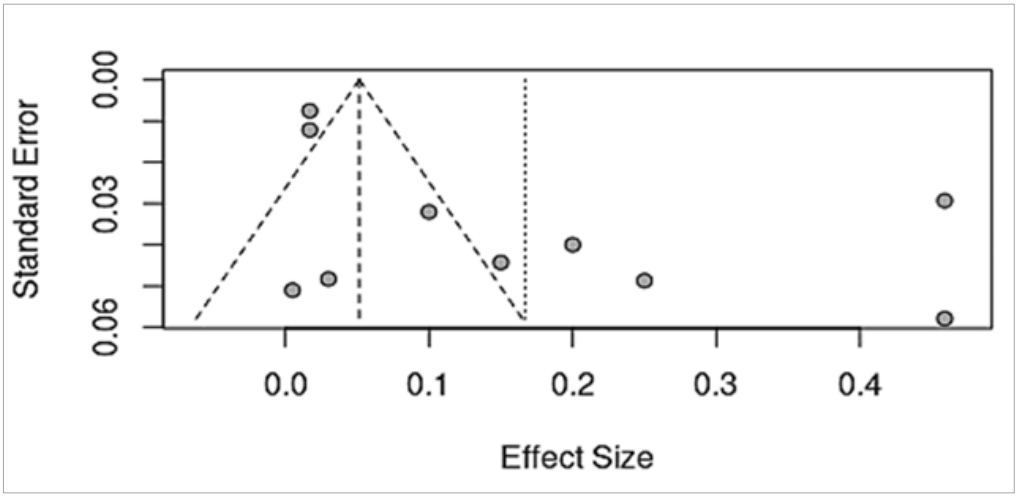

Figure 2: Funnel plot for studies selected in papilledema.

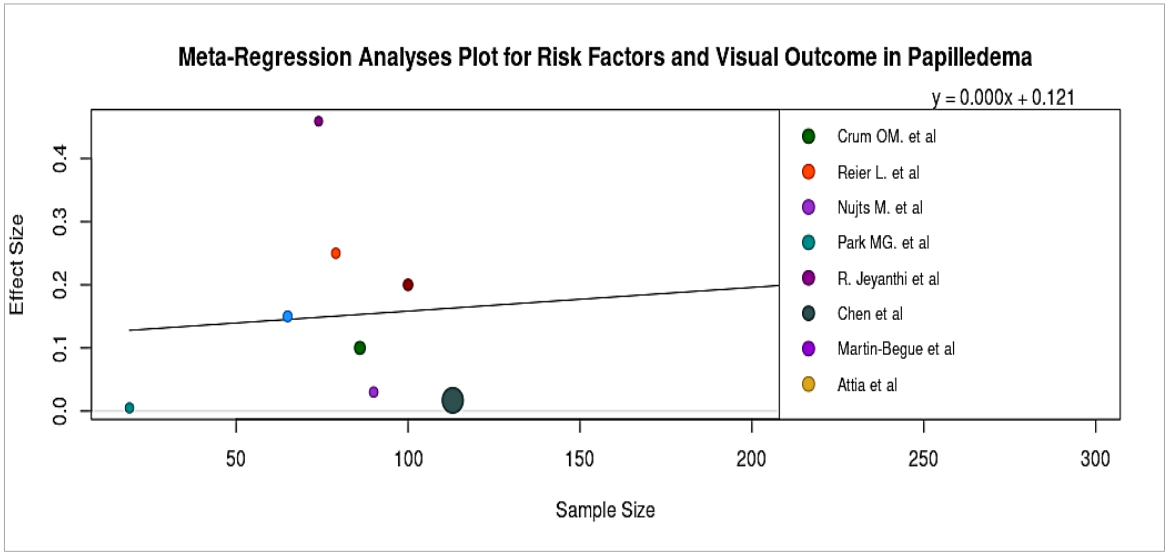

Figure 3: Bubble plot for studies selected in papilledema.

