Assessment of the Prevalence and Associated Risk Factors of Pediatric Hydrocephalus in Diagnostic Centers in Addis Ababa, Ethiopia

Blein Mulugeta
Addis Ababa University
Girma Gedion Seyoum (girma91@yahoo.com)
Addis Ababa University
Abebe Mekonnen
Addis Ababa University
Elbet Ketema
Addis Ababa University

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Abstract

Background: Hydrocephalus (HCP) is defined as pathophysiology with disturbed cerebrospinal fluid. Neither qualitatively nor quantitatively are there adequate data to determine the prevalence and incidence of HCP in the developing world. HCP is a treatable condition that when left untreated, has fatal consequences.

Objective: The objective of this study was to assess the prevalence of pediatric HCP and associated risk factors in diagnostic centers in Addis Ababa.

Methods: A cross-sectional facility-based study was conducted over a retrospective and prospective data collection periods. Children aged 5 years and below who came to the four diagnostic centers for MRI/CT examination were studied. The collected data were analyzed using binary logistic regression.

Result: The retrospective study included 639(58%) males, 462 (42%) females, and 753 (68.4%) infants were aged younger than 24 months. The mean age calculated was 22.3 months. Children diagnosed with HCP were 245 (22.3%); of these HCP cases, 153(62.4%) were classified as non-communicating HCP. This study identified infants aged younger than 24 months to be significantly associated with HCP ($P<0.05$). Regarding the gender and age distribution of the prospective study, 57(57.6%) males, 42 (42.4%) females; a mean age of 24.9 months and 60 (60.6%) infants aged younger than 24 months were included. Children diagnosed with HCP were 23 (23.2%); of these HCP cases, 13(56.5%) were classified as non-communicating HCP. Inadequate consumption of folic acid and the familial association of HCP were found to be statistically significant ($P<0.05$).

Conclusion: The results of this study suggest that the high prevalence of HCP was due to the high prevalence of aqueductal stenosis and neural tube defects; with a small contribution of post-infectious causes. The majority of infants who present with HCP were aged younger than 24months.

Background

Hydrocephalus (HCP) has been repeatedly defined as a pathophysiology with disturbed cerebrospinal fluid (CSF) circulation (1). Infants with this disorder commonly present with progressive macrocephaly while those children older than 2 years often present with indications of intracranial hypertension (2). In the developed world, the incidence of congenital HCP has been estimated to be about 0.5 cases per 1000 live births with an overall incidence of neonatal HCP estimated to be about 3 to 5 cases per 1000 live births (3). There aren't enough or adequate data to determine the prevalence and incidence of HCP in the developing world, especially in sub-Saharan Africa, where this condition appears to be much more frequent than in developed countries. Taking some very conservative estimates in Uganda, as an example, between 1000 and 2000 new cases of infant HCP occurs every year, with this most likely being an underestimate. Generalizing this to other regions, 6500 new cases of HCP occur per year in East Africa and more than 45,000 new cases per year in the entire sub-Saharan Africa (4). HCP is a treatable condition that when left untreated, has fatal consequences. Data on the burden of HCP in low-income

countries are limited, given a lack of radiologic resources for the diagnosis of this condition (5). In Ethiopia, the limited resources faced in terms of finance, limited access to health care, and low level of literacy; have all made it not only difficult to assess the prevalence of this disorder but also impossible to determine or estimate the general characteristics of the disease with respect to the etiology, type, gender or age composition of the patients. The etiology and incidence rates of HCP in Ethiopia has been attributed to infectious causes; similar to other East African countries. As mentioned earlier due to the lack of resources, diagnosis and treatment of these infants with this disorder presents an enormous challenge as only a few hundred each year are properly diagnosed and receive proper treatment. If the estimates on new cases of pediatric HCP in Ethiopia are valid, these children represent an enormous challenge for the nation (6). HCP could be due to congenital causes, most commonly involving aqueduct stenosis. It could also be due to acquired causes, mostly from pathological processes that affect subarachnoid space function (2). Significant morbidity and mortality from this disorder can be accomplished with continued research and education (4).

Hence, this study has assessed the prevalence and possible risk factors of pediatric HCP from a large sample of CT and MRI scans of the head performed at selected diagnostic centers in Addis Ababa, Ethiopia, a low-income country in Africa. The findings of this study will give focus on the management of HCP, and will create awareness for the importance of prenatal care given to mothers during their pregnancy.

Methods And Materials

This study was performed in four of the diagnostic centers that work in close association with Addis Ababa University, Wudassie Diagnostic Center (WDC), Dr.Alia Diagnostic Center, Pioneer Diagnostic Center, and BMY Diagnostic Center; all chosen randomly. This study was conducted from January 2018 to February 2020. A cross-sectional facility-based study was conducted over a two-time period, i.e. a 2-year retrospective data collection from January 2018 to January 2020 and a prospective data collection from May 2019 to February 2020. The study design involved children aged 5 years and below who came to the selected diagnostic centers for MRI/CT examination during the data collection periods.

A 2-year retrospective data collection yielded 1,101 patients and the prospective data collection yielded 99 patients. All children of either gender aged 5 years and below admitted for MRI /CT examination of the Brain during the data collection periods were included in the study. Patients, who had surgery for HCP before the study period started, patients who had imaging examinations besides the Brain, and parents/caretakers not willing to participate in the study were excluded.

