Original Article

Management and Outcomes of Fetal Hydrops in a Tertiary Care Centre in Singapore

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Abstract

Introduction: Fetal hydrops is a serious condition which can be caused by immune and non-immune aetiologies. We aimed to review the management of fetal hydrops at our hospital. **Materials and Methods:** A retrospective review of all cases of fetal hydrops diagnosed in our institution from 2006 to 2013 was carried out. **Results:** Out of the 30 cases of fetal hydrops diagnosed antenatally, 17 were cases of Bart's hydrops which were all terminated in-utero. Of the remaining 13 cases, 11 cases consisted of non-immune causes of hydrops. Planned antenatal interventions including in-utero blood transfusions (n = 4) and thoracentesis (n = 5) as well as planned caesarean deliveries (n = 11) were performed in the majority of cases. Postnatal neonatal intensive care with interventions including chest drainage and transfusions were also performed. A majority, 92%, of the cases survived the perinatal period following a variable length of hospital stay ranging from a week to 3 months. **Conclusion:** Management of fetal hydrops is complex. Close coordination between the obstetric and neonatal teams was the key to good short-term survival of neonates with antenatally diagnosed hydrops, as it allows timely antenatal intervention and anticipation of potential perinatal complications.

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Introduction

Fetal hydrops, or hydrops fetalis, is a serious antenatal finding, with several studies around the world quoting similar perinatal survival rates of only 40% to 50%.[1-5] It indicates the presence of excessive fluid in 2 or more fetal compartments, which can include the abdominal cavity, pleural space, pericardial space, and subcutaneous tissue. The aetiology can be divided into immune and non-immune causes. Immune-mediated hydrops fetalis is typically due to fetal anaemia resulting from red blood cell alloimmunisation between mother and fetus.[3] Non-immune hydrops, on the other hand, is defined as the presence of fetal subcutaneous tissue oedema associated with a significant effusion in one or more cavities in the absence of atypical red cell antibodies[2] and has been the main cause for fetal hydrops for more than a decade.[1,3,6] Common causes include fetal cardiac arrhythmias, vascular and lymphatic malformations causing circulation obstruction, chromosomal abnormalities and metabolic conditions such as lysosomal storage diseases.[7,8]

Despite the ability to identify this condition early from the antenatal period, the morbidity and mortality rates from hydrops fetalis reported in current literature are often significant. However, with the advent of in-utero fetal therapy, the experience in our centre has been different, with positive outcomes in most of our cases of non-immune hydrops, apart from those with Bart's hydrops. This prompted us to do a detailed retrospective case series study, in an attempt to review the outcomes of in-utero treatment of fetal hydrops from our hospital. We hoped to understand the strength in our areas of management of hydrops fetalis

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that could be pivotal in positively influencing survival outcomes for these children.

Materials and Methods

We conducted a retrospective review of all the cases of fetal hydrops diagnosed via antenatal ultrasound at the Fetal Care Centre in National University Hospital (NUH) from 2006 to 2013. Cases were obtained from the database of records from the Obstetrics and Gynaecology Department, NUH, which is a tertiary referral centre. The approval from the Domain Specific Review Board (DSRB) was obtained for the study.

Of the total of 30 cases of hydrops diagnosed, 17 pregnancies were cases of Bart's hydrops, due to alpha thalassaemia major. These 17 cases were terminated in-utero after confirmation of the Bart's hydrops with genotyping performed prior to the development of hydrops. The case records of the remaining 13 cases were then studied in detail from diagnosis to the perinatal period until discharge or death of the infant. None of these 13 cases defaulted or were delivered in another healthcare institution, hence there were no dropouts.

Identification of Hydrops

Antenatal scans were performed by trained ultrasonographers who are either certified by the American Registry for Diagnostic Medical Sonography (ARDMS) or who hold a diploma in Diagnostic Medical Ultrasound (DMU). The scans were performed using either General Electrics (GE) Voluson 730 Expert or GE Voluson E8 machines, both of which are manufactured in California, United States of America. Scans performed were then verified by the consultant obstetricians (Wong YC or Biswas A). Inclusion criteria for the 13 cases were ultrasound findings of excessive fluid in at least 2 preformed spaces of the fetus (ascites, pleural effusion or pericardial effusion), or fluid in 1 preformed space associated with skin oedema.

