*Review Article*

# Normal Pressure Hydrocephalus in the Elderly: A Narrative Review of Diagnostic Complexity, Biomarker Potential, and Surgical Outcomes

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**Abstract:** *Normal pressure hydrocephalus (NPH) is a reversible cause of dementia in older adults, characterized by the clinical triad of gait disturbance, cognitive decline, and urinary incontinence. Owing to overlapping symptoms and low cerebrospinal fluid (CSF) Aβ42 levels, NPH is frequently misdiagnosed as Alzheimer's or Parkinson's disease.* **Objective:** *To provide a comprehensive narrative review of the pathophysiology, diagnostic challenges, treatment options, and prognostic markers of NPH, with a particular focus on implications for low- and middle-income countries (LMICs).* **Methods:** *Relevant literature published between 2000 and 2025 was retrieved from PubMed, Scopus, and Google Scholar using the keywords "normal pressure hydrocephalus," "cerebrospinal fluid dynamics," "ventriculoperitoneal shunting," and "biomarkers." Both clinical and experimental studies addressing NPH's pathophysiology, diagnostic modalities, and treatment outcomes were reviewed, with emphasis on studies applicable to LMIC contexts such as Pakistan.* **Results:** *Evidence indicates that disrupted CSF circulation and ventriculomegaly underlie NPH, with diffusion tensor imaging and arterial spin-labelling MRI offering diagnostic refinement. However, limited access to advanced neuroimaging and cultural perceptions of symptoms as "normal aging" contribute to underdiagnosis in LMICs. Ventriculoperitoneal shunting, particularly with fixed-pressure devices, consistently improves gait performance, while cognitive and urinary outcomes are variable. Post-shunt changes in CSF biomarkers (Aβ42, tau) and serum markers (BDNF, TRPV4) demonstrate potential prognostic value. Functional imaging further correlates reduced cerebral blood flow with symptom severity.* **Conclusion:** *NPH remains an under-recognized yet treatable neurological disorder. Increasing awareness, developing simplified diagnostic approaches, and ensuring cost-effective treatment strategies are essential to optimizing patient outcomes, particularly in resource-constrained settings.*

**Keywords:** Normal Pressure Hydrocephalus, Elderly, Dementia, Ventriculoperitoneal Shunt, Gait Disturbance, Pakistan, Narrative Review

## Introduction

Normal pressure hydrocephalus (NPH) is a chronic neurological condition characterized by the accumulation of excessive cerebrospinal fluid (CSF) within the brain's ventricles, leading to ventriculomegaly without significantly elevated intracranial pressure. This disorder predominantly affects older adults, presenting with a clinical triad of gait disturbance, cognitive impairment, and urinary incontinence, commonly referred to as the Adams and Hakim triad (1). As global populations age, the prevalence of NPH is expected to increase, particularly among the Early identification and treatment are crucial (5). Diagnostic difficulties are, however, compounded by comorbidities that are mostly encountered in old age, as well as the absence of standard guidelines in limited-resource settings. The paper is part of a comprehensive review that discusses the pathophysiology, diagnostic measures, management, and associated problems of NPH in older adults, particularly in developing countries such as Pakistan, and aims to overcome these obstacles to enhance patient outcomes through appropriate Diagnosis and early treatment strategies. NPH management in elderly patients is not merely a medical issue; it is also a social and psychological concern. However, it is a societal issue as well, since an undiagnosed patient leads to disability, caregiver burden, and medical costs. The aging brain is a special case, as the condition may not be noticed for many years due to the subtlety of the associated symptoms, making early intervention even more challenging.

elderly, where it remains a significant yet underdiagnosed condition. The Pakistan demographic, within the LMIC, such as Pakistan, has an epidemic that is distinct due to the paucity of healthcare infrastructure and social thinking that overlooks the symptoms as a part of normal aging (2). The presence of neurodegenerative manifestations (including Alzheimer's disease (AD), Parkinson's disease (PD), and vascular dementia) overlapping with the symptomatic presentation of the disorder makes it difficult to diagnose and, as a result, it is often misdiagnosed or treatment occurs too late (3, 4). NPH is also unique in that it is one of the potentially reversible causes of dementia, so very few people are aware of it, and Early clinical suspicion is thus as important as the tools themselves for Diagnosis.

