Journal of Neonatal-Perinatal Medicine 5 (2012) 357–362
DOI 10.3233/NPM-1261512
IOS Press



# Can Doppler studies predict mortality in fetuses with congenital hydrocephalus?

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Received 12 March 2012
Revised 1 May 2012
Accepted 3 July 2012

**Abstract**. *Objectives*: To evaluate the changes in middle cerebral artery (MCA) Doppler blood flow in fetuses with congenital hydrocephalus in relationship with perinatal mortality.

*Methods*: This a prospective study conducted in King Fahad Medical City, Riyadh, Saudi Arabia from January 2008 to December 2010. All fetuses diagnosed with congenital hydrocephalus had detailed morphology scans. The associated congenital anomalies, cortical mental thickness measurement, and MCA Doppler abnormalities ware marked. Perinatal mortality rates were evaluated in relation to those three findings. The main outcome measures were MCA Doppler changes and perinatal mortality rate.

*Results*: We managed 116 cases of congenital ventriculomegaly and hydrocephalus (35 cases with mild ventriculomegaly, 29 cases with severe ventriculomegaly, and 52 cases with hydrocephalus). The birth incidence of congenital hydrocephalus was 3.52 per 1,000 live births and the total perinatal mortality rate was 40.4% (21/52). Out of 52 cases of hydrocephalus, 9 fetuses were diagnosed with abnormal MCA Doppler (absent or reverse diastolic flow). All nine fetuses died before the age of 24 hours. Abnormal MCA Doppler and a cortical mental thickness measurement of less than 10 mm were significantly associated with higher perinatal mortality rates with a relative risk of 4.42 and 3.58 respectively. The association of congenital hydrocephalus with other congenital anomalies was not statistically associated with higher perinatal mortality.

*Conclusion*: Congenital Hydrocephalus is a common abnormality that is associated with high perinatal mortality. Abnormal MCA Doppler blood flow appears to be a marker of poor prognosis and high perinatal mortality.

Keywords: Congenital hydrocephalus, middle cerebral artery, reversed diastolic flow

## 1. Introduction

Congenital hydrocephalus is defined as abnormal dilatation of the lateral ventricular system with marked enlargement of the cranium. The incidence of congenital hydrocephalus has been estimated between 0.4–0.8 per 1,000 live and stillbirths [1, 2]. The etiology of congenital hydrocephalus is heterogeneous [3], X-linked hydrocephalus is the most common form of the inherited hydrocephalus [2].

MCA Doppler blood flow has a significant role in the diagnosis of fetal anemia, as in cases of rhesus alloisoimmune disease [4] and in monitoring of growth restricted fetuses [5]. To our knowledge, no study looked at the changed in MCA Doppler blood flow with congenital hydrocephalus as a marker or predictor of perinatal mortality.

The objective of this study was to evaluate the MCA Doppler blood flow abnormalities (absent/reverse diastolic flow) in fetuses with congenital hydrocephalus as antenatal ultrasound indicator or marker for perinatal

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mortality. Also, to compare MCA Doppler with the two previously suggested ultrasound markers; association with other congenital anomalies and cortical mental thickness (CMT) of less than 10 mm; in relation to early neonatal mortality. In addition to evaluate the incidence of congenital hydrocephalus and the perinatal mortality rates in our population.

## 2. Material and methods

This is a prospective cohort study conducted in Maternal-Fetal Medicine Department, Women's Specialized Hospital, King Fahad Medical City, during the period from January 2008 to December 2010. The study population involve all booked obstetrics patient who had antenatal morphology scan and diagnosed to have singleton fetuses with congenital ventriculomegaly or hydrocephalus. The Exclusion criteria were (1) all cases of ventriculomegaly or hydrocephalus that aborted before 22 weeks of gestational age and (2) all Cases of ventriculomegaly a or hydrocephalus secondary to cranial anomalies (such as cases of arachnoid cyst, Dandy Walker malformation, or occipital encephalocele). The maternal demographic data were recorded from the ultrasound data base.

All obstetrics patients were scheduled for morphology scan from 18 to 22 weeks of gestation or later upon booking. All fetuses diagnosed with major congenital anomalies are referred to the fetal developmental clinic (FDC). The fetuses with ventriculomegaly or hydrocephalus were allocated into three groups (1) mild ventriculomegaly, where the lateral ventricle width was 11–14.9 mm, (2) severe ventriculomegaly where the lateral ventricle width was 15 mm or more, and (3) hydrocephalus when there is severe ventriculomegaly with marked enlargement of the cranium.

