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ORIGINAL ARTICLE

The impact of fetal middle cerebral artery Doppler on the outcome of congenital hydrocephalus

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ABSTRACT

Objectives: The objective of this study is to investigate the impact of abnormal middle cerebral artery (MCA) Doppler on the perinatal mortality in fetuses with congenital hydrocephalus (CH).

Methods: A prospective study of all fetuses with CH who delivered at our hospital over a period of 7 years. Data were obtained from the ultrasound, Labor room and intensive neonatal care unit (NICU) database. The Perinatal mortality rates were evaluated in relation to the following measures, associated congenital anomalies, cortical mantle thickness (CMT), and MCA Doppler abnormalities (absent or reversed diastole). The main outcome measure was perinatal mortality rate in relation to MCA Doppler changes.

Results: A total of 85 cases of CH were diagnosed and managed. The birth prevalence of CH was 2.44 per 1000 live births. On one hand, the perinatal mortality rate was higher in those fetuses with non-isolated hydrocephalus, (37.25% (19/51) versus (35.29% (12/34, $p = 0.854$ and in those cases with CMT <10 mm, 38.78% (19/49) versus 33.33% (12/36) in those with CMT >10 mm, $p = 0.607$. On the other hand, the perinatal mortality rate was significantly higher in those fetuses with abnormal MCA Doppler, (100% (13/13) versus 25% (18/72), OR = 78.0, 95% CI (5.52–44085124.60), $p < 0.001$.

Conclusions: Abnormal fetal MCA Doppler (absent or reversed diastole) appears to be a poor prognostic indicator with significantly high perinatal mortality in fetuses with CH.

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Introduction

Hydrocephalus is a multifactorial disorder, defined as an abnormal dilatation of the lateral cerebral ventricular system due to excessive accumulation of cerebrospinal fluid (CSF) leading to increased intra-ventricular pressure and then marked cranial enlargement. This could be due to obstruction of CSF pathway, overproduction, or impaired absorption [1,2]. Hydrocephalus can be congenital or acquired. The incidence of congenital hydrocephalus has been estimated between 0.4 and 0.8 per 1000 live and still births [1–4]. The X-linked hydrocephalus is the most common form of the inherited hydrocephalus [3]. Although some antenatal prognostic factors were suggested to predict the postnatal prognosis of congenital hydrocephalus as associated other congenital anomalies and the cortical mantle thickness (CMT) of less than 10 mm, there is no specific antenatal prognostic criteria for congenital hydrocephalus [5–8].

Some studies had investigated the role of the transcranial Doppler (TCD) of cerebral vessels in children and adult patients with hydrocephalus; they found that TCD of cerebral vessels is a useful and valid method for the confirmation of cerebral circulatory arrest [9,10]. Abnormal middle cerebral artery (MCA) Doppler has been reported as a feature of brain death or vegetative state [11,12]. Furthermore, MCA Doppler has significant role in diagnosis of fetal anemia [13], and in monitoring of growth-restricted fetuses [14]. Moreover, MCA Doppler can determine the difference between active and resting behavioral states in healthy fetuses aged 30–32 weeks [15]. However, to our knowledge, few studies evaluated the role of antenatal MCA Doppler as a predictor of perinatal mortality in congenital hydrocephalus, apart from our previous study on the same subject but was done on few cases and included all cases of ventriculomegaly [16]. In addition, another two previous studies had demonstrated that an abnormal fetal intracranial arterial velocity waveform can be seen as a sign of increased perinatal risk in hydrocephalic fetuses; however, both these studies evaluated only few cases of fetal

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hydrocephalus and one of them didn't focus only on hydrocephalus [17,18].

The aim of our study to further evaluate the benefit of antenatal MCA Doppler as an indicator for perinatal mortality in fetuses with congenital hydrocephalus, and to compare it with the two previously suggested ultrasound markers; association with other congenital anomalies and CMT of less than 10 mm.

Materials and methods

A prospective study was conducted over 7 years from January 2008 to December 2014 to evaluate the impact of antenatal MCA Doppler as an indicator for perinatal mortality in fetuses with congenital hydrocephalus in a tertiary care hospital in Riyadh/Kingdom of Saudi Arabia (KSA): Women's Specialized Hospital (WSH)/King Fahad Medical City (KFMC). This study was approved by the internal review board in KFMC (IRB: 08–103, IRB Registry No. with KACST: H-01-R-012), informed consent was obtained from the patients. KFMC is a tertiary referral hospital serving wide geographical area in KSA with a current average delivery rate of 5000 per year.