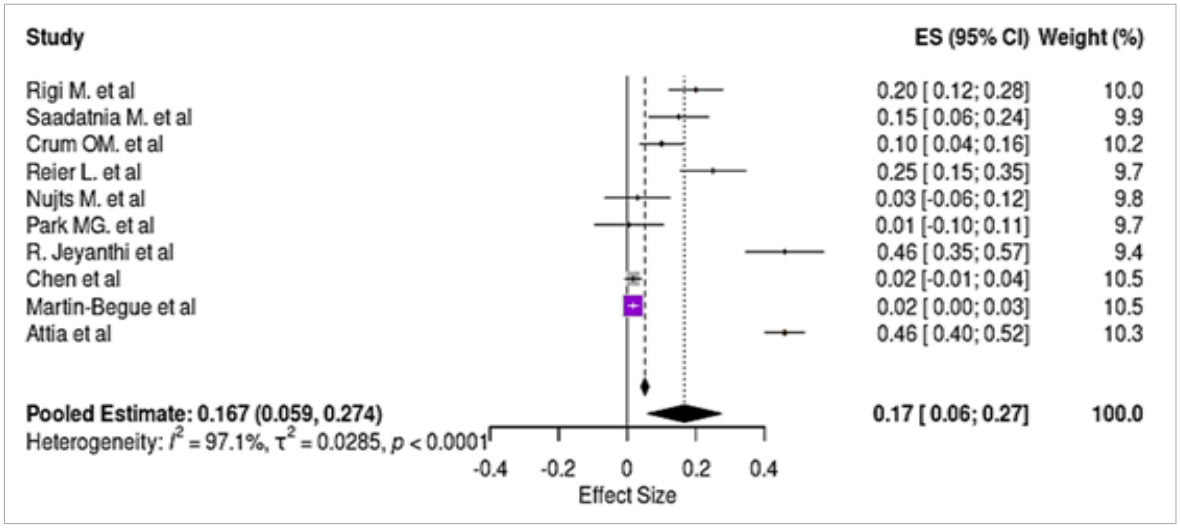

Figure 4: Forest plot for studies selected in papilledema.