## Methodology

This article presents a literature narrative review of normal pressure hydrocephalus (NPH) in the aged population. An informal search was conducted using databases such as PubMed, Google Scholar, and ScienceDirect, with a focus on articles published between 2000 and 2025. They consisted of keywords related to normal pressure hydrocephalus, elderly hydrocephalus, VP shunt outcomes, and NPH Diagnosis. A selection of studies was conducted based on their relevance to clinical presentation, diagnostics, treatment outcomes, and challenges in low and middle-income countries. The new peer-reviewed publications,

systematic reviews, and clinical trials were preferably selected. There are also other references identified through backward citation tracking. This approach enabled the synthesis of the current state of knowledge in great detail and with adaptability, highlighting the most clinically relevant challenges and local barriers in treating NPH.

## What is NPH?
### Pathophysiology
NPH consists of compromised cerebrospinal fluid circulation that causes enlargement of the ventricles regardless of a normal or slightly increased intracranial pressure (1). The exact pathophysiological processes involved in NPH are not yet fully understood. However, recent findings indicate that this is a multifactorial disease involving defective CSF absorption, vascular disease, congenital abnormalities, and a genetic propensity (6). According to studies using electroencephalography (EEG), there is impaired activity in the occipital alpha rhythm, visual perception network, and self-referential network, which have been shown to exert their functions and lead to cognitive and gait disabilities in NPH patients (7). Additionally, the pathophysiology is complicated by the presence of vascular comorbidities, such as microangiopathy, as well as neurodegenerative changes, which are more common among the aged population (8). This combination of elements causes ventriculomegaly, which puts pressure on other parts of the brain, resulting in the triad of clinical symptoms.

### CSF Dynamics
The pathophysiology of NPH is centered on the dynamics of CSF flow and clearance. Their main parameters (resistance to CSF outflow (Rout), compliance) are the crucial predictors of responsiveness to such surgical interventions as shunting (1). These dynamics can be evaluated by measures such as continuous spinal drainage, which is typically conducted within three days; however, this method remains invasive and challenging to perform in elderly patients due to their frailty and comorbidities (1). Other diagnostic tests, although less invasive, such as the CSF tap test, where 40-50 mL of CSF is removed, are widely used to assess the possibility of shunt responsiveness. The test may be repeated on several consecutive days to increase its predictive validity; however, its application in patients with concomitant neurodegenerative disorders is limited (1, 9). Additional sophisticated techniques, such as lumboventricular perfusion, are highly accurate but require specialized expertise; therefore, they are not regularly useful (10).

### Classification: Idiopathic vs. Secondary
NPH can be defined as idiopathic (iNPH) and secondary. Idiopathic NPH does not have a known cause, whereas secondary NPH exists as a result of the damage caused by a head trauma, subarachnoid hemorrhage, or meningitis. The term idiopathic has been disputed, with newer studies showing that factors such as body mass index, age, sex, and vascular disease, among others, affect CSF pressure and, thus, are probably etiologically more complex (6). This has resulted in the suggestion that iNPH should be renamed Hakim syndrome, after the person who discovered it, to reflect its multifactorial characteristic and diminish the implication of a novel cause (6). Idiopathic and secondary NPH are distinct, and differentiating between the two is necessary because the underlying causes can determine which treatment to use and its outcome in secondary cases. Although a classification makes Diagnosis and treatment processes more efficient, it is essential to keep in mind that the range of symptoms and the dynamics of NPH development may vary significantly among individuals. In clinical practice, such a categorical division is not always relevant to the patient's condition, especially in older samples where comorbidities often overlap.

### Epidemiology
NPH accounts for approximately 6% of all dementia cases, making it a relatively rare but significant condition in the elderly (5). Studies report a mean age of onset between 71 and 78 years, with a higher prevalence in aging populations (2, 8, 11). No specific epidemiological data for Pakistan were provided in the reviewed studies, but global trends suggest an increasing burden in LMICs due to aging demographics and limited diagnostic resources (2). The lack of specialized care and awareness in such settings likely underestimates NPH prevalence, emphasizing the need for improved screening and diagnostic protocols.