The retrospective data were collected by the employment of a checklist that included the patient's clinical indication, the type of modality used, confirmation of HCP, and type of HCP confirmed. The prospective data were collected through a pre-tested semi-structured questionnaire that consisted of socio-demographic and economic factors, maternal conditions, and radiological results of the study participants. To ensure the validity and reliability of the tools, impartial personnel, public Health expert

was used; supervision was also carried out by the principal investigator to check completeness and consistency to keep the quality of the data.

The data were entered, cleaned, and analyzed using SPSS software version 23.0. The data collected was analyzed by descriptive analysis. Binary logistic regression analysis with a 95% confidence interval (CI) was calculated to test the degree of association between dependent and independent variables and applied to identify possible risk factors. Multivariate analysis was applied to identify predictors of the outcome variable. A P-value of less than 0.05 was taken as statistically significant. Ethical clearance was obtained from the postgraduate office of Anatomy, College of Health Sciences; Addis Ababa University. Permission was obtained from the office of selected diagnostic centers. The purpose and importance of the study were explained to each study participant and they were informed that no personal identifiers were used in the data. Verbal and written consent was also obtained from each participant. Participants had the right to be excluded from the study if they were not voluntary to participate.

Results

Concerning the retrospective data, 639(58%) males and 462(42%) females participated. Their age ranged from 1 to 60 months with a mean age of 22.3 months and a standard deviation of ± 18.8. MRI was used to image 736(66.8%) and 365(33.2%) were imaged using a CT machine. There were 753 (68.4%) children aged younger than 24 months. Fifty-seven (57.6%) males and 42(42.4%) females were included in the prospective data with their age ranging from 1 to 60 months; with a mean age of 24.9 months and a standard deviation of ± 19.2. Ninety-three (93.9) were imaged using MRI and 6(6.1%) were imaged using CT. This data set had 60 (60.6%) children aged younger than 24 months. The prevalence of HCP was calculated separately for both study periods. The number of children diagnosed with HCP during the retrospective study was 245 (22.3%), and of these HCP cases, 153(62.4%) were classified as non-communicating HCP and 92 (37.6%) as communicating HCP based on MRI and CT images. Males were relatively higher to be diagnosed with HCP in this study (140 patients accounting for 57.14% of all patients diagnosed with HCP). Prevalence of HCP calculated during the prospective study was 23 (23.2%); and of these HCP cases, 13(56.5%) were classified as non-communicating HCP and 10(43.5%) as communicating HCP based on MRI and CT images. Females were relatively higher to be diagnosed with HCP in this study (12 patients accounting for 52.17% of all patients diagnosed with HCP). Regarding the maternal history, those aged 18–23 were 23 (23.7%), those aged 24–29 were 45 (46.4%), those aged 29–34 were 17 (17.5%), and those aged 35–40 were 12 (12.4%). Concerning the mother's educational level, those that did not attend school were 22(24.2%), on the other hand, those who attended elementary school we 29 (31.9%), those that went to high school were 22(24.2%) and those that had a diploma and above were 18(19.8%). Forty-nine (49.5%) of the mothers interviewed were from the rural area and 50 (50.5%) were from Urban area. Seventy-four (81.3%) were housewives and 17 (18.7%) were employed. Seventy-five (82.4%) of the mothers reported that they attended the antenatal clinic during the pregnancy while 16 (17.6%) of mothers did not attend their antenatal follow-ups. Twenty-nine (32.2%) of mothers did not take their folic acid nutritional supplement while 61 (67.8%) of mothers took their supplement, 58 (58.6) started consuming the folic supplement after conceiving and 3 (3.3%) started consuming before

conceiving; and 54 (58.7%) of them were scanned by Ultrasound during their prenatal follow-up visits. The majority of these mothers had vaginal delivery 71 (78.0%) as opposed to 19 (20.9%) of Caesarean deliveries. History of HCP among families was found to account for 46 (46.5%) of all the interviewed cases. Also, it was identified that 55.6% of the families had a first-degree relative and 22.2% had second and third-degree relatives with HCP.

Risk Factors Associated with HCP in the Retrospective Study

The risk factors associated with pediatric HCP were also calculated separately for the two study periods. The retrospective study identified 753 (68.4%) were children younger than 24 months; accounting for the majority. With a statistical significance of (AOR = 1.90 [95% CI = 1.36, 2.26], P < 0.05), the study has found that out of all patients diagnosed with HCP, 192 (78.3%) children were younger than 24 months; accounting for the majority of the HCP patients. (Table 1)

Table 1
Associated Risk factors of HCP of the Retrospective Data within the Selected Diagnostic Centers in Addis Ababa, Ethiopia, 2018–2020

Variables	Category	Diagnosis		COR (CI 95%)	AOR (CI 95%)
Variable		Diagnosis		COR (CI 95%)	AOR (CI 95%)
		Yes	No		
Age of the child	≥ 24 months	53	293	1	1
	≤ 24 months	192	559	1.89 (1.36, 2.65)*	1.90 (1.36, 2.26)*
Gender	Male	140	497	1	1
	Female	105	355	0.95(0.72, 1.27)	1.01 (0.75, 1.35)

