

AN OBSERVATIONAL STUDY OF PRE AND POST SHUNT PITUITARY FUNCTION IN PAEDIATRIC PATIENTS WITH HYDROCEPHALUS

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Received : 01/10/2023
Received in revised form : 13/11/2023
Accepted : 01/12/2023

Keywords:

Pre and Post Shunt, Pituitary Function, Paediatric Patients, Hydrocephalus.

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DOI: 10.47009/jamp.2023.5.6.298

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (6); 1453-1458



Abstract

Background: In this study we have attempted to delineate the nature of anterior pituitary hormonal derangements of these patients, and to follow them up over the course of their illness and surgical treatment to demonstrate what role shunt surgery has in the evolution of their pituitary function over time. However due to constraints of resources and time, and our follow-up duration was limited to 6 months, limiting the scope of our observations. **Materials and Methods:** Prospective Nonrandomised Observational Study with a Follow-up Duration of 6 Months was conducted in the Department of Neurosurgery PMCH And Department Of Endocrinology And Metabolism, PMCH, Patna, Bihar. Study Population Children with Hydrocephalus (Aged From Birth Up to 15 Years) Admitted For VP Shunt Surgery At Study Period PMCH, Patna Bihar From September 2022 To August 2023. A Minimum Of 40 Cases Planned. Total 45 Patients Completed the Study. Children With Hydrocephalus Aged From Birth Up To 15 Years Admitted Under The Department Of Neurosurgery In Patna Medical College And Hospital for VP Shunt Surgery. **Result:** In all of these patients pituitary function was monitored before and after a ventriculoperitoneal shunt. For the 8 patients with Dandy Walker or equivalent posterior fossa cysts, steroids were not prescribed, and a cystoperitoneal shunt was not deemed necessary on analysis of clinicoradiological findings. Only those patients who underwent a single shunt procedure were chosen for the study. **Conclusion:** We propose that baseline testing of pituitary hormones should become a part of routine preoperative investigations in paediatric hydrocephalus, due to the high prevalence of pituitary dysfunction and its long reaching consequences in these patients.

INTRODUCTION

Children with hydrocephalus are often suffering from undiagnosed hypopituitarism, stunted growth and precocious puberty. The nature of their pituitary dysfunction often changes with progression of the illness, and also with interventions such as ventriculoperitoneal shunt insertion or endoscopic third ventriculostomy.^[1]

Developing countries face the greatest burden of paediatric hydrocephalus due to high birth rates and greater risk of neonatal infections. In developed countries, the incidence of congenital hydrocephalus is 0.5–1/1000 live births, while neonatal acquired hydrocephalus is 3–5/1000 live births.^[2] It is estimated that 1% of children who survive bacterial meningitis will develop hydrocephalus.^[3] Approximately 4% of all patients who suffer head trauma will require CSF diversion due to hydrocephalus.^[4] Males have a particular sex

predilection in the form of aqueductal stenosis with adducted thumbs in X-Linked hydrocephalus. X-linked hydrocephalus comprises less than 4% of all cases of hydrocephalus, but it accounts for 8–15% of primary hydrocephalus in boys.^[5] Approximately 85% of children with posterior fossa tumours present with some degree of hydrocephalus, and about 20–30% develop permanent hydrocephalus.^[6] Approximately 12% of children with syndromic craniosynostosis develop hydrocephalus.^[7] The majority of children who present with hydrocephalus do so before 2 years of age, with most of these cases related either to congenital conditions or to complications of premature birth. After 2 years of age, the incidence decreases with increasing age, with most of these cases resulting from obstructive tumours or aqueductal stenosis.^[8]

Indian studies on epidemiology of paediatric hydrocephalus have been few. The World Health Organization Situation Analysis on the South East Asian Region published in 2013 indicates that

hydrocephalus affects 11.20 children per 10000 live births every year in India, with 30240 children affected per year.^[9]

Shunts are the mainstay treatment of hydrocephalus, and even in patients with severe hydrocephalus, shunt insertion can have a dramatic effect on the re-expansion of the cortical mantle, particularly in children.^[10]

In this study we have attempted to delineate the nature of anterior pituitary hormonal derangements of these patients, and to follow them up over the course of their illness and surgical treatment to demonstrate what role shunt surgery has in the evolution of their pituitary function over time. However due to constraints of resources and time, our study duration was of 18 months, and our follow-up duration was limited to 6 months, limiting the scope of our observations.