### Clinical Triad & Presentation
The hallmark of NPH is its clinical triad of gait disturbance, urinary incontinence, and cognitive decline, often presenting sequentially with gait impairment as the earliest and most prominent feature (1). Gait disturbance, described as "magnetic" or hypokinetic, is characterized by short, shuffling steps, as if the patient's feet are "glued to the floor" (5). In mild iNPH, intermittent gait disturbance (IGD) manifests as a progressive decline in gait speed and step length during extended walking, as observed in the 6-minute walk test (6MWT), with significant improvement following CSF drainage (12). Urinary symptoms, including urgency, frequency, and incontinence during both day and night, are not as effectively responsive to treatment as gait issues (1, 5). The type of cognitive impairment usually consists of executive dysfunction, which is close to subcortical dementia, yet can resemble AD, complicating the process of differential Diagnosis (3). There are also situations when cognitive symptoms appear even before the motor deficit, which complicates the Diagnosis (3). These symptoms among the elderly are normally caused by normal aging or other neurodegenerative disorders such as AD or PD, which explains their underdiagnosis (4). Due to comorbidities, vascular disease, or AD pathology in particular, the issue of Diagnosis becomes more complicated and affects treatment outcome (13). A comprehensive clinical assessment, with an emphasis on the prevalence of gait disturbance and its responsiveness to CSF drainage, is key to the proper Diagnosis of NPH and the exclusion of imitative disorders. The triad may not be immediately apparent in most outpatient settings, and patients may initially present with only one or two symptoms. It becomes essential for clinicians to look beyond isolated complaints and consider NPH in the differential Diagnosis when any of the triad components are present — particularly if gait issues precede cognitive concerns. Over-reliance on typical presentations risks missing early-stage cases.

### Diagnostic Challenges
Diagnosing NPH in the elderly is fraught with challenges due to its symptomatic overlap with AD, PD, vascular dementia, and spinal stenosis (3, 4). Approximately 19% of patients with suspected NPH have concurrent AD pathology, which significantly reduces shunt responsiveness (14). Neuroimaging plays a pivotal role in Diagnosis, with MRI and CT used to assess ventriculomegaly. The Evans Index, measuring the ratio of ventricular width to skull diameter, and the corpus callosum angle on MRI help distinguish NPH from cerebral atrophy (1). CT findings, such as periventricular low density and expanded temporal horns, are strongly associated with shunt success (10). Novel 3-directional (3D) linear measures, such as the z-Evans Index and Brain-to-Ventricle Ratio (BVR), enhance diagnostic precision and predict CSF responsiveness (8). The CSF tap test, which involves the removal of 40-50 mL of CSF, is a standard diagnostic tool; however, its efficacy is reduced in patients with AD pathology, where only 18.2% show improvement, compared to 44.6% in NPH-only cases (14). Repeating the test over consecutive days or using external lumbar drainage (ELD) improves predictive accuracy, but this approach is less feasible in elderly patients due to its invasiveness (6). Misdiagnosis is common in the elderly due to the high prevalence of comorbidities, necessitating serial neuroimaging and careful clinical follow-up to confirm NPH and rule out other conditions (3). CSF biomarkers for AD, such as β-amyloid and tau proteins, can further aid in distinguishing NPH from neurodegenerative diseases (9). Moreover, the diagnostic journey is rarely straightforward. In elderly patients, overlapping pathologies can obscure the clinical picture, making it necessary to adopt a holistic approach that combines imaging, functional testing, and longitudinal assessment. Family input and cognitive scoring tools can also assist in tracking symptom progression when imaging results are ambiguous.