Note: *significance; p < 0.05

Risk Factors Associated with HCP in the Prospective Study

The prospective study identified the majority of children 60 (60.6%) were younger than 24 months. Out of all patients diagnosed with HCP, 15 (65.2%) children were younger than 24 months; though this accounted for the majority of the HCP patients, it was not found to have statistical significance (P > 0.05). No statistical significance was identified among the gender of these patients either (P > 0.05). Mothers who did not take folic acid nutritional supplements were 29 (32.8%). These mothers were identified to be significantly associated with HCP occurrence (OR = 6.107 [95% CI = 1.32, 28.35], P < 0.05). Concerning the utilization of supplements only once after they found out they were pregnant, there is a significant association of HCP development at P < 0.05 with a proportion of 58 (58.6%). History of HCP was found to have a significant association with the occurrence of HCP (OR = 4.52 [95% CI = 1.624–12.984], P < 0.05). (Table 2) This study identified that interviewed mothers who had Pre-eclampsia were (9.9%), chronic

hypertension (8.8%), and Diabetes mellitus (2.2%) during their gestation. Though these variables were studied as risk factors, a significant association with HCP was not found (P > 0.05). Sexually transmitted infections were identified among 4.4% of the interviewed mothers but this did not reach significance (P > 0.05). This study also did not find any association between the use of alcohol and cigarette smoking among mothers interviewed (P > 0.05). This study identified that mothers who took medication (prescribed or otherwise) were (10.1%) and these mothers that took this medication in the first-trimester were (33.3%), the second trimester was (55.6%) and in the third trimester were (11.1%); however, this did not reach statistical significance (P > 0.05) Table 2

Table 2
Associated Risk factors of HCP of the Prospective data within the Selected Diagnostic Centers in Addis Ababa, Ethiopia, 2019–2020.

Variables	Category	Diagnosis		COR (CI 95%)	AOR (CI 95%)
Age of child		Yes	No		
	≥ 24 months	8	31	1	1
	≤ 24 months	15	45	1.2(0.08–1.3)	1.3 (0.6–1.7)
Gender	Male	11	46	1	1
	Female	12	30	0.59(0.23–1.52)	1.69 (0.63–4.54)
Age of mother	18–23	2	21	1	1
	24–29	14	31	0.21(0.04–1.03)	0.22 (0.04–1.08)
	29–34	5	12	0.23 (0.038–1.36)	0.24 (0.04–1.43)
	35–40	2	10	0.48(0.06–3.88)	0.43 (0.05–3.58)
The educational level of the mother	Did not attend school	8	14	1	1
	Elementary school(1–8)	6	23	2.2(0.63–7.64)	2.04 (0.54–7.79)
	High school(9–12)	4	18	2.6(0.64–10.31)	2.61 (0.57–11.7)
	Diploma and above	3	15	2.8(0.63–12.9)	3.92 (0.78–19.5)
Antenatal care attendance	Yes	19	56	1	1
	No	2	14	2.38(0.49–11.41)	0.34 (0.06–1.78)
Consumption of folic acid	Yes	19	42	1	1
	No	2	27	6.107(1.32–28.35)*	1.64 (0.052–51.5)*
Use of folic acid	Before conceiving	2	1	1	1
	After conceiving	17	41	0.59(0.04–0.804)*	0.27 (0.009–8.32)*
History of HCP in the family	Yes	17	29	1	1

Note: *significance; P < 0.05

Variables	Category	Diagnosis		COR (CI 95%)	AOR (CI 95%)
	No	6	47	4.52 (1.624–12.984)*	4.89 (0.64–3.23)*
Trauma to the mother during pregnancy	Yes	4	4	1	1
	No	17	66	3.882(0.88–17.140)	2.93 (0.56–15.3)
Note: *significance; P < 0.05					

Prevalence of Congenital and Acquired Hydrocephalus

Prevalence of Congenital and Acquired HCP within the Retrospective Study

Prevalence of congenital and acquired HCP in both study periods was studied separately based on MRI and CT images, of all children diagnosed with HCP (22.3%). Congenital HCP was described in terms of Aqudectal stenosis and NTDs. Aqudectal stenosis, accounting for 17.6%, was identified to be the most prevalent. NTDs were found as the second most common type of congenital HCP. These NTDs were further studied and explained through Chari II 41(16.7%), and Chari III malformations 1(0.4), Dandy-Walker variant 28(11.4%), and Colpocephaly 8(3.2%). NTDs associated with MMC 2(0.89%), Encephalocele 5(2.04%), and Meningoencephalocele 3(1.2%) were further identified. These NTDs accounted for 35.91% in total. The acquired HCP was described in terms of Post-infectious, Post-hemorrhagic, Adhesion of Foramen of Monroe, and tumor-related causes. Post-infectious HCP (PIH) (3.2%), was determined according to the child's clinical indication and CT and MRI imaging findings. PIH was defined in terms of chronic in-utero infection (TORCH- Toxoplasmosis, Rubella, Cytomegalovirus, and Herpes), Ventriculitis, Cerebral and Cerebellar abscess, and Tuberculoma that led to the development of HCP. Post-meningitis complications (6.9%) due to Pyogenic and Tuberculous causes were also included in this group. This same technique was applied to diagnose post-hemorrhagic complications leading to HCP. Subdural hematoma (0.4%), hypoxic-ischemic cerebral injury (1.2%), perinatal ischemic insult (1.2%), Cystic Encephalomalacia (0.8%), and Dural venous malformation (0.4%) were investigated and included in this group as well. Tumor-related HCP was diagnosed according to imaging investigations and was identified in terms of Medulloblastoma-Teratoid Rhabdoid Variant 12(4.8%), Craniophangioma (0.8%), Pineal gland Glioma (0.4%), and Ependymoma (0.4%). Another etiology of HCP identified in this study was the Adhesion of Foramen of Monroe (0.4%)