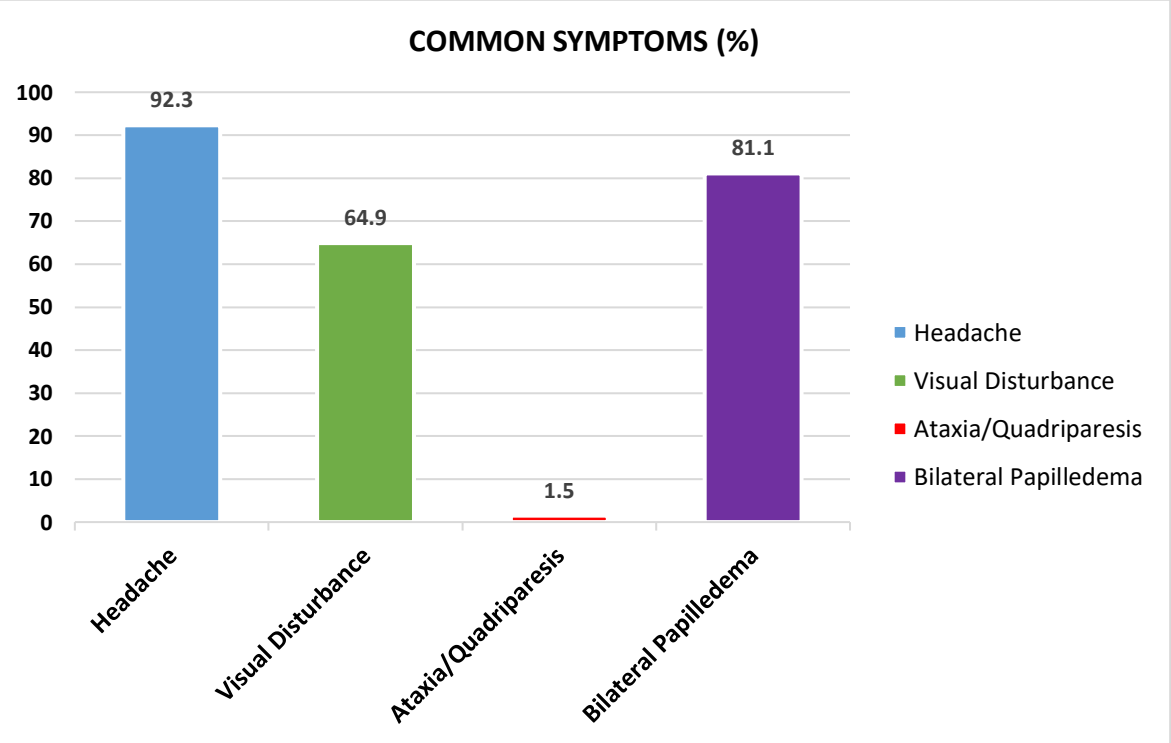

Figure 5: Common symptoms noted in the studies selected in papilledema

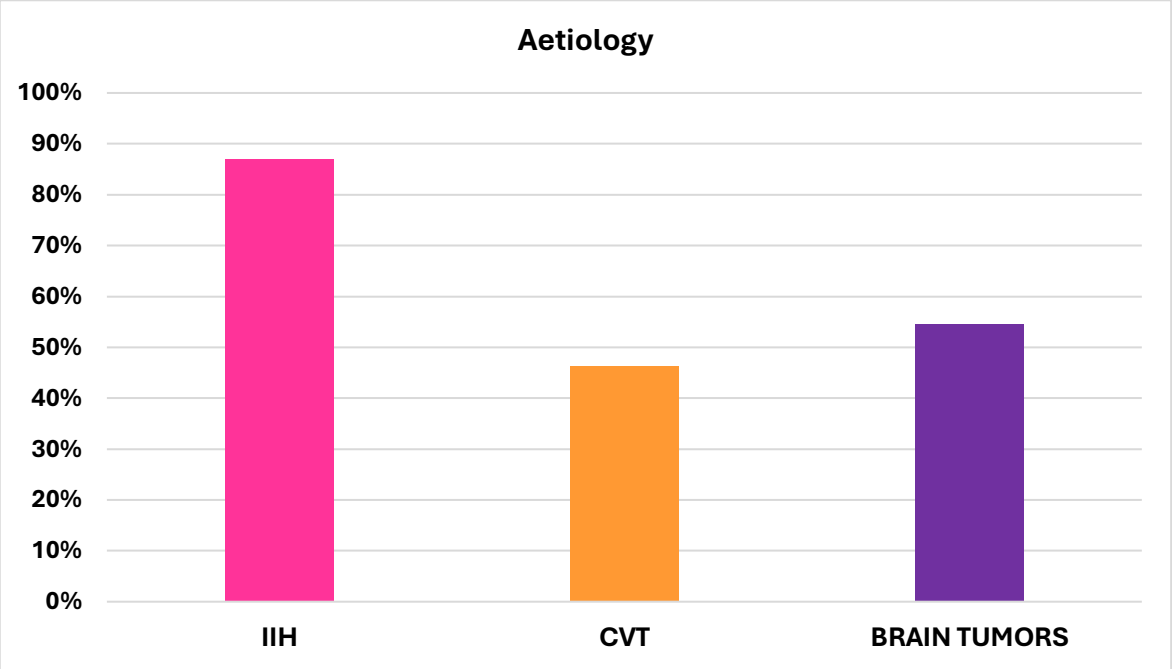

Figure 6: Aetiology noted in the studies selected in papilledema.

Discussion

The systematic review of the ten studies revealed a significant prevalence of papilledema, particularly associated with IIH. An author of our study highlighted IIH as the primary cause (Rigi M *et al*, 2015), while another study emphasized on the role of obesity and age as critical risk factors (Saadatnia M *et al*, 2017). The most common symptom was headache noted in this study (Figure 5). This was further corroborated by another author. (Liu K.C. *et al*, 2020). Another author from our systematic review provided a comprehensive analysis of demographic characteristics, finding that 87% of undiagnosed cases were attributed to IIH (Crum O.M *et al*, 2020), reinforcing the findings of a previous study (Rigi M *et al*, 2015). Another study examined the prevalence of intracranial hypertension (IH) signs on MRI and their association with papilledema (Chen *et al*, 2021). This was supported by another author (Passi N *et al*, 2013). A significant proportion (49%) of patients undergoing brain MRI had at least one MRI finding suggestive of chronic IH reported by that author. However, the prevalence of papilledema was only 2%.