### Surgical Interventions
Ventriculoperitoneal (VP) shunting is the cornerstone treatment for NPH, diverting CSF from the ventricles to the peritoneal cavity to alleviate

symptoms (4). In developing countries, fixed-pressure gravitational shunts, such as the MIETKE GAV, provide a cost-effective alternative to programmable shunts, achieving an 81.3% improvement rate after initial or revision surgery (2). Programmable shunts allow for pressure adjustments but require frequent follow-up, which is often impractical in resource-limited settings due to cost and travel barriers (2). Patients with prominent gait disturbance or the full clinical triad are most likely to benefit from shunting, with neuroimaging findings like periventricular low density and a positive CSF tap test serving as strong predictors of success (1, 10). CSF biomarkers indicative of AD pathology also predict shunt responsiveness, with AD-like profiles associated with better outcomes (9). Younger patients, those with shorter symptom durations, and those without significant comorbidities tend to show superior outcomes (11, 16). Endoscopic third ventriculostomy (ETV) is rarely mentioned in the context of NPH, suggesting its limited applicability compared to VP shunting. Careful patient selection, guided by clinical and imaging predictors, is crucial for maximizing the benefits of surgical intervention while minimizing risks. Preoperative counseling plays a vital role, especially for elderly patients and their families, in setting realistic expectations regarding symptom relief and potential complications. Many patients believe that surgery will restore all functions completely, but explaining the variability of outcomes — particularly regarding cognition and bladder control — ensures better satisfaction and follow-up compliance.

## Post-Surgical Outcomes

VP shunting yields significant improvements in gait, with studies reporting a 23.2% enhancement in mobility scores at 1-year follow-up, often evident within 6 months (12, 16). Cognitive recovery is less consistent, with Mini-Mental State Examination (MMSE) scores showing significant improvement at 1 and 3 years, though to a lesser extent than gait (11). Urinary incontinence demonstrates the least improvement, often persisting post-surgery (1). Quality of life (QOL) metrics, including mobility, cognition, and social participation, improve significantly within 6 months and remain sustained at 1 year (16). However, shunt complications, such as infection, overdrainage, and chronic subdural collections, occur in 46.3% of cases, with higher revision rates in pediatric patients (15). Positive prognostic indicators include a typical NPH pattern on cisternography, CSF pressure greater than 100 mm, and frequent B-waves on overnight monitoring (10). Conversely, coexisting AD pathology, vascular disease, or prolonged preoperative symptoms reduce shunt success (11, 14). Factors such as male sex, smoking, and lower education level are associated with poorer long-term outcomes at 3 years (11). Regular postoperative monitoring is essential to manage complications and optimize recovery, particularly in the elderly with comorbidities. Importantly, post-operative care must extend beyond the hospital setting. Elderly patients recovering from shunt placement benefit from physical therapy, cognitive support, and home-based rehabilitation programs. Without such multidisciplinary follow-up, initial gains from surgery may plateau or decline over time, especially in those with frailty or social isolation.

## The Role of Diffusion Tensor Imaging in NPH Differential Diagnosis

The differentiation of NPH from overlapping conditions like Alzheimer's disease (AD) remains a diagnostic challenge, necessitating advanced imaging techniques. Diffusion tensor imaging (DTI) has emerged as a promising tool, as highlighted in the document, offering insights into white matter integrity that structural imaging alone cannot provide. It is demonstrated that the DTI of the corpus callosum, posterior limb of the internal capsule, hippocampus, and fornix, in conjunction with the Evans Index, is a potential MRI biomarker for distinguishing between NPH and AD, as well as other dementias (17). The given strategy will utilize microstructural alterations of brain tissue to indicate the level of damage caused by hydrocephalus. DTI may provide clinicians with an adequate suggestion for implementing applicable interventions by improving the process of differential Diagnosis; however, its particularity should be validated in various patient groups, including those in resource-poor areas, such as Pakistan.

## Exploring Novel CSF Dynamics and Biomarker Changes Post-Shunting

Understanding the dynamic changes in cerebrospinal fluid (CSF) biomarkers following ventriculoperitoneal (VP) shunting provides critical insights into NPH pathophysiology and treatment response. The document reveals that pre-shunt NPH exhibits low levels of Aβ42, total tau (t-tau), and phospho-tau (p-tau), mimicking AD, but these increase post-shunting due to enhanced interstitial fluid drainage (18, 19). Longitudinal studies show that while t-tau, p-tau, and neurogranin stabilize post-surgery, Aβ42 diverges based on AD pathology in brain biopsies, suggesting its utility as a prognostic marker (20). This decompression effect on the interstitial space and protein clearance offers a mechanistic explanation for misleading pre-shunt biomarkers, highlighting the need for post-shunt monitoring to refine Diagnosis and predict outcomes in elderly NPH patients.