Aims and Objectives

- To establish whether there was any change in the parameters studied during the postoperative period after undergoing VP shunt.
- To characterise whether any pituitary dysfunction in shunted paediatric hydrocephalus patients appeared newly after the procedure/represented a worsening of a pre-existing defect/represented an improvement of a pre-existing defect.
- To establish whether routine preoperative pituitary function tests should become the norm in investigating children with hydrocephalus.

MATERIALS AND METHODS

Prospective Nonrandomised Observational Study with a Followup Duration of 6 Months was conducted in the Department Of Neurosurgery PMCH And Department Of Endocrinology And Metabolism, PMCH, Patna, Bihar. Study Population Children With Hydrocephalus (Aged From Birth Up To 15 Years) Admitted For VP Shunt Surgery At Study Period PMCH, Patna Bihar From September 2022 To August 2023. A Minimum Of 40 Cases Planned. Total 45 Patients Completed The Study. Children With Hydrocephalus Aged From Birth Up To 15 Years Admitted Under The Department Of Neurosurgery In Patna Medical College And Hospital for VP Shunt Surgery.

Exclusion Criteria

Seller or suprasellar mass lesion

Open neural tube defects

Known drug therapy (phenobarbitone and analogues) which alters IGF 1 and IGF bp3

Deranged liver function test (alters IGF 1 and IGF BP3)

Anterior or middle or posterior cranial fossa mass lesion or any other lesion requiring corticosteroid administration

Instances where the shunt got infected/malfunctioned/displaced and had to be removed

Death of the patient during the study period/loss of follow-up

Inclusion Criteria

Communicating hydrocephalus; post infection cases are included. Tb meningitis induced hydrocephalus is included

Hydrocephalus in cases of chiari malformations/craniosynostoses

Obstructive hydrocephalus due to primary or secondary aqueductal obstruction

History and clinical examination records, pre and postoperative blood and imaging investigation reports, operative procedure related data. Baseline (before shunt) and 6 month post shunt levels of gh, igf-1, igf-bp3 (under 5yrs age group), tsh,s total t3, total t4, fsh, lh, prolactin and acth were done at pmch, patna . Samples were collected at 8am in the morning, with patients in fasting state, via cold syringe (precooled in refrigerator) and collected into precooled edta and serum vials. Samples were immediately put on ice and transferred to lab for assay. A total of 15ml blood was collected for each assay (edta 3.5ml, serum vial 1-3 carrying 4ml).

Ventriculoperitoneal shunt using the surgiwear™ chhabra™ medium pressure ventriculoperitoneal shunt device was performed at pmch, department of neurosurgery, following which the patients were discharged. At 6 months' follow-up the entire set of baseline parameters were reevaluated (anthropometry, sexual maturity, hormone levels and bone age). Data was stored in digital media for analysis using standard statistical analysis software such as ibm's spss™ at the conclusion of the study duration. Plan for analysis of data contingency were drawn up for baseline and 6 months follow-up anthropometric, bone age and sexual maturity rating parameters and significance of changes assessed by using the chi-square or fisher's exact tests. Statistical analysis was performed for the different pituitary hormone levels and significant changes will be documented accordingly.