Antenatal Investigations to Identify Aetiology

Maternal medical and past obstetrical histories were reviewed for possible aetiologies for hydrops. Maternal antenatal testing results were reviewed and these included tests for in-utero infections such as tests for hepatitis B (HBsAg, HBeAg), human immunodeficiency virus (HIV) via antigen-antibody screen, syphilis (VRDL and TPR) and TORCH screen (comprising serology for antibodies against toxoplasmosis and rubella, PCR for cytomegalovirus and for herpes simplex). Other maternal results reviewed included maternal tests for anaemia, thalassaemia, blood group, rhesus typing and also antibody titres that were

performed routinely.

Fetal antenatal investigations reviewed included chromosomal karyotype in the survivors and thalassaemia genotyping obtained via chorionic villus blood sampling for those with Bart's hydrops. Antenatal ultrasound assessments were reviewed for any possible structural abnormalities, in particular major cardiac malformation and cardiac rhythm abnormalities and other structural malformation in the thoracic and also renal malformations were performed for all cases. In cases with anaemia, fetal doppler assessment of blood velocity in the fetal middle cerebral arteries (MCA) was used for assessment. Cordocentesis was performed in all those cases with fetal anaemia when the peak systolic velocity of the MCA exceeds more than 1.5 MoM (multiple of median). Confirmation of fetal anaemia and investigations to determine the aetiology of the anaemia were performed prior to blood transfusions. Placental abnormalities were also examined to determine potential causes of hydrops. Follow-up ultrasounds were performed 2 to 4 weekly to monitor the fetal condition in-utero and the progression of the hydrops, depending on the in-utero treatment required. In addition, the various in-utero treatments undertaken were also reviewed.

Neonatal Investigations and Data Collection

The neonatal medical records were reviewed to identify the possible aetiology of hydrops, the perinatal resuscitation required and outcomes such as Apgar scores and level of metabolic acidaemia on blood gas, neonatal course and ventilation mode required, postnatal evaluation and investigations, the treatment required including blood transfusion, thoracocentesis and surgical treatment if needed, the length of stay and eventual survival outcome. None were first diagnosed postnatally as neonatal intensive care admission records for the last 7 years were also counter-checked to identify any undiagnosed cases. Laboratory investigations performed in the neonate to determine the aetiologies of hydrops were also reviewed and these included full blood count, rhesus and blood type, liver function tests, urea, creatinine and also assessment for TORCH and parvovirus infections. Neonatal procedures reviewed included cardiac assessment including echocardiography and cardiac rhythm monitoring. Chest x-rays and pleural fluid, if present, were sent to determine for triglycerides, protein analysis and microbiology. Abdominal x-rays and contrast studies were performed for those with suspected gut atresia prior to surgical explorations.

Statistical Analysis

Statistical analysis was performed using SPSS version 20 from IBM. Continuous data were described as mean
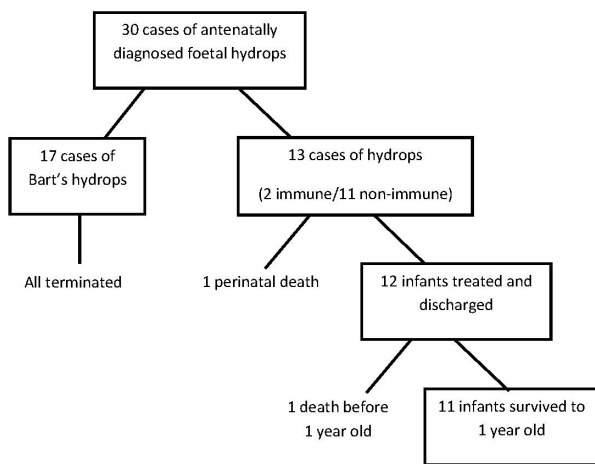
Fig. 1. Chart showing the study subjects.

with its standard deviation or median with appropriate range, while absolute and relative frequencies were used for categorical values. Chi square tests were performed to compare the dichotomous data between the fetus received in-utero therapy and those that did not. Descriptive data was presented for the comparison with the other 2 published studies. A *P* value of less than 0.05 was considered to be statistically different.