All patients with ventriculomegaly or hydrocephalus underwent level II morphology scan performed by maternal fetal medicine (MFM) consultant and most of the patients had more than one ultrasound scan. Congenital hydrocephalus was marked as either isolated hydrocephalus or non-isolated hydrocephalus if associated with other anomalies (i.e. Spina bifida). MCA Doppler blood flow examination and the CMT were measured in all fetuses with hydrocephalus. All ultrasound examinations were performed by one ultrasound systems, Philips IU 22 and the data was stored in our electronic ultrasound data base.

The MCA Doppler blood flow was sampled at the lower third close to the origin of the artery before branching. MCA flow velocity waveforms were obtained for three times or more, and marked as normal or as an abnormal in cases of absent or reversed diastolic flow. Caution was observed in minimizing the transducer pressure especially when there was abnormal diastolic flow. The CMT was measured in the fronto-parietal cortex at the level of transventricular view. We marked the cases as severe hydrocephalus if the CMT was less than 10 mm. Umbilical artery Doppler blood flow and electronic fetal heart monitoring were performed in all cases. In addition, karyotyping was offered to all patients.

Later on, all the cases were discussed in a multidisciplinary prenatal planning meeting, in the presence of neonatologist, genetic consultant, and pediatric neurosurgeons. All the patients delivered in our institution. The mode of delivery was deliberated based on obstetric indications. MCA Doppler blood flow findings did not change or influence the mode of delivery plan. Fetal craniocentesis was performed in seven patients either prepartum or intrapartum to facilitate vaginal delivery. The neonatal resuscitation team with the neonatologist on call attended all deliveries and resuscitated all newborns. Pediatric Neurosurgeons were consulted for all live newborns. Postnatal data were collected from the labor room and the neonatal intensive care unit (NICU) data base. The newborns were followed in the NICU till discharged from the hospital.

The study was approved by the Institutional Review Board (IRB). IRB Number 11–103 and IRB Register number KACST: H-01-R-012. We used Fisher exact test to build up the statistical data and use SPSS 18.0 for data analysis.

## 3. Results

During the study period, 14,767 patients delivered in our institution. We have diagnosed a total of 116 fetuses with congenital ventriculomegaly or hydrocephalus, including 35 fetuses of mild ventriculomegaly, 29 fetuses of severe ventriculomegaly and 52 fetuses of hydrocephalus. Maternal data, gestational age, and outcomes of the three groups are shown in Table 1. Umbilical artery Doppler blood flow and electronic fetal heart monitoring were unremarkable in all cases. Genetic testing was offered to all patients but only 24 mothers accepted the procedure. Four fetuses were

Table 1
Maternal data, gestational age, and perinatal outcomes for the three studied groups

| | Mild ventriculomegaly | Severe ventriculomegaly | Hydrocephalus |
|---|---|---|---|
| Number | 35 | 29 | 52 |
| Maternal age in years[a] | 31 (22–53) | 28 (19–41) | 28.5 (16–44) |
| Consanguinity | 14 (40%) | 14 (48.3%) | 28 (53.8%) |
| Recurrent history | 8 (22.9%) | 4 (13.8%) | 10 (19.2%) |
| Non-isolated | 24 (68.6%) | 16 (55.2%) | 28 (53.8%) |
| Diagnosis gestational age in weeks[a] | 29 (17–38) | 32 (15–40) | 33 (19–40) |
| Delivery gestational age in weeks[a] | 37 (22–43) | 38 (24–41) | 38 (25–41) |
| Perinatal mortality | 19 (54.3%) | 6 (20.7%) | 21 (40.4%) |

[a]Data are presented as medians. Other data are presented in numbers (%).

found to have abnormal chromosomal studies (two fetuses with trisomy 18, one fetus with trisomy 13, and one fetus with trisomy 21).

We managed a total of 52 fetuses of hydrocephalus; the birth prevalence of congenital hydrocephalus in our hospital population was 3.52 per 1,000 live births. The most common associated congenital anomalies with hydrocephalus were spina bifida (23.3%), club foot (17.2%), renal anomalies (17.2%), and cardiac anomalies (9.5%).

In the 52 fetuses with congenital hydrocephalus, 24 fetuses were diagnosed with isolated hydrocephalus and 28 fetuses were diagnosed with non-isolated hydrocephalus. The MCA Doppler blood flow was abnormal (absent or reversed diastolic flow) in 9 fetuses, in 4 fetuses with isolated hydrocephalus (Fig. 1) and in 5 fetuses with non-isolated hydrocephalus (Fig. 2). All live newborns were admitted to the NICU. The total perinatal mortality rate was 40.4% (21/52) including fetal and neonatal deaths.