RESULTS

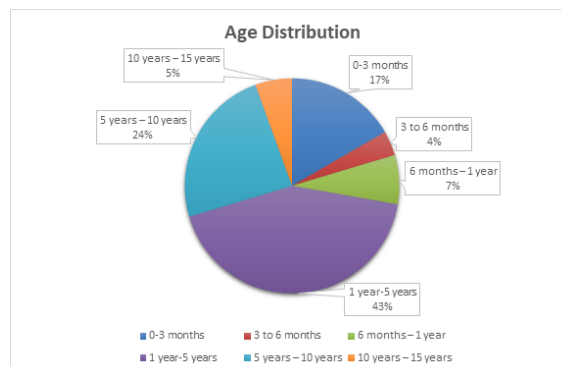


Figure 1: Pie Diagram Showing age Distribution of Patients

The study population consisted of 40 children who fulfilled all the inclusion and exclusion criteria and

were able to complete the study. The age distribution of the patients studied is depicted in the following pie diagram and table. 28% of the patients were under the age of 1 year, and 43% in the next age bracket up to 5 years. Only 16 (29%) patients were above the age of 5 years. The youngest patient was aged 19 days and the oldest aged 12 years.

The sex distribution of the patients studied is as per the following pie diagram and table. 54% were male and 46% female.

Gender	Number of patients	Percentage
Male	29	54%
Female	11	46%

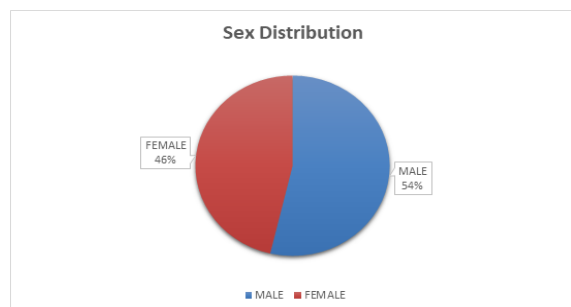


Figure 2: Pie Diagram Showings Distribution of Patients Parameters from Clinical Examination

The Patients Had Several Symptom Groups, With Presentations Occurring As Various Combinations Of Increasing Head Size, Failure To Thrive, Nausea And Vomiting, Visual Deficits, Headache/Irritability, Fever, Neck Rigidity, Papilledema And Cranial Nerve Palsies.

The Following Table Indicates The Percentage Of Patients Who Had/Did Not Have The Aforementioned Symptoms. The Data Is Illustrated With A Stacked Bar Graph.

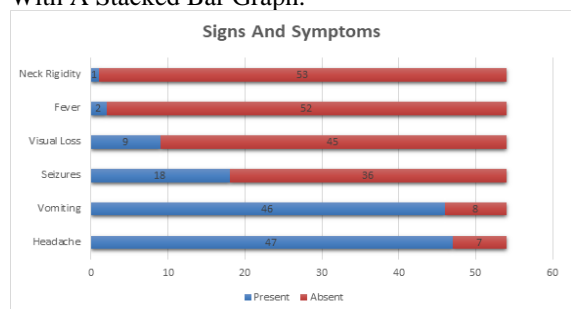


Figure 3: Stacked Bar Diagram Showing Signs and Symptoms

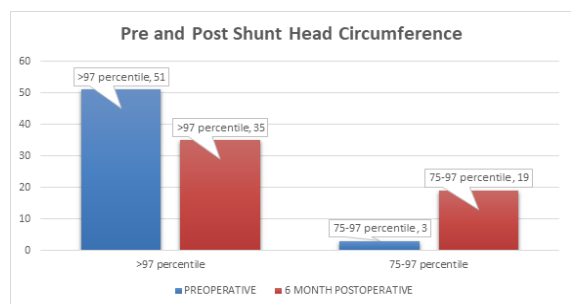


Figure 4: Bar Diagram Showing Pre and Post Shunt Head Circumference

From MRI and CT scan, And the History of Birth Asphyxia and Neonatal Sepsis/Meningitis, It Was Possible to arrive at the Etiological Classes of Hydrocephalus in All the Patients. The Following Table and Bar Diagram Show This Data. In all of these patients pituitary function was monitored before and after a ventriculoperitoneal shunt. For the 8 patients with Dandy Walker or equivalent posterior fossa cysts, steroids were not prescribed, and a cystoperitoneal shunt was not deemed necessary on analysis of clinicoradiological findings. Only those patients who underwent a single shunt procedure were chosen for the study. The Surgiwear TMChabra medium pressure Slit n SpringTM VP shunt was chosen for the operation in all cases.