Prevalence of Congenital and Acquired HCP within the Prospective Study

This study has also tried to understand the prevalence of congenital and acquired HCP separately similar to the retrospective study; of the total pediatric patients diagnosed with HCP (23.2%). Congenital HCP

was again described in terms of Aqudectal stenosis and NTDs. The congenital pediatric HCP identified five different causes. Of which, the largest, a little more than a quarter was attributable to aqueductal stenosis (26.1%). This, on the other hand, was followed by NTDs further studied in terms of Dandy-Walker malformation (17.4%), and Chari II malformation (8.7%). HCP associated with MMC (8.69%) and Meningoencephalocele (8.69%) were also included in this category. These NTDs accounted for 43.48% in total. The acquired pediatric HCP, similar to the retrospective study, also identified post-infection related post-meningitis complications, post-hemorrhagic, and tumor-related HCP. The same diagnosis criteria used in the retrospective study were applied here as well. Post-meningitis complications due to Pyogenic and Tuberculous causes account for (8.69%). Perinatal hypoxic-ischemic injury and post-perinatal hypoxic-ischemic injury due to Ex-vacuo ventriculomegaly were studied as post-hemorrhagic complications. Ex-vacuo ventriculomegaly was not defined as a type of HCP in this study, but its development due to post-perinatal hypoxic-ischemic cerebral injury (21.7%) and perinatal hypoxic-ischemic cerebral injury (13.04%) was identified and investigated as a post-hemorrhagic complication. This group also included Subdural hematomas (21.7%). This study has also identified tumor-related HCP and has diagnosed it using results of imaging investigations. Medulloblastoma-Teratoid Rhabdoid Variant, Germinoma, and Craniophangioma each accounting for 8.69% were included in this group. Figure 1 Finding(s): Superior vermian arachnoid cyst compressing the superior vermix and the tectal plate and effacing the aqueduct causing severe aqueductal stenosis and obstructive HCP

Discussions

Demographics: Sex, Age and Patient Characteristics of both studies

As opposed to their female counterparts, males had a relatively higher chance of being diagnosed with HCP (140 patients accounting for 57.14%). This finding is similar with published studies in other African countries which have shown that majority of pediatric patients with HCP were males; 64.6% of the population in a study from Tanzania and 53% in a study from Kenya (7); 60.5% in a study from Nigeria (8), as well as a predominance of 51.9% in a study from Uganda (9). The finding also is in agreement with a published study in Ethiopia which similarly found males to be predominant both in isolated HCP (38 male patients accounting for 66.7% of all patients with isolated HCP) and in the MMC associated HCP group (30 male patients accounting for 53.6% of the patients in that group) (6). However, the prospective study had a different finding; as it was found that females had a relatively higher chance of being diagnosed with HCP (12 patients accounting for 52.17% of all patients diagnosed with HCP). In this study, sex was not considered as one of the risk factors of HCP. As a result, the relatively higher prevalence of HCP among males in retrospective study and females in prospective studies was not further investigated. In this study, age distribution ranged from 1 to 60 months; there was a slight increment in the mean age of pediatric patients from 22.3 months to 24.9 months in the two study

periods but the difference was not statistically significant. A statistically significant association between age and the development of HCP was found (P<0.05), in the retrospective study, among children aged younger than 24 months; 192 children (78.3%) out of all patients diagnosed with HCP. These children were observed to have a higher risk of developing HCP 1.9 times as opposed to those aged older than 24months. (Table 1) This is similar to an article published in the journal of the International Society for Pediatric Neurosurgery (ISPN) and the National Organization of Rare Disorders (NORD) both of which reported the majority of children who present with HCP do so before 2 years of age (10, 11). Non-communicating HCP (obstructive HCP) was predominant in both populations, 62.4% in the retrospective and 56.5% in the prospective study. This is in agreement with the Ethiopian study that also found obstructive HCP to be predominant in two of their study periods, 64.7 % during the first period, and 62.2 % in the second (6).

Prevalence of HCP

In developed countries, the incidence of congenital HCP is estimated at three to five cases per 1000 live births (3). This study had a different finding as it identified the prevalence in the population studied during the retrospective study to be 222.72 per 1,000 births (2,222.72 per 10,000 births) and the prevalence observed during the prospective study period to be 232.3 per 1,000 (2,323.2 per 10,000 births). The observed prevalence of pediatric HCP in both studies is much higher than prevalence rates of 20.3 per 10,000 births seen in northern China (12), 4.65 per 10,000 births in four European regions (13), 11 per 10,000 births in Denmark (14), 5.9 per 10,000 births for California (15), and prevalence of 28.7 per 10,000 births in a region of Nigeria (16). However, the results of this study are in agreement with the study conducted in Uganda-from CURE Children's Hospital of Uganda (CCHU) which demonstrated infant HCP among 3,684 children. The study estimated the infant HCP prevalence rate between 1,000 and 2,000 cases every year (4). This study is also similar to research conducted here in Addis Ababa, Ethiopia that used the estimates applied in the Ugandan research and presented an estimate between 2,000 and 4,000 new cases of pediatric HCP per year (6). As described earlier, this high prevalence rate of HCP in Ethiopia has been attributed to high percentages of Aqueductal stenosis, NTDs, and a small contribution of post-infectious causes observed in both study periods. In presenting the causes and incidence rates of HCP from East Africa (6), where it served as a reference for Ethiopia, there is a contradiction concerning the cause of HCP.