The study group included all fetuses diagnosed with congenital hydrocephalus where the head biometry above 2 standard deviations of the normal for the stated gestational age (GA). All fetuses with ventriculomegaly but normal head biometry and those with other major intracranial anomalies (i.e. Holoprosencephaly, Dandy Walker, and others) were excluded from the study.

The MFM unit at our hospital provides good perinatal care for our patients including routine morphology scan at 18–22 weeks gestation, interventional procedures like amniocentesis, cordocentesis, and others as well as managing high risk patients. All patients with congenital hydrocephalus were scanned by maternal–fetal medicine (MFM) specialist with a caution of not applying pressure during Doppler study. Most of the patients had more than one ultrasound scan. The MCA Doppler was marked as normal or abnormal (absent or reversed diastole). Congenital hydrocephalus was marked as either isolated hydrocephalus or non-isolated hydrocephalus if associated with other anomalies (i.e. Spina bifida). MCA Doppler examination and the CMT were measured in all fetuses with hydrocephalus. All ultrasound examinations were performed by one ultrasound systems, Philips IU 22 (Philips, Amsterdam, Netherlands), and the data were stored in our electronic ultrasound database.

The MCA Doppler was sampled at the lower third of the artery (Figure 1). Three or more MCA Doppler studies were obtained every scan for each case; however, in those cases with reversed flow we obtained more than seven Doppler studies just to ensure the consistency of the findings. We confirmed the findings by repeating the MCA Doppler several times every scan and performing another scan within 2 weeks, so every time we scan, the patient with hydrocephalus MCA was performed.

The CMT was measured in the fronto-parietal cortex at the level of trans-ventricular view. Cases of severe hydrocephalus were diagnosed if the CMT was $<$10 mm. Karyotyping was offered to all patients.

All cases were discussed in a multidisciplinary prenatal planning meeting, in the presence of neonatologist, genetic consultant, and pediatric neurosurgeons.

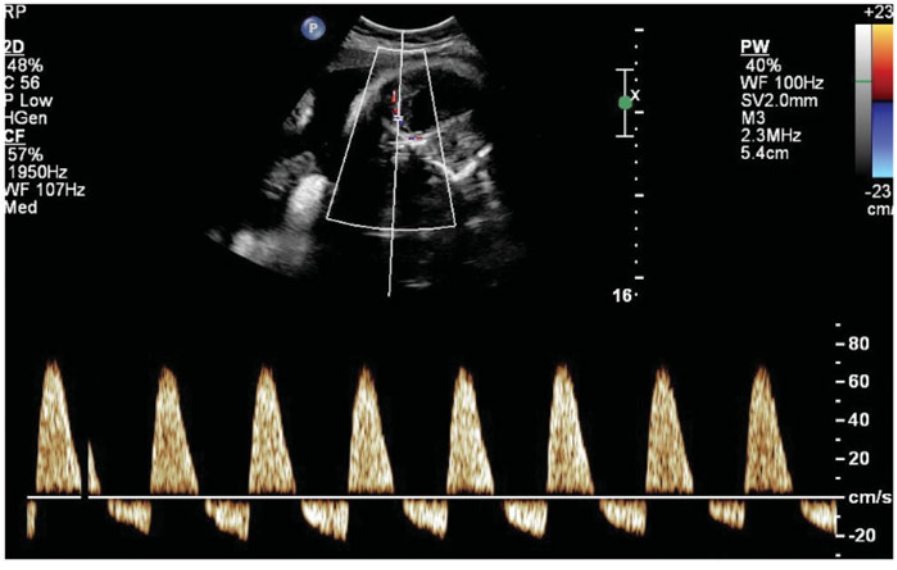

Figure 1. Reversed diastole of middle cerbral artery Doppler.