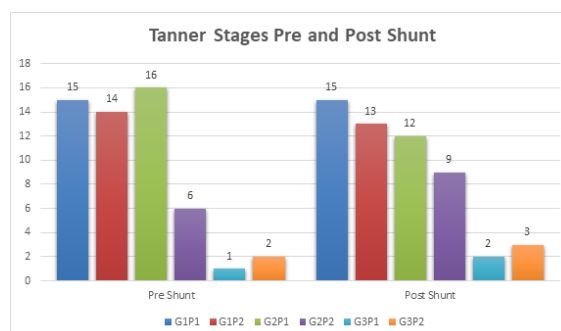


Figure 5: Bar Diagram Showing Tanner Stages Pre and Post Shunt

Hand bone age was estimated by comparing ap hand (left) radiographs with standard age specific atlases of greulich and pyle. Concordance was seen in 94.4% patients pre shunt and 92.5% patients post shunt. P value was 0.6956 signifying no significant changes between the groups.

DISCUSSION

The study population comprised 40 children of the age range 19 days to 12 years, mean age of 4.12 years, with most children in the age group of 1-5 years (43%), the next largest group being of 5-10 years (24%). 54% were male and 46% female. 83% came from rural areas, with 17% residing in urban areas. 43 patients came from various districts of UP, 2 from Jharkhand, 6 from Bihar and 3 from Jharkhand. 63% had one working parent, while in 37% both parents were working to sustain their family. 85% patients were born in a hospital, while 15% were non institutional births at home. This is in contrast to the Coverage Evaluation Survey data of 2009 (Ministry of Health and Family Welfare, Govt of India) where Institutional births were 68% (rural) and 86% (urban) for all of India, and 63.3% (rural) and 85.5% (urban) for Bihar.^[11]

Periconceptional folate (from before conception till 12 weeks gestation) supplementation is not a routine practice in India. Only 9% patients' mothers (mostly being treated for incidentally diagnosed anaemia) were receiving folate in the periconceptional period. 61% patients had a complete immunisation status (as

per National Immunisation Schedule Card) at presentation.

The most common symptom was headache (in children old enough to complain) or irritability and failure to thrive (in infants), being present in 87% patients. Vomiting was next commonest, being present in 85% patients. 33% patients had seizures at the time of presentation. 17% patients had some degree of vision impairment. Papilledema grades were 37%- Grade 1, 33% - Grade 2, 17% - Grade 3 and 13% - Grade 4. Only 2 patients had fever and 1 had neck rigidity at presentation, and antibiotics were administered to both to successfully reduce symptoms prior to shunting. Symptom duration was less than 1 month in 28%, 1-3 months in 54%, 3-6 months in 17% and >6months in 1%.

Preoperatively 94.4% patients had occipitofrontal head circumference in the 97 percentile and higher range according to IAP/WHO head circumference charts. Postoperatively 64.8% had head circumference above 97th percentile, and 35.2% had head circumference in 85-97 percentile range. [p= 0.0000207].

26% patients had aqueductal stenosis causing obstructive hydrocephalus. 15% had post hemorrhagic hydrocephalus secondary to germinal matrix bleed in perinatal period. 13% had postmeningitic/postventriculitic hydrocephalus. 9% had tubercular meningitis, while 4% was due to Chari malformation and 15% was due to Dandy Walker malformations or variants. 18% had communicating hydrocephalus of primary origin.

Standing height or length was measured and recorded as percentile values pre and post shunt. Before shunting, 74% patients had height in the 75 to 97 percentile, 14.8% in the 50-75 percentile range, 1.9% in the >97 percentile range, and 9.3% in the <50 percentile range. 6 months after shunting, 83.4% patients had height in the 75 to 97 percentile, 11.1% in the 50-75 percentile range, 0% in the >97 percentile range, and 5.5% in the <50 percentile range. [p= 0.556, no significant change post shunt].