Prevalence of Congenital and Acquired HCP

Aqueductal stenosis and Neural tube defects (NTDs)

This study has identified Aqueductal stenosis (17.9%) as the most prevalent type of congenital HCP. Aqueductal stenosis is a narrowing of the aqueduct of Sylvius which blocks the flow of CSF in the ventricular system. The aqueduct of Sylvius, a channel that connects the third to the fourth ventricle,

because of its small size, is the most likely place for a blockage of CSF in the ventricular system (17). Reports that aqueductal stenosis causes the majority of the Obstructive HCP (17), have been reviewed by this study and it similarly has attributed the non-communicating HCP (Obstructive HCP) predominance in both populations, i.e. 62.4% in the retrospective and 56.5% in the prospective study to Aqueductal stenosis. Following this, NTDs have been identified as the second most prevalent type of congenital HCP. NTDs compiled within the retrospective data were Chari II malformation, Dandy-Walker malformation, and MMC. This result is in agreement with a study conducted in three African countries; Zambia, Zimbabwe, and Malawi, that stated the most common cause of HCP to be congenital, associated with Aqueductal stenosis and NTDs (18). A similar distribution was also found when compiling the prospective data, Aqueductal stenosis accounting for 26.1%, followed by NTDs (Dandy walker malformation, MMC and Chari II malformation). In contrast, this study differed from the study in Uganda which indicated HCP secondary to CNS infection to be the single most common cause of infant HCP accounting for 60% of cases (19). The results of this study may be explained by the diagnosis of typical characteristics of NTDs and level of obstruction of the cerebral aqueduct on MR neuroimaging of the children's brain and clinical history acquired during the interview process that was able to show the classic features of HCP, that is, increase in head size, sun-setting eyes, vomiting, and seizures in the patients. This study also found HCP associated with MMC accounting for 0.81% retrospectively and 8.69% prospectively. This result is different from the Ugandan study which found MMC associated HCP to account for 14% (4). This finding is also contrary to the study conducted here in Ethiopia that found MMC associated HCP among children aged under 5 years to account for 44.5% (6). This study also differed from the study in Kenya which found MMC (Spinal Bifida) associated HCP to account for 43.4% (20), south-western Saudi Arabian study that found Spinal Bifida Cystica accounting for (95.8%) (21), and the Tanzanian study that reported MMC to account for 16% of their cases (22). MMC cases were not encountered as much as expected in this study because it was conducted within diagnostic centers and these patients had better chances of being treated in public hospitals since they were detected early and diagnosed clinically; not a lot of imaging investigations were referred out to diagnostic centers. Besides, there is no centrally managed database of the patient's clinical history in public and private health institutes.

Post-infectious HCP (PIH)

Studies in Uganda (4), Tanzania (22), and Kenya (20); have reported PIH prevalence of 57%, 22.4%, and 27.7%. In our study, however, a prevalence of only 10.1% and 8.69% have been observed in the retrospective and prospective study periods respectively. This discrepancy may be explained by differences in methodology. In the Ugandan study, for example, PIH was defined in terms of the absence of HCP at birth, history of febrile illness or seizure preceding the onset of HCP, and convincing evidence of prior ventriculitis based on imaging or ventriculoscopic findings if the history was unclear (4). In this study, however, PIH was defined in terms of the patient's clinical history and post-natal CT and MRI imaging investigations only; thus defining PIH in terms of post-natal diagnosis. This study has identified PIH related post-meningitis complications due to Pyogenic and Tuberculous causes accounting for 6.9%

and 8.69% within the retrospective and prospective data respectively. In contrast, this study had a lower percentage when compared with the south-western Saudi Arabia study that found post-meningitis causes accounting for 14.8% (21). This study however agrees with the study conducted in three African countries; Zambia, Zimbabwe, and Malawi, that identified post-meningitic HCP as the most frequent cause next to NTDs and aqueductal stenosis (18). A similar study in Kenya was observed to show the same finding where it classified post-meningitis HCP within the PIH group which was again identified as the second most common cause of HCP following Spinal Bifida (20).

The Risk Factors Associated with Pediatric HCP

Prenatal care given to mothers and HCP

This prospective study identified that 82.4% of the interviewed mothers attended their antenatal visits. Statistical significance was not reached among those mothers that did not attend their visits (17.6%). This study hypothesized that those mothers that said they went to their visits may not have attended all the visits they were supposed to go to. This may be explained by poor antenatal follow-ups and this could have resulted in NTDs, which in turn lead to HCP. This study is supported by a study conducted in Atlanta that has suggested that getting adequate prenatal care might help prevent birth defects, HCP being one of them (23). In this study, no association was found with the onset of prenatal care given to the mother and HCP development ($P>0.05$). This finding is supported by the study from Mississippi that similarly studied potential risk factors of congenital HCP, which similarly did not find any association among prenatal care given to mothers and HCP occurrence (24).