## Barriers in Pakistan/Developing Countries

Managing NPH in developing countries, such as Pakistan, is hindered by multiple barriers. The scarcity of neurosurgeons limits access to specialized care, particularly in rural areas, where patients may need to travel long distances for Diagnosis and treatment (2). The absence of standardized geriatric protocols for NPH complicates identification, especially given the overlap with neurodegenerative conditions like AD and vascular dementia (2). Programmable shunts, due to the frequency of reprogramming, are expensive and logistically demanding, as patients in rural areas often face significant challenges in following up with routine appointments (2). An alternative approach is the use of fixed-pressure gravitational shunts, such as the MIETKE GAV, which has demonstrated an 81.3 percent improvement rate in patients treated with it (2). The cultural stigma that is used to refer to the NPH, such as referring to its symptoms as part of normal effects of old age, consequently delays the Diagnosis and treatment, especially where primary care provider awareness is low (2). Such misrepresentation is aggravated by the fact that access to advanced means of Diagnosis, such as MRI or CT, which are fundamental towards accurate Diagnosis, is never available. The improvement of these barriers should involve the provision of cost-effective solutions to treat the condition, as well as increased training of healthcare workers, and campaigns on health awareness that will educate the population about NPH as a distinct disease, rather than a normal part of aging. Additionally, due to the lack of awareness among frontline medical staff, such as general practitioners and rural medical officers, there is a high level of misdiagnosis or outright rejection of patients. One way to fill this diagnostic gap and ensure better long-term results is to utilize continuing medical education and rural health campaign programs, including NPH awareness initiatives.

## Implications of Cerebral Blood Flow and Oxygen Metabolism in NPH

Functional imaging, which measures cerebral blood flow (CBF) and oxygen metabolism, is gaining prominence in the prognosis of NPH. The document highlights that arterial spin-labeling (ASL) MRI indicates a decrease in perfusion in the periventricular white matter, lentiform nucleus, and thalamus associated with cognitive decline (21). In contrast, oxygen extraction fraction (OEF) mapping indicates a decrease in metabolism accompanied by ventricular enlargement (22). These results suggest that impaired CBF and oxygen utilization indicate the severity of NPH, with the potential to predict responder shunts. Assessing them along with clinical assessments may lead to better patient selection, but the practical application in a geography like Pakistan necessitates discussing concerns about imaging accessibility, which is why this area is a good focus for future research and adaptation.

## Conclusion

Normal pressure hydrocephalus (NPH) is one of the least known but curable disorders of neurology. It is often confused with Alzheimer's disease and Parkinson's disease, and has a clinical triad attributed to age, but it is common in low-resource settings and frequently misdiagnosed. However, the functional decline can be rescued by early Diagnosis and

treatment of the patient, and the quality of life shot up drastically. This review highlights advances in managing NPH, as well as the roles of CSF biomarkers, neuroimaging, and surgical interventions. New methodologies, such as diffusion tensor imaging and arterial spin labeling MRI, can be very useful in terms of prognosis. Nevertheless, obstacles in such countries as Pakistan (imaging is insufficient, cultural misunderstanding, and ignorance among providers) slow down acknowledging and treating the disease. Shunting is the most vital therapy, mainly ventriculoperitoneal fixed-pressure systems, which are applicable in LMICs. However, surgery is not sufficient. Postoperative intensive care, rehabilitation, and clinical follow-up are crucial to maintaining recovery. Increased awareness, screening at an early age, and inexpensive methods of Diagnosis hold the key to improving the situation. Appreciation of core reversible forms of dementia transforms NPH from an inconvenient high-cost pressure into an opportunity to treat dementia and provide hope, operation, and dignity to some populations that live too long.

## Declarations

### Data Availability statement
All data generated or analysed during the study are included in the manuscript.
### Consent for publication
Approved
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Not applicable

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This review is purely academic and educational in nature. It does not represent or reflect the views, policies, or official stance of any institute, organization, or department. The content is intended solely for learning and knowledge-sharing purposes.

### Conflict of interest

The authors declared the absence of a conflict of interest.

### Author Contribution

**AQS**
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