Body weight was measured and recorded as percentile values pre and post shunt. Before shunting, 18.5% patients had weight in <50 percentile, 20.4% patients in 50-75 percentile, 61.1% in 75-97 percentile, and 0% in >97 percentile. 6 months after shunting, 0% patients had weight in <50 percentile, 18.6% patients in 50-75 percentile, 74% in 75-97 percentile, and 7.4% in >97 percentile. [p= 0.0021, significant change post shunt].

Body mass index was measured and recorded as percentile values with reference to age pre and post shunt. Before shunting, 9.2% patients had BMI in <50 percentile, 37% patients in 50 percentile to 23 adult equivalent, 46.4% in 23 to 27 adult equivalent, and 7.4% in >27 adult equivalent. 6 months after shunting, 3.7% patients had BMI in <50 percentile, 33.3% patients in 50 percentile to 23 adult equivalent, 57.4% in 23 to 27 adult equivalent, and 5.6% in >27 adult equivalent. [p= 0.5359, no significant change post shunt].

In most of the patients, waist hip ratio (done only for children above 5 years of age, n=16) was in the normal range (0.75-0.90) accounting for 62.5%. The post shunt group also had similar findings, with the same number of children in the normal group. P value was 0.8924 by a Fisher's exact test (two tailed), signifying no statistically significant difference between the pre and post shunt groups.

The Tanner Stages of Sexual Maturity were used to score the secondary sexual characters of the patients studied pre and post shunt. However due to the short follow-up durations used in the study, and the paucity of pubertal subjects, there was no significant development in the post shunt period in secondary sexual characters. P value by a Chi Square test was calculated to be 0.8835, signifying no statistically significant difference between pre and post shunt populations.

Hand bone age was estimated by comparing AP hand (left) radiographs with standard age specific atlases of Greulich and Pyle. Concordance was seen in 94.4% patients pre shunt and 92.5% patients post shunt. P value was 0.6956 signifying no significant changes.

Lopponen et al in their series noted a reduced relative height, increased waist hip ratio and increased body fat percentage while maintaining similar BMI in males and a slightly higher BMI in females. There was accelerated pubertal (gonadal as well as pubic hair criteria in the Tanner stages) development, as well as earlier menarche. There was an exclusively post shunt cohort, and pre and post shunt estimation of anthropometry was not done.^[12]

This was reflected only partially in our study population, with there being retarded linear growth in only 26% of our patients in baseline state, and reduced to 5.5% at 6 months post shunt. High BMI (above 23 adult equivalents) was present in 53.8% of our patients in the baseline state, and in 63% patients 6 months after shunt. Waist hip ratio was mostly in the normal range in our study population.

Most patients had normal baseline serum cortisol (pre shunt=94.4%, post shunt 96.3%). P value was 0.499 implying no significant difference between pre and post shunt groups. All subjects had normal test results for ACTH in both pre and 6 month post shunt setting. While 42.6% subjects had below reference range levels (as per Tanner stage) for growth hormone at baseline, the figure improved to 11.1% in the 6 month post shunt tests. The p value is 0.0039 implying high statistical significance. While 48% children initially had low levels of IGF-1, the number worsened in the 6 month post shunt period and reached 81%. P=0.0005 suggested a highly significant drop in IGF 1 in the 6 month post shunt period. IGF-BP3 levels (done for under 5 patients only, n=38) were below reference range in 18.5% patients before shunt. At 6 months' followup, the levels normalised in all patients. p=0.0009 suggested a highly significant finding. Prolactin levels pre shunt was deranged in 45%, with lower than baseline levels in 17% and high levels in 28%. In the 6 month post shunt period there

was dramatic improvement with 94% patients reaching normal blood levels. $P=0.00009$ suggests a highly significant finding.