Folic acid Supplementation and HCP

Folate deficiency has a recognized teratogenic effect, resulting in an increased risk of NTDs (16). This study argues that the incidence of these NTDs that eventually lead to HCP and other CNS anomalies could have resulted due to the inadequate consumption of folic acid. In this study, mothers who did not take folic acid nutritional supplements were significantly associated with HCP occurrence ($P<0.05$). (Table2) During early development, folic acid helps form the neural tube hence, it plays an important role in the prevention of some major birth defects of an infant's brain i.e. (Anencephaly) and spine (Spinal Bifida) (25). Although the majority (67.8%) of the interviewed mothers in this study did take their folic acid supplement, it was discovered that they took their supplements once they had found out they had conceived and within their late first trimester period and about 32.2 % of these mothers did not take their supplements at all. This study also found that mothers who took their supplements after they had conceived (58.6%) were significantly associated with HCP development ($P<0.05$). This study has gathered from this that these mothers did not plan their pregnancy and early consumption of folic acid was not considered. The fact that these mothers did not take their supplements before pregnancy and during their early pregnancy periods could explain the high prevalence of NTDs identified during both

study periods. This study is also in agreement with the study from the Enugu region of Nigeria that similarly suggested that the high incidence of NTDs among the study cohort attributed to the lack of use of folic acid by the majority of the mothers studied, 57 (79.2%) of the affected children (16). This study is also similar to another study that suggested the consumption of adequate amounts of folic acid by women before pregnancy and during early pregnancy decreases their risk for having a pregnancy affected by NTDs (26). This study again goes following the study conducted in Northern China that found the supplementation of folic acid reduced the incidence of HCP and NTDs in their study population (12). This study supports the findings above. Nevertheless, multivariate analysis of this study was not able to show the inadequate consumption of folic acid as the predictor of HCP occurrence. This has been attributed to the small sample size in the studied population. However, bivariate analysis of this study has found that mothers who did not take the folic acid nutritional supplement were significantly associated with HCP occurrence. As Ethiopia is one of the largest producers of Wheat in Sub-Saharan Africa (27), and most Ethiopian's diet commonly use Wheat in bread, fortification of wheat flour is an effective, and simple strategy for supplying folic acid and iron to its population (28), thereby reducing the incidence of NTDs that have the potential to lead to HCP.

Advanced maternal age and HCP

Although an association was expected between advanced maternal age and occurrence of HCP, this study did not find a significant relationship between the two ($P>0.05$). It was difficult to find association as the number of interviewed mothers aged above 35 accounted for only 12.4% and these mother's risk of having a child with HCP was not found to have increased; whereby only 8.6% of these mothers had an infant with HCP. This is in agreement with the study conducted in Mississippi that similarly did not find any association with advanced maternal age and HCP occurrence ($P=0.976$) (24). This study has however found that the majority of mothers (46.4%) were aged 24-29; of these mothers (60.8%) were found to have a child with HCP. This finding among the young mother's age group goes following the study from Atlanta which has also identified HCP without NTDs among young mothers and has reported 1.56 times increased risk among this sect of the population. It was suggested that the most likely explanation for the increased risk for birth defects observed in these young mothers may be due to different lifestyle factors like inadequate prenatal care, lower intake of vitamins, lowest awareness of folic acid, unhealthy diet, exposure to alcohol, smoking and/or drugs (23). Young maternal age and advanced maternal age are both associated with increased risks for some types of non-chromosomal birth defects and mothers under 20 and over 35 have a higher risk of giving birth to an infant with a birth defect (23). However, this study was not designed to determine the mechanism by which birth defects occur among different age groups of mothers but further investigation is needed to understand the effects of maternal age on HCP and other birth defects.

Familial Association and HCP

This study was able to show an association between the history of HCP among family members and the development of congenital HCP with a statistical significance of ($P<0.05$) (Table 2); when performing the bivariate analysis. However, the multivariate analysis was not able to show this as a predictor of HCP development and this as mentioned before has been attributed to the small number of study participants. History of HCP among family members was found to account for 73.9% of all the diagnosed cases of HCP. This is similar to a study conducted in Mississippi which reported 72 of 596 congenital HCP cases (12.1%) had at least one additional family member with HCP (24). Although in this study significant association among different degrees of relatives and the development of HCP was not found, it was identified that of the children with HCP, 8.69% had a first degree relative with congenital HCP. This result is in agreement with a study conducted in Denmark that also found a significant association of HCP among individuals with first- or second relatives with congenital HCP. The Denmark study suggested that familial aggregation and both the genetic and the maternal effects play important roles in congenital HCP pathogenesis (29). This study was unable to adequately analyze genetic sequences due to the lack of genetic laboratories and clinics. Though this study did not investigate genetic agents as a risk factor for HCP, it does recognize its significance and recommends further exploration into the topic for future researches.