By the evaluation of the three suggested ultrasound markers in relation with perinatal mortality rates; CMT of less than 10 mm and abnormal MCA Doppler were significantly associated with higher perinatal mortality rates, *P* values were <0.001 and relative risks were

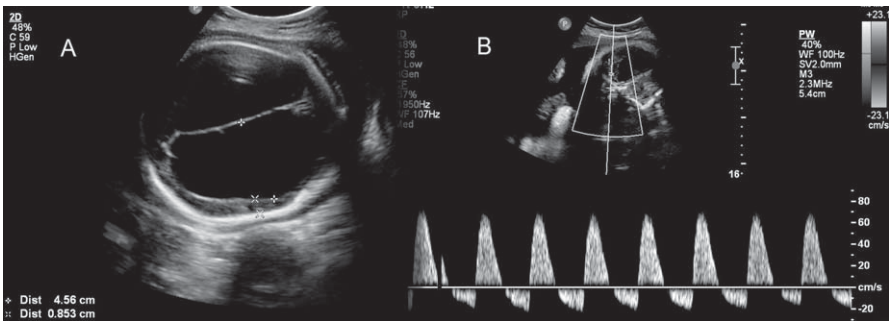


Fig. 1. Ultrasound images of fetus with isolated hydrocephalus, A: cortical mental thickness of 8.5 mm. B: middle cerebral artery Doppler blood flow showing reversed diastolic flow.

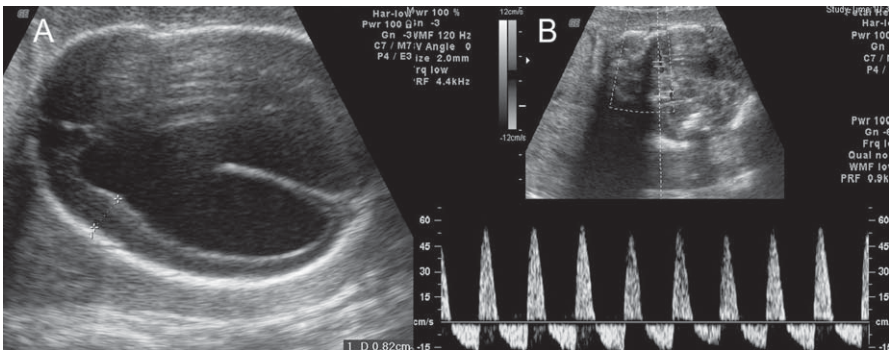


Fig. 2. Ultrasound images of fetus with hydrocephalus and multicystic kidneys, A: cortical mental thickness of 8.2 mm. B: middle cerebral artery Doppler blood flow showing reversed diastolic flow.

Table 2
Congenital hydrocephalus perinatal mortality rate in relation to the three suggested prognostic markers; other associated congenital anomalies, cortical mental thickness (CMT), and middle cerebral artery (MCA) Doppler

| Abnormality findings | Mortality | | RR | *P* value |
|---|---|---|---|---|
| Hydrocephalus (*N* = 52) | Isolate | Non-isolate | | |
| | 7/24 (29.3%) | 14/28 (50%) | 1.71 | 0.129 |
| Hydrocephalus (*N* = 52) | CMT >10 mm | CMT <10 mm | | |
| | 3/22 (13.6%) | 18/30 (60%) | 4.42 | <0.001 |
| Hydrocephalus (*N* = 52) | MCA normal | MCA abnormal | | |
| | 12/43 (27.9%) | 9/9 (100%) | 3.58 | <0.001 |
| Severe hydrocephalus | Isolated | Non-isolated | | |
| CMT <10 mm (*N* = 30) | 6/13 (46.2%) | 12/17 (70.6%) | 1.53 | 0.176 |
| Severe hydrocephalus | MCA normal | MCA abnormal | | |
| CMT <10 mm (*N* = 30) | 9/21 (42.9%) | 9 /9 (100%) | 2.33 | 0.003 |

Data are presented in numbers (%); RR: relative riak.

4.42 and 3.58 respectively. The association of congenital hydrocephalus with other congenital anomalies was not significantly associated with increases perinatal mortality rate, *P* values was 0.129 with a relative risk of 1.71. The details of prenatal mortality rates for isolated hydrocephalus and non-isolated hydrocephalus in relation to CMT and MCA Doppler blood flow are shown in Table 2.