Results

Antenatal Diagnoses and Management

Of the 30 cases of hydrops, the most common aetiology was found to be due to Bart's hydrops, as confirmed on chorionic villus sampling and genetic sequencing for alpha thalassaemia in 17 cases (56.7%) (Fig. 1). These 17 cases were terminated in-utero.

All of the remaining 13 cases of fetal hydrops were delivered at late preterm period. Demographics of the neonates at birth are shown in Table 1. Diagnosis was made via ultrasonography, at variable gestational ages, with some cases occurring late in pregnancy, whereas others were cases booked initially in another antenatal centre and referred to our centre upon identification of hydrops. Amniocentesis was performed for fetal karyotyping in 84.6% of cases, with no chromosomal abnormalities identified in the cases studied.

There was no dropout, thus the data of all 13 cases of hydrops diagnosed antenatally or referred to our centre were used for analysis in the current study.

The majority of cases (n = 11, 84.6%) were born via lower segment caesarean section (LSCS). These included elective planned caesarean sections, and also emergency cases as indicated by maternal and fetal conditions. The mean gestation age of these newborns was 34.6 weeks (range:

31.3 to 39.2 weeks). Causes of hydrops were predominantly non-immune in origin, of which chylothorax was found to be the most common (36.4%). Chylothorax was confirmed on postnatal testing of the fluid composition and no infective aetiologies were detected. Specific testing for associated conditions such as Noonan syndrome and lymphangiogram were not performed as none of the infants were dysmorphic and the chylothorax resolved with time. Two infants with separate diagnoses of chylothorax and congenital dyserythropoietic anaemia were born to mothers who were chronic hepatitis B carriers; 3 fetuses with chylothorax and 2 with pulmonary sequestration underwent a total of 3 to 6 in-utero thoracentesis for pleural effusion. Four cases of anaemia were found in fetuses with diagnoses of rhesus isoimmunisation (n = 2), congenital dyserythropoietic anaemia (n = 1) and midgut atresia (n = 1). These fetuses with anaemia were given in-utero packed cell transfusion

Table 1. Demographic Characteristic of Infants with Fetal Hydrops Delivered

Characteristics	n = 13
Gender – male/female (n, %)	7/6 (53/47)
Gestational age at birth (mean, range in weeks)	34.6 +/- 2.8 (31.3 to 39.2)
Antenatal procedure (diagnostic intent)	
Amniocentesis (n, %)	11 (84.6)
Aetiology of hydrops	
Immune (n, %)	2 (15.4)
Rhesus isoimmunisation	2
Non-immune (n, %)	11 (84.6)
Congenital dyserythropoietic anaemia	1
Chylothorax	4
Pulmonary sequestration	2
Gut atresia (midgut, ileal, colonic)	3
Intrauterine growth restriction (due to maternal preeclampsia)	1
Birth weight (mean,+/-SD, range in g)	2572 +/- 677 (1479 to 3725)
Antenatal procedures (therapeutic intent)	9 (69.2)
Packed cell transfusions	4 (30.8%)
Thoracentesis	5 (38.5%)
Mode of delivery	
Lower section caesarean section (LSCS, %)	11 (84.6)
Normal vaginal delivery (NVD, %)	2 (15.4)
Median Apgar score at 5 minutes (range)	9 (5-9)
Mean base excess within 1st hour of life	-4.2 +/- 4.2 (-13 to 1)
Resuscitation required at birth (n, %)	3 (23.1)
Outcomes	
Death before discharge	1 (7.7)
Survived until discharge (n, %)	12 (92.3)
Survivors at 1 year of age (n, %)	11 (84.6)

(PCT) using O negative type blood at intervals of 3 to 5 weeks, with the median number of 3 PCTs given to each fetus. The remaining 4 fetuses were diagnosed with fetal hydrops late in the course of the pregnancy, and antenatal interventions could not be administered in time prior to delivery. Of these 4 fetuses, 1 had intrauterine growth restriction associated with maternal preeclampsia.

Prior to the planned date of delivery, these cases were discussed at a multidisciplinary meeting involving the neonatal and obstetrics team. Discussion was made with regards to the antenatal interventions performed, the optimal delivery time after antenatal intervention when possible and the planned neonatal resuscitation team at delivery. Regular updates were made by the obstetrics team with the neonatal team, in order to allow the neonatal team to anticipate and prepare for stabilisation of the hydropic fetus at birth. In addition, at least 2 neonatal specialists skilled in resuscitation were available during the planned delivery.