Trauma during Pregnancy

In this study, trauma to the mother during the pregnancy period was not significantly associated with pediatric HCP. This study, however, indicated that 17.3% of mothers of children with HCP suffered from trauma during their gestation. Nonetheless, this did not show statistical significance. This is in agreement with a similar study conducted in Mississippi that identified trauma to the mother during her gestation (3%) and traumatic birth (19.5%) as risk factors for the development of HCP; this study from Mississippi nevertheless did not find this to be statistically significant (24). In this prospective study, vaginal delivery (78%) and caesarian section delivery (20.9%) accounted for the total number of modes of deliveries questioned. Instrumental delivery was considered a traumatic birth that could have the potential to cause brain injury leading to HCP. Falling accidents during the gestational period were also considered to be causes of fetal brain damage. This goes following a study in Washington State, USA, that reported brain injury as one of the severe birth traumas observed among hospital singleton live births (30). However, this study was not able to acquire sufficient information from mothers about the details of delivery and only a few of the mothers interviewed were able to recall falling during their pregnancy time. This made it difficult to assess the association; thus making it hard to conclude that birth traumas and accidents were exactly the causes that lead to HCP development. Nonetheless, it hypothesizes that post-hemorrhagic complications that resulted from these traumas could have the potential to lead to HCP. Even though the etiologies of acquired infant HCP associated with post-hemorrhagic HCP of prematurity were reported to be the most common cause of HCP in more economically developed countries (4), this study has described earlier the contribution of post-hemorrhagic HCP i.e. hypoxic-ischemic cerebral injury, perinatal ischemic insult, subdural hematoma, IVH and cystic encephalomalacia here in Addis Ababa, Ethiopia, a

low-income country. Following the initial hypothesis, this study has attributed the occurrence of these post-hemorrhagic complications of acquired HCP to post-traumatic reasons.

The Educational Level of the Mother

Ethiopia has been grouped as one of the nations with a low literacy rate of 49.1% along with Liberia (literacy rate of 47.6%), Chad (literacy rate of 40.2%), and Mali (literacy rate of 38.7%) (31). By the year 2017 the literacy rate of male and female adults in Ethiopia, was 59.24% and 44.2% respectively which puts Ethiopia's literacy rate the lowest in the world (32, 33). It was presumed in this study that the low level of literacy Ethiopia faces especially in its female population particularly among rural communities would be one factor for the limited knowledge of these mothers regarding the health of their child. Going in line with this presumption, we found 49.5% of the interviewed mothers to be from the rural population, and 81.3% to be housewives. The findings of this study could be attributed to sociocultural factors, for example, gender violence, early marriage, and the burden of housework that affects women and girls to not pursue and complete their education. Of the mothers from the rural side, 16.16% of them had a child diagnosed with HCP. In this study, 87.9% of the mothers interviewed did not have any awareness about HCP and had never even heard about it. This study is in line with the article published by Indiana University that reported low health literacy negatively affects a woman's health knowledge, ability to navigate the health care system, and ability to care for her children (34). Despite not being able to establish a statistically significant association between the mother's educational level and HCP occurrence, different works of literature this study has reviewed has explained its assumptions about the fact that mother's education is important not only to empower these women but to have a better awareness about their child's health. In this study, mothers with an educational level of diploma and above had a reduced rate of children with HCP, about 3.29% were identified. This study is in line with another study conducted where parental occupation was examined as a risk factor for HCP. This study found that engineers' and architects' infants had a reduced risk as compared to janitors who showed a higher risk of HCP among their infants (35).

Maternal Pathologies and Infections

Maternal chronic hypertension, pre-eclampsia, and maternal diabetes (pre-gestational and gestational) were investigated as risk factors of HCP development, these associations had no statistical significance. This goes in line with reports from the study that similarly did not find statistical significance between maternal diabetes and preeclampsia with HCP development (36). Reports of the prevalence of diabetes and preeclampsia are limited in the developing country setting as opposed to the Western world. For example, a study from Mississippi has identified maternal hypertension during pregnancy to be significantly associated with HCP (24). Unlike this, a study conducted within the eastern zone of Tigray, in Ethiopia has reported the prevalence rate of gestational diabetes mellitus to be only 3.7% (37). In this study, intrauterine infections, for example, TORCH infections were identified among 9.9% of the mothers. These infections were diagnosed while CT and MRI imaging of the child's brain was performed and HCP

was diagnosed. This is in agreement with the study conducted at the University of Athens which also reported an association between maternal infections of toxoplasmosis and cytomegalovirus with congenital HCP but was not able to establish a statistical significance (36). This study found it difficult to reach a statistical significance as the mothers were neither able to explain the type of infection they were diagnosed with nor were they able to know whether they had an infection in the first place. This study has attributed this to the fact that the majority of these mothers were not educated, as previously reported, only 19.8% of the interviewed mothers had a diploma and above. Besides, as some of the viral infections stayed dormant with no clinical signs, this study did not find it surprising these mothers were unaware of the infections. In this study, sexually transmitted infections during pregnancy were identified among 4.4% of mothers. These identified infections were not confirmed by laboratory investigations in this study rather they were gathered from mothers during the interview process. Though this did not reach statistical significance, it goes following the study from Mississippi that similarly reported sexually transmitted infections at the time of delivery were 1.2% but this was not statistically significant (24).