In the subgroup of 30 fetuses with severe hydrocephalus with CMT less than 10 mm, 13 fetuses had isolated hydrocephalus and 17 fetuses had non-isolated hydrocephalus, the perinatal mortality rates was not significantly increased with associated congenital anomalies, the *P* values was 0.176 with a relative risk of 1.53. In the same subgroup, MCA Doppler was normal in 21 fetuses and abnormal in 9 fetuses, the perinatal mortality rate was significantly higher with abnormal MCA Doppler blood flow, the *P* values was 0.003 with a relative risk of 2.33, Table 2.

## 4. Discussion

Women's Specializes Hospital, King Fahad Medical City is a tertiary referral centre for the ministry of health, receiving referrals from all over Saudi Arabia. The marked high prevalence of congenital hydrocephalus in our study in comparison to the internationally published reports could be explained by several reasons; first, KFMC is a referral centre for Saudi Arabia, second, consanguinity rate was high in our study population that may add an unknown genetic factors, and third, termination of pregnancy of congenitally malformed fetuses is not practiced in our community.

In cases of congenital hydrocephalus, the dilated ventricular system containing an excessive amount of cerebrospinal fluid (CSF) leads to increased intracranial pressure, which results in thinning of the cerebral mantle. With the increasing intracranial pressure, the vascular system is compressed, and the venous pressure increases, resulting in a decrease in end-diastolic flow in cerebral vessels and ischemia caused by decreasing cerebral perfusion pressure [6]. We excluded the cases of Dandy-Walker malformations, arachnoid cysts, and encephalocele, because those cases have poor prognosis. Mixing those heterogeneous groups of fetuses with fetuses with hydrocephalus secondary to increased intracranial pressure will affect the results, because we are looking for markers of poor perinatal prognosis in fetuses with hydrocephalus that generally have a favorable prognosis.

In healthy fetuses, the diameter of the middle cerebral artery (MCA) increases with advancing gestation and there is a continuous forward flow in the all the cerebral arteries throughout the cardiac cycle even during diastole [7, 8]. Abnormal MCA Doppler blood flow as absent or reversed diastolic flow was reported to be a benign transient event except in one case where persistent reversed diastolic flow proceeded intrauterine fetal death [9]. In a severely growth-restricted fetus, reverse flow in the MCA was reported as one of the terminal hemodynamic events that preceded fetal death [10].

The prognosis of fetuses with congenital hydrocephalus is variable. For neonates with congenital hydrocephalus, a favorable outcome is expected in patients with a CMT of two cm and more [11]. On the other hand, there are no specific criteria or indicators to predict postnatal prognosis during antenatal evaluation. The association of other congenital anomalies with hydrocephalus and fronto-parietal CMT was suggest as prognostic indicators for perinatal outcome. However, the ratio of the size of the lateral ventricles to CMT was found to be weak indicator for long-term prognosis [12].

Trans cranial Doppler (TCD) has been investigated widely in pediatric and adult patients. In children with hydrocephalus, TCD was an effective method to evaluate cerebral circulation and increased intracranial pressure [13]. In adult patients, TCD of cerebral vessels is a useful and valid method for the confirmation of cerebral circulatory arrest [14]. Abnormal MCA Doppler blood flow, absent or reversed end diastolic flow, has been reported as features of brain death or vegetative state [15]. More studies showed that reversed flow in the MCA often preceded loss of brain stem function, reliably predictive of brain death [16] and is considered as characteristic of cerebral circulatory arrest. The specificity of TCD examination of the MCA in confirming brain death was reported to be 100% [17].

The antenatal diagnosis of congenital hydrocephalus carries poor prognosis, with higher perinatal mortality rate if associated with other anomalies, although it was not statistically significant, it is clinically significant. The same result was reported recently, that severe ventriculomegaly carries poor prognosis and associated anomalies worsened the prognosis.

Although CMT less than 10 mm was associated with higher perinatal mortality rate, it was clinically difficult to acquire especially when the intracranial anatomy was severely disturbed. The finding of abnormal MCA Doppler blood flow was significantly associated with higher perinatal mortality rate (100%). MCA Doppler blood flow sampling was relatively easy even with disturbed intracranial morphology. To our knowledge, this is the first study reporting abnormal MCA Doppler blood flow (absent/reverse diastolic flow) in fetuses with congenital hydrocephalus. Even though, the results were statically significant, we believe that further studies are needed to evaluate the same result.

The assumption that severe dilatation of the fetal ventricles leads to increased intracranial pressure and increased resistance to the cerebral blood flow which disrupts cerebral perfusion, seems to be confirmed by the presence of abnormal Doppler blood flow in such cases. Our data goes in favor of poor prognosis, as all fetuses with abnormal MCA Doppler blood flow died in the early neonatal period. We believe that MCA Doppler blood flow should be used as an assessment parameter during antenatal evaluation of fetuses with hydrocephalus or other intracranial anomalies. Further larger studies are needed to evaluate these findings.