Perinatal Management

At birth, 3 neonates (23.1%) required aggressive resuscitation including cardiopulmonary resuscitation (CPR), use of adrenaline and mechanical ventilation for support. Subsequent management of the remaining neonates involved a prolonged stay in the neonatal unit, with a mean duration of 26.5 days of hospitalisation (range 7 to 69 days). Respiratory issues were a major concern for these neonates in the perinatal period. Mechanical ventilation was required in the majority of patients eventually over the course of their stay (n = 11, 84.6%), with 1 infant having severe respiratory compromise requiring escalation of support with high frequency oscillatory ventilation. Seven neonates (53.8%) required postnatal thoracocentesis; these included 4 of the 5 infants who had previously undergone antenatal thoracocentesis. All 3 infants with gut atresia received complete surgical repair and recovered from the procedure prior to discharge. Somatostatin and total parenteral nutrition was used to treat the infants with chylothorax. One neonate with chylothorax unfortunately passed away after a day in the neonatal intensive care unit despite extensive antenatal and postnatal interventions including thoracocentesis. The cause for demise was a combination of respiratory insufficiency and inability to support ventilation, and prematurity (child was born the most premature amongst the 13 cases, at 31 weeks and 3 days).

Comparison of Outcomes between Groups of Subjects With and Without Antenatal Interventions

Infants who received antenatal interventions tended to be slightly more mature, with the median gestational age at 35.0 weeks which is 1 week more than those infants who

did not receive interventions antenatally (*P* = 0.35). The former group also tended to be heavier with a mean weight of 2705 g (compared with 2207 g in the latter group) (*P* = 0.30), and had better perinatal outcomes (as represented by higher Apgar score at birth and lower acidosis recorded) (*P* = 0.23) without needing aggressive resuscitation (Table 2). Nevertheless, the combined outcomes in infants of both groups remained good, with a high survival rate until discharge of 92.3% (12 out of 13 infants).

Outcomes following Discharge from Neonatal Unit

Of the 12 infants who survived until discharge, 1 infant with congenital dyserythropoietic anaemia passed away before the age of 1 year due to sepsis with liver failure. Another infant left Singapore and was lost to follow-up, but was noted to have been well during the last outpatient review in our centre. The remaining 10 infants (76.9%) were followed up until 1 year of age and were noted to have good overall outcomes, with no significant neurological impairment.

Discussion

In our study, the most common cause of fetal hydrops in our centre was Bart's hydrops. The parents were alpha-thalassaemia trait carriers. However, all of these pregnancies did not survive beyond the antenatal period due to termination of pregnancy. These pregnancies were terminated after detailed counselling by the obstetrics team with the expecting parents due to potentially life threatening maternal complications and extremely poor prognosis and invariable death of the fetus in-utero or shortly after birth.[9]

Of the remaining cases, non-immune hydrops remained the predominant cause (84.6%), with chylothorax being at the top of the list of non-immune aetiologies. Other causes

Table 2. Comparison of Characteristics of Neonates with Fetal Hydrops Requiring Antenatal Interventions and Not Requiring the Antenatal Intervention

Demographics (n = 13)	No In-Utero Intervention (n = 4)	In-Utero Intervention (n = 9)	*P* Value
Gender, males (%)	1 (25)	6 (66.7)	0.27
Mean gestational age (weeks)	33.9	35.0	0.35
Mean birth weight (g)	2274	2705	0.30
Aggressive resuscitation (%)	50.3	11.1	0.23
Median Apgar score (5 minutes)	7	9	0.68
Mean base excess (first blood gas)	-6.3	-3.3	0.20

included congenital dyserythropoietic anaemia, pulmonary sequestration, gut atresia involving the small and large bowel, and maternal preeclampsia (or Mirror syndrome). The predominance of non-immune causes for hydrops is similarly found in the Turkish review done by Takci et al,[1] which was a large retrospective review performed in recent years to investigate mortality risk factors in fetal hydrops and also in a recent Chinese retrospective study done by An X et al.[10] The encouraging results of decreasing numbers of immune-related hydrops is proof of the success of widespread efforts in recent years in identifying rhesus negative mothers early in pregnancy, and the widespread and appropriate use of anti-D immunoglobulins to reduce isoimmunisation in these rhesus negative mothers.[11,12]

We compared our findings with 2 studies done over the same period, namely that of Takci S et al,[1] who studied 62 cases of hydrops fetalis in the Turkish centre of Hacettepe University Ihsan Dogramaci Children's' Hospital from 2002 to 2011 and Ng et al[4] who studied 23 cases of non-immune fetal hydrops in our local population in Singapore from 2005 to 2010 (Tables 3 and 4). The demographics of the neonates such as gender distribution, gestational age at birth and birth weight were generally similar in the 2 published studies, and both studies focused on non-immune cases of hydrops fetalis, as in the current study.