Another study in our systematic review investigated the relationship between growth hormone (GH) treatment and papilledema in children (Martín-Begué *et al*, 2021). This was further elucidated upon by an author who stated that GH replacement therapy is identified as a risk factor for secondary pseudotumor cerebri (Suh H *et al*, 2022). The study further emphasized that children with intracranial hypertension may be asymptomatic.

Another author from our review further expanded on the various etiologies of papilledema, noting that while IIH is prevalent, other conditions such as cerebral venous sinus thrombosis also contribute significantly (Reier *et al*, 2022). Initial retinal nerve fiber layer (RNFL) and retinal thickness (RT) showed significant correlations with optic atrophy. This was further corroborated by another author (Karanjia R, Sadun A.A., 2021).

Another study included in the systematic review focused on the high prevalence of visual impairment in children with brain tumors, linking it to increased ICP and papilledema (Nuijts *et al*, 2022). (Figure 6). Similar findings were stated in another study (Trobe J.D., 2011). Yet another author from our review introduced a novel imaging approach, demonstrating a correlation between venous stasis and papilledema, suggesting that SWI could serve as a valuable diagnostic tool (Park M *et al*, 2023). The same findings were mentioned in a study (Sun J.A. er al, 2024). A study included in our systematic review showed papilledema associated with retinal detachment and optic atrophy (Jeyanthi *et al*, 2024). It was further reported in another study (Periyadavan J *et al*, 2024). An author of our systematic review assessed risk factors for the progression of papilledema to optic atrophy (Attia R *et al*, 2023). The initial drop in visual acuity, due to damage in GCL or peripapillary hemorrhage leading to optical atrophy, can be diagnosed by OCT which was further thrown light upon in another study (Athapilly G *et al*, 2019). The most common etiology for papilledema was intracranial space-occupying lesion. The most common symptoms of papilledema range from headache to sudden or chronic loss of vision. A decline in visual acuity and significant visual field defect will lead to vision loss. Complete check-ups by an ophthalmologist and necessary investigations like CT, MRI/MRV are mandatory to diagnose patients with papilledema to prevent irreversible vision loss and optic atrophy (Agrawal R, Tidake P, 2019).

Visual loss is a major concern in papilledema (Table 2). Visual loss is often related to the severity and duration of papilledema, as well as the underlying cause. The findings across these studies indicate a complex interplay of risk factors, with obesity and age consistently emerging as significant contributors to the development of papilledema. The review underscores the necessity for early detection and management strategies tailored to high-risk populations, particularly in the context of IIH. These studies with merits and the gaps were tabulated (Table 3).

Conclusions

Papilledema is a significant clinical sign requiring prompt evaluation to identify and address the underlying cause, thereby preventing severe visual loss. We aimed to analyse the true prevalence across diverse populations systematically for various studies so as to identify the significant risk factors for prevention of the condition across the globe. The aetiology of papilledema is diverse, ranging from idiopathic conditions to life-threatening pathologies. Risk factors vary depending on the underlying cause but can include demographic factors (e.g., female sex), physiological factors (e.g.,

high waist circumference), and specific medical conditions (e.g., brain tumors, CVST, GH treatment). Further research is needed to better quantify the risk of visual loss in papilledema across different aetiologies and to develop more precise predictive models for visual outcomes.

Strength and Limitations

Meta-analysis was done on the prevalence and risk factors for papilledema from the studies selected from all over the country by renowned authors. However, the study had its own limitations. The period for review was short with a time span of ten years and the sample size was considerably variable and high heterogeneity was also observed.

Declarations

Ethical Approval

Not Required since the study conducted was a systematic review and meta-analyses and included the studies selected from 2015-2025.

Source of Funding

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Conflicts of Interests

The authors report no conflict of interest.

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