All of them delivered in KFMC. The mode of delivery was based on obstetric indications. MCA Doppler findings did not influence the mode of delivery. Fetal cephalocentesis was performed either antepartum or intrapartum to facilitate vaginal delivery in 11 patients, seven fetuses with normal MCA Doppler, and four fetuses with reversed diastolic flow. Six fetuses were stillbirth and five fetuses had early neonatal death. We preformed cephalocentesis for 11 fetuses. The indication for cephalocentesis was cephalo-pelvic disproportion. The procedure was performed if the patient requested trial of vaginal delivery. Patient with previous cesarean section or patient declining the procedure went for cesarean section based on obstetrics indications. So the mode of delivery for the entire population was centered totally on clinical judgments and taking into consideration patients' requests. The median gestational age at delivery was 38 weeks, most of the patient delivered at term. Only 14 patients delivered before 34 weeks of gestation. The neonatologist on call attended all deliveries and resuscitated all newborns. Pediatric neurosurgeons were consulted for all live newborns.

The maternal demographic data were recorded from the ultrasound database. Postnatal data were recorded from the labor room and intensive neonatal care unit (NICU) database. The perinatal outcome included NICU admissions and perinatal death (Table 1).

The associated congenital anomalies, cortical mental thickness (CMT) measurement, and MCA Doppler abnormalities were marked for all cases. Perinatal mortality rates were evaluated in relation to those three findings. The main outcome measures were MCA Doppler changes and perinatal mortality rate.

Fisher's exact and Chi-square tests were used for categorical data and use of SPSS 18.0 (SPSS Inc., Chicago, IL) for data analysis. Statistical comparisons were performed with descriptive techniques and two-tailed *t* tests were used for continuous data. A *p* value <0.05 was considered statistically significant.

Results

About 34 841 patients were delivered during the study period. A total of 85 cases of congenital hydrocephalus were diagnosed and managed. The birth prevalence of congenital hydrocephalus was 2.44 per 1000 live births. Out of the 85 cases, 34 fetuses were diagnosed with isolated hydrocephalus and 51 fetuses were diagnosed with non-isolated hydrocephalus, the most common associated anomaly was spina bifida in 37 cases. The perinatal mortality rates for isolated and non-isolated hydrocephalus were 35.29% (12/34) and 37.25% (19/51), respectively, OR = 1.09, 95% CI (0.40–2.97), $p = 0.854$ (Table 2).

CMT was less than 10 mm in 49 cases and between 11 and 20 mm in 36 cases. The perinatal mortality for fetuses with CMT was less than 10 mm and between 11 and 20 mm was 38.78% (19/49) and 33.33% (12/36), respectively, OR = 0.79, 95% CI (0.29–2.13), $p = 0.607$ (Table 3). There was no difference in CMT in fetuses with or without MCA reverse diastolic flow, in the contrary, most of the fetuses with CMT less than 10 mm had normal MCA Doppler flow and few fetuses with CMT more than 10 mm had abnormal MCA Doppler with reverse diastolic flow.

MCA Doppler was abnormal (absent/reverse diastolic flow) in 13 fetuses, in seven fetuses with isolated hydrocephalus, and in six fetuses with non-isolated hydrocephalus. All the 13 fetuses died either before delivery or within 24 h of age (six stillbirths and seven neonatal deaths). The perinatal mortality with normal

Table 2. Perinatal mortality rates in relation to associated anomalies.

	Outcome		
Hydrocephalus	Survived	Died	Total
Isolated	22	12	34
Non-Isolated	32	19	51
Total	54	31	85
OR =1.09, 95% CI (0.40–2.97), $p = 0.854$			

Table 3. Perinatal mortality rates in relation to CMT.

	Outcome		
CMT (min)	Survived	Died	Total
≤10	30	19	49
11–20	24	12	36
Total	54	31	85
OR =0.79, 95% CI (0.29–2.13), $p = 0.607$			

CMT: cortical mental thickness.

Table 1. Maternal demographic data and perinatal mortality.

	Total hydrocephalus	Isolated	Non-isolated
Number	85	34	51
Maternal age (median)	28 (18–44)	28 (21–44)	27 (18–41)
Parity median	1 (0–9)	2 (0–9)	1 (0–7)
Diagnosis gestational age (median)	33 (19–41)	34 (19–40)	33 (19–41)
Family history	15/85 (17.6%)	7/34 (20.6%)	8/51 (15.7%)
Consanguinity	39/85 (45.9%)	17/34 (50%)	22/51 (43.1%)
Delivery gestational age	38 (25–42)	37 (25–41)	38 (25–42)
Perinatal mortality	31/85 (36.47%)	12/34 (35.29%)	19/51 (37.25%)

Table 4. Perinatal mortality rates in relation to MCA Doppler abnormalities.