92.6% patients had normal values of TSH in the preop setting, with 7.4% having below reference range levels. In the postop setting, 94.4% had normal levels of TSH. $P=0.6033$ suggests no significant alteration between pre and 6 month post shunt setting. Observed FSH levels (reference ranges taken as per Tanner stage) were from 0.01 to 4.1 mIU/ml. FSH levels were within reference ranges in 96.3% patients pre-shunt, and 94.4% post-shunt. $P=0.4712$ suggests no significant alteration in post shunt population. Observed LH levels (reference ranges taken as per Tanner stage) were from 0.1 to 9.5 mIU/ml. LH levels were within reference ranges in 98.1% patients pre-shunt, and 96.3% post-shunt. $P=0.5526$ suggests no significant alteration in post shunt population.

In the series published by Lopponen et al,^[13] there was accelerated pubertal (gonadal as well as pubic hair criteria in the Tanner stages) development, as well as earlier menarche. Higher basal FSH, LH was noted in the prepubertal as well as pubertal populations. No abnormalities were seen in the estradiol or testosterone levels. Bone age estimation showed retarded bone age at prepubertal age groups, but there was an early pubertal growth spurt and bone age appeared advanced after that stage, leading to an overall reduced final height. This is in contrast to our series which found near normal bone age in prepubertal subjects, and normal basal FSH and LH. However due to our study limitations we cannot comment on final height, and estradiol and testosterone levels were not estimated as part of our study.^[14] However our study aimed to evaluate total anterior pituitary function, and we had attempted to evaluate thyrotroph and corticotroph function as well. While Lopponen et al performed stimulation testing with GH and LH/FSH axes to further characterise the deficits, we did not perform any stimulation tests due to resource constraints. Observed T3 levels were from 30 to 168 ng/dl. T3 levels were within reference ranges in 90.7% patients pre-shunt, and 94.4% post-shunt. $P=0.3478$ suggests no significant alteration in post shunt population. Observed T4 levels were from 2.8 to 14.1 µg/dl. T4 levels were within reference ranges in 87% patients pre-shunt, and 96.3% post-shunt. $P=0.0812$ suggests no significant alteration in post shunt population.^[15,16]

CONCLUSION

In this study, we attempted to establish whether any pituitary dysfunction exists in paediatric hydrocephalus, and whether the nature and character of such dysfunction changes after Ventriculoperitoneal Shunt. We studied a total of 40 children over a period of 6 months follow-up duration for each patient, and obtained baseline and 6 month postoperative data on anthropometry, bone and sexual maturity, and pituitary function testing (no

stimulated single samples only). A single model of VP shunt (the Surgiwear Chhabra™ Slit and Spring Medium Pressure Shunt) was used to provide consistent CSF dynamics and comparable results. Our study population consisted of 54% males and 46% females, 83% hailing from a rural background, 95% under the age of 10 years, mostly from low income families, and of an Eastern Indian racial heritage. 26% patients had aqueductal stenosis causing obstructive hydrocephalus. 15% had post hemorrhagic hydrocephalus secondary to germinal matrix bleed in perinatal period. 13% had postmeningitic/postventriculitic hydrocephalus. 9% had tubercular meningitis, while 4% was due to Chari malformation and 15% was due to Dandy Walker malformations or variants. 18% had communicating hydrocephalus of primary origin. Most of the patients were prepubertal at presentation and did not achieve puberty during the course of the study. A few patients had retarded linear growth at presentation, but mostly reverted to acceptable growth in height after 6 months post shunt. There was no significant retardation in bone maturity in the study population (94.4% pre shunt and 92.5% post shunt had normal imaging). Pituitary hormone levels showed no significant consistent derangement in ACTH. Cortisol, TSH, T3, T4, FSH and LH levels were normal in most patients (more than 94% before and more than 96% after shunt).

We propose that baseline testing of pituitary hormones should become a part of routine preoperative investigations in paediatric hydrocephalus, due to the high prevalence of pituitary dysfunction and its long reaching consequences in these patients.

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