STRENGTHS AND LIMITATIONS OF THE STUDY

- The strength of this study was; cross-sectional facility-based study design employed across the four selected diagnostic centers allowed this study to be representative of the study population and the limitation of this study was; the limited amount of time and resource the prospective study had and failure of the MRI machine to work during this data collection period, as a result, has decreased the total studied population.

Conclusions

1. High prevalence observed in the pediatric population of both study periods i.e. the retrospective study was 22% and the prospective study was 23%. 2. Aqueductal stenosis was found to be the most prevalent type of congenital HCP, followed by NTDs. 3. Hydrocephalus that developed secondary to infection was minimal whereby 10.1% and 8.69% were observed in the first and second study periods respectively. 4. This study has observed non-communicating HCP predominance in both study periods and was attributed to Aqueductal stenosis. 5. Advanced maternal age, maternal parity, maternal pathologies, the educational level of the mother, attendance of antenatal clinic, and trauma during pregnancy were all studied as potential risk factors for HCP development but statistical significance was not found. Inadequate consumption of folic acid during pregnancy, the onset at which the mothers took their supplement, and history of HCP within the family were significantly associated with the development of HCP but this study was not able to show these as major predictors of the outcome variable. However, infants aged younger than 24months were identified as risk factors (major predictor) that were significantly associated with the development of HCP. 6. There is a high association between the amount of folic acid consumption in early pregnancy and the incidence of NTDs. Sufficient utilization reduces the incidence of having a child with NTDs. 7. In this study post-hemorrhagic complications of acquired HCP

resulted due to post-traumatic reasons. 8. The majority of HCP diagnosed patients had first-degree relatives with congenital HCP.

RECOMMENDATIONS

It would be ideal if public teaching hospitals affiliated with universities, public and private medical schools, and diagnostic centers across the country conducted similar research regarding the prevalence and risk factors of HCP. This would help in formulating a guideline that can be used across the nation and better understand its public health impact. Further investigation is recommended to understand maternal risk factors associated with the occurrence of congenital and acquired HCP. If a centrally managed database of patient's clinical history among public and private health institutes was organized under the Ministry of Health, it would help keep records for better management of the patient and will also serve as a medical and public health policy input.

Abbreviations

HCP- Hydrocephalus, MRI- Magnetic Resonance Imaging, CT- Computed Tomography, CSF, Cerebrospinal fluid, MMC- Mennigomyocele, NTD- Neural Tube Defects

Declarations

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the institutional review board of collage of health science of Addis Ababa University. The performed study's protocol was following the principles of the declaration of Helsinki. After presenting the study aims and adequate explanations about the research, and receiving a written informed consent as well as verbal agreement from the parents/ guardians of the children, were included in the study.

CONSENTFORPUBLICATION

Not applicable

AVAILABILITY OF DATA AND MATERIALS

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

FUNDING

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COMPETING INTERESTS

We declare that we have no conflict of interest.

AUTHORS' CONTRIBUTION

BM and GS analyzed and interpreted the data regarding the prevalence and associated risk factors of the pediatric patients. AM interpreted the radiologic images acquired i.e. CT and MRI images of the brain of the pediatric patients. EK guided the statistical analysis. All authors have read and approved the manuscript.

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Figures

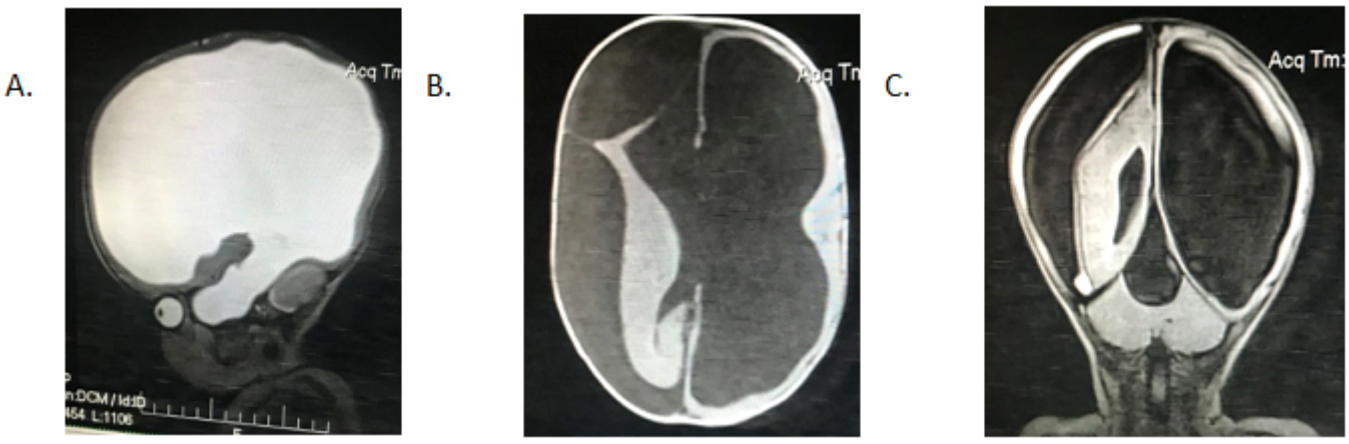

Figure 1

MRI Image of a 4 months old male infant represented by A. T2 Sagittal B. T1 Axial and C. T2 Coronal FLAIR(fluid attenuation inversion recovery) The image was performed by the assigned Medical Radiologic Technologist within the diagnostic center