	Perinatal outcome		
MCA Doppler blood	Survived	Died	Total
Normal	54	18	72
Abnormal	0	13	13
Total	54	31	85

OR =78.0, 95% CI (5.52–44085124.60), $p < 0.001$.

MCA: middle cerebral artery.

MCA Doppler flow and abnormal MCA Doppler flow were 25% (18/72) and 100% (13/13), respectively, OR = 78.0, 95% CI (5.52–44085124.60), $p < 0.001$ (Table 4).

Abnormal MCA Doppler was statistically significant in prediction of perinatal mortality in fetuses diagnosed with congenital hydrocephlus. The CMT and the presence of extra-cranial congenital anomalies associated with congenital hydrocephalus were not statistically significant in prediction of perinatal mortality.

Discussion

Although there are no confirmed antenatal indicators to predict the postnatal prognosis of congenital hydrocephalus, some indicators were suggested like the association with other congenital anomalies and the CMT. The prognosis varies; a favorable outcome is expected in those cases with a CMT of ≥ 2 and the absence of other anomalies [6,7]. However, in our study, the presence of other anomalies was not statistically significant, although it is clinically significant. Furthermore, CMT < 10 mm was statistically significant and associated with higher perinatal mortality rate in our study; it was clinically difficult to acquire especially when the intracranial anatomy was severely disturbed.

In healthy fetuses, the diameter of the MCA increases with gestation with a continuous forward flow in all the cerebral arteries throughout the cardiac cycle [19,20]. On the other hand, the persistent abnormality of MCA Doppler especially if it is reversed diastole was reported to proceed intrauterine fetal death in a severely growth-restricted fetuses [21,22].

In cases of congenital hydrocephalus, the excessive amount of CSF within the dilated ventricular system leads to increased intracranial pressure, and subsequently thinning of the cerebral mantle and compression of the vascular system with an increase in the venous pressure resulting in a decrease in diastolic flow and ischemia in cerebral vessels [23]. TCD of cerebral vessels has been investigated widely in pediatric and adult patients; it was an effective method to evaluate the cerebral circulation and the increase in intracranial pressure and thus it was a useful and valid method for the confirmation of cerebral circulatory arrest [10]. Furthermore, some studies have reliably confirmed the predictive value of the abnormal MCA Doppler (absent or reversed diastole in brain death or vegetative state in adults [11]. In addition, more studies showed that reversed flow in the MCA often preceded the loss of brain stem function and thus was considered as characteristic of cerebral circulatory arrest [12]. The specificity of TCD examination of the MCA in confirming brain death was reported to be 100% [24].

Congenital hydrocephalus is usually associated with high perinatal mortality [1,25]. To our knowledge, this study is the only one to confirm the impact of abnormal MCA Doppler (absent/reverse diastolic flow) in the perinatal outcome of congenital hydrocephalus; the previous study was conducted on smaller sample size and for all cases of ventriculomegaly over 3 years [16] and the other studies were done on very few cases [17,18]. The findings of abnormal MCA Doppler were significantly associated with higher perinatal mortality rate (100%), as all fetuses with abnormal MCA Doppler died in the early neonatal period. Unlike CMT, MCA Doppler blood flow sampling was relatively easy even with disturbed intracranial morphology.

In our study, MCA Doppler studies were obtained three times at least every scan and more than seven times in those cases with reversed flow to ensure the consistency of the findings. Furthermore, these findings were confirmed by repeating the MCA Doppler several times, each scan every two weeks. Although our results are statistically significant, we believe that further larger studies are needed to investigate this new subject so we can apply it in our practice.

Conclusions

Fetal MCA Doppler has significant impact on the perinatal mortality of congenital hydrocephalus, as abnormal MCA Doppler (absent or reversed diastole) appears to be a poor prognostic indicator with significantly high perinatal mortality. However, further larger studies are needed to investigate these findings.

Disclosure statement

The authors declare that they have no conflicts of interest.

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