## 5. Conclusion

Congenital hydrocephalus is common in our tertiary center population with high perinatal mortality rates. Persistent abnormal MCA Doppler blood flow (Absent/reversed diastolic flow) in fetuses with congenital hydrocephalus is a sign of poor prognosis and an indicator for fetal and perinatal mortality.

## Financial disclosure statment

All the authors have no potential conflicts of interest in this study.

## References

[1] Willems PJ, Brouwer OF, Dijkstra I, Wilmink J. X-linked hydrocephalus. Am J Med Genet 1987;27:921-8.
[2] Schrander-Stumpel C, Fryns JP. Congenital hydrocephalus: Nosology and guidelines for clinical approach and genetic counseling. Eur J Pediatr 1998;157:355-62.
[3] Blackburn BL, Fineman RM. Epidemiology of congenital hydrocephalus in Utah, 1940–1979: Report of an iatrogenically related epidemic. Am J Med Genet 1994;52:123-9.
[4] Mari G, Deter RL, Carpenter RL, Rahman F, Zimmerman R, Moise KJ, et al., Noninvasive diagnosis by Doppler ultrasonography of fetal anemia due to maternal red-cell alloimmunization. Collaborative group for Doppler assessment of the blood velocity in anemic fetuses. N Engl J Med 2000;342:9-14.
[5] Fong KW, Ohlsson A, Hannah ME, Grisaru S, Kingdom J, Cohen H, et al., Prediction of perinatal outcome in fetuses suspected to have intrauterine growth restriction: Doppler US study of fetal cerebral, renal, and umbilical arteries. Radiology 1999;213:681-9.
[6] Duschek S, Schandry R. Reduced brain perfusion and cognitive performance due to constitutional hypotension. Clin Auton Res 2007;17:69-76.
[7] Mari G, Adrignolo A, Abuhamad AZ, Pirhonen J, Jones DC, Ludomirsky A, et al., Diagnosis of fetal anemia with Doppler ultrasound in the pregnancy complicated by maternal blood group immunization. Ultrasound Obstet Gynecol 1995;5: 400-5.

[8] Harrington K, Carpenter RG, Nguyen M, Campbell S. Changes observed in Doppler studies of the fetal circulation in pregnancies complicated by pre-eclampsia or the delivery of small or gestational age baby. I. Cross-sectional analysis. Ultrasound Obstet Gynecol 1995;6:19-28.

[9] Respondek M, Woch A, Kaczmarek P, Borowski D. Reversal of diastolic flow in the middle cerebral artery of the fetus during the second half of pregnancy. Ultrasound Obstet Gynecol 1997;9:324-9.

[10] Sepulveda W, Shennan AH, Peek MJ. Reverse end-diastolic flow in the middle cerebral artery: An agonal pattern in the human fetus. Am J Obstet Gynecol 1996;174:1645-7.

[11] Jamjoom AB, Khalaf NF, Mohammed AA, Jamjoom ZA, Kashoggi TY, Abdelbasit OB, et al., Factors affecting the outcome of foetal hydrocephaly. Acta Neurochir (Wien) 1998;140:1121-5.

[12] Levitsky DB, Mack LA, Nyberg DA, Shurtleff DB, Shields LA, Nghiem HV, et al. Fetal aqueductal stenosis diagnosed sonographically: How grave is the prognosis? AJR Am J Roentgenol 1995;164:725-30.

[13] Ahmad I, Wahab S, Chana RS, Khan RA, Wahab A. Role of Transcranial Doppler and Pressure Provocation in Evaluation of Cerebral Compliance in Children with Hydrocephalus. HK J Paediatr (New Series) 2008;13:110-5.

[14] Azevedo E, Teixera J, Neves JC, Vaz R. Transcranial Doppler and brain death. Transplant Proc 2000;32:2579-81.

[15] Shan G, Yining H, Xia H, Yicheng Z, Bo W, Shunwei L. Transcranial Doppler characteristic in persistent vegetative status, locked-in syndrome and brain death. Chin Med Sci J 1999;14:211-4.

[16] Shiogai T, Sato E, Tokitsu M, Hara M, Takeuchi K. Transcranial Doppler monitoring in severe brain damage: Relationships between intracranial haemodynamics, brain dysfunction and outcome. Neurol Res 1990;12:205-13.

[17] Kuo JR, Chen CF, Chio CC, Chang CH, Wang CC, Yang CM, et al., Time dependent validity in the diagnosis of brain death using transcranial Doppler sonography. J Neurol Neurosurg Psychiatry 2006;77:646-9.