In all 3 studies, LSCS was the predominant mode of delivery. Aggressive resuscitation was required in the majority of cases as evident from most studies with rates

in our centre (23.1%). Postnatal interventions used by our centre were also common in other centres, especially in the support of the respiratory system. This is evident from the high percentage of mechanical ventilation rates required in all 3 centres, with rates of up to 84.6% shown in our study and in the study by Takci S et al.[1]

Factors affecting survival are many, with some studies attributing aetiology of the hydrops as a main prognostic factor for survival[4] while other studies suggest that the severity of disease, indicated by the number of fluid collection sites, is a main factor in predicting the risk of neonatal deaths.[5,13] Importantly, the condition of the newborn infant, including gestational age at birth is key to the prediction of survival.[4] Prematurity is known to be one of the poor prognostic factors.[5] The latter 2 causes are amenable to interventions by the neonatal and obstetrics team taking care of the mother and unborn child.

The antenatal interventions could play a role in improving survival; 69% of our cases had in-utero blood transfusions for anaemia or thoracocentesis for pleural effusions. This is comparable to 58% of antenatal interventions for the fetuses with hydrops in Takci et al's study.[1] Importantly, with these antenatal interventions used in our study, the extravascular fluid collections were reduced to decrease the risk of spontaneous preterm delivery, which is likely the contributing cause to our infants being born at more matured gestational age closer to late preterm. The long-term positive impact on fetal growth was also significant, as

Table 3. Comparison of Demographic Characteristics of Liveborns with Fetal Hydrops in the Perinatal Period with Published Studies

Demographics	NUH (n = 13)	Takci, et al (n = 62)[*]	Ng, et al (n = 19)[†]
Males (%)	53.8	46.8	68
Mean gestational age (wks)	34.6 ± 2.8	33.1 ± 2.9	33
Mean birth weight (g)	2572 ± 677	2350 ± 640	2480[‡]
Mode of delivery (NVD/LSCS [% LSCS])	2/11 (84.6)	9/53 (85%)	7/12 (63%)
Aggressive resuscitation at birth i.e. mechanical ventilation/CPR/drugs (%)	23.1	72.6	89
Median Apgar score (5 minutes)	9	5.7	7

CPR: Cardiopulmonary resuscitation; LSCS: Lower segment caesarean section; NUH: National University Hospital; NVD: Normal vaginal delivery
[*]Takci S, Gharibzadeh M, Yurdakok M, Ozyuncu O, Korkmaz A, Akcoren Z, et al. Etiology and outcome of hydrops fetalis: report of 62 cases. Pediatr Neonatol 2014;55:108-13.
[†]Ng ZM, Seet MJ, Erng MN, Buendia F, Chang AS, Sriram B. Nonimmune hydrops fetalis in a children's hospital: a six-year series. Singapore Med J 2013;54:487-90.
[‡]Median.

Table 4. Comparison of Postnatal Interventions Used

Intervention	NUH (n = 13)	Takci, et al (n = 62)[*]	Ng, et al (n = 19)[†]
Thoracentesis (%)	53.8	50.0[‡]	57.9
Ventilation (%)	84.6	88.7	57.9
HFOV (%)	7.7	27.1	36.8
PCT (%)	30.8	50.0	-
Mean length of stay (days)	26.5	8.5	-

HFOV: High frequency oscillatory ventilation; NUH: National University Hospital; PCT: Packed cell transfusion
[*]Takci S, Gharibzadeh M, Yurdakok M, Ozyuncu O, Korkmaz A, Akcoren Z, et al. Etiology and outcome of hydrops fetalis: report of 62 cases. Pediatr Neonatol 2014;55:108-13.
[†]Ng ZM, Seet MJ, Erng MN, Buendia F, Chang AS, Sriram B. Nonimmune hydrops fetalis in a children's hospital: a six-year series. Singapore Med J 2013;54:487-90.
[‡]Data provided in Table 3 of the original paper stated "thoracoparacentesis and/or blood transfusion at birth". A total tally of these 2 procedures was provided.

transfusions to correct fetal anaemia helped to reduce effect of heart failure and perpetuation of the hydropic state in the fetus, and also helps to ensure oxygen delivery to growing organs during the crucial developmental period in-utero. Thoracocentesis, on the other hand, reduces the restriction of growth of the developing fetal lungs caused by pleural effusion, minimising the outcome of lung hypoplasia in these infants. These interventions were repeated as required for the fetus since no premature labour was being triggered as a result of these procedures, proving that these essential procedures can be done safely with adequate expertise to improve the survival rates of infants with hydrops. Antenatal steroids were also administered to the mothers during pregnancy, to improve lung maturity, as preterm delivery of the fetuses with hydrops was anticipated. The overall lower rates of perinatal resuscitation required in the group who did not receive antenatal interventions compared to those who had some form of antenatal interventions for their hydrops condition (Table 2) is testament to the positive impact that antenatal interventions can make on the perinatal condition of the child, which again is pivotal in influencing the overall survival outcome. We do, however, understand that antenatal interventions performed may not be curative as evident in our study in which further thoracocentesis were required even in those infants who had already received antenatal thoracocentesis for chylothorax.

The timeliness of interventions could also have played a significant supporting role. A study by Zohra Hasnani-Samnani et al[14] looking at non-immune cases of hydrops in Qatar from 2003 to 2011 showed a high perinatal mortality rate, with 10 out of 64 births, or 16%, surviving beyond the delivery and 40% of the surviving newborns passing away within the first 6 months. Of note, 8.6% of these cases of hydrops diagnosed antenatally had been monitored closely without immediate intervention, and had eventual spontaneous resolution of symptoms. Within this group, there was an eventual demise of a fetus at 33 weeks due to intrauterine death despite the resolution of hydropic appearance on ultrasound. All in all, only 2 cases of antenatal interventions were performed.[14] This suggests that the decision on how soon the interventions ought to be performed following identification of features of hydrops on antenatal scan may influence the eventual survival outcome of these infants. In our centre, we intervene within 2 weeks of diagnosis of hydrops on antenatal ultrasound. The significantly higher rates of intervention noted in our study implies the aggressiveness and speed in instituting treatment for the fetuses at our centre, which are again important considerations for the eventual positive outcome of our hydropic fetuses.

Another possible factor that was likely to contribute to the good early survival rates was the immediate postnatal management of these infants. The median 5-minute Apgar score for our neonates with hydrops was 9. Looking at the perinatal conditions including mode of delivery and rate of aggressive resuscitation, we noted that the high rates of planned caesarean section, along with resuscitation at birth contributed hand-in-hand to provide a good immediate postnatal outcome for our neonates with hydrops. Following the immediate resuscitation, the subsequent management of the newborn was also equally important, as evident by the common use of interventions including mechanical ventilation (conventional, and high frequency oscillatory ventilation), thoracocentesis for persistent effusions to improve respiratory status and transfusions for anaemia across the 3 centres including ours. We postulate that there may be reduced necessity for postnatal interventions following the high rates of antenatal interventions that could have already positively modulated earlier issues such as pleural effusion and pulmonary hypoplasia.

Importantly, all these interventions were possible as there was close and frequent antenatal follow-up ultrasound assessment of the cases, availability of antenatal fetal interventions, and involvement of neonatologists early in the care of the cases of fetal hydrops upon diagnosis. Contribution of expertise from both the obstetrics and neonatology teams were evident from frequent discussion about the planned antenatal procedures to improve perinatal outcome, and expected condition of the fetuses at birth. The neonatologists were frequently and regularly updated on the progress of the fetus antenatally, allowing them to have a good grasp of the condition of the hydropic neonate at birth. The planning of expected perinatal procedures was possible as a result, allowing adequate nursing and medical staff in both the neonatal and obstetrics team to be available on the expected day of delivery, as well as ensuring equipment for procedures such as thoracocentesis and ventilator support were all ready for use during the same period. In addition, it was helpful for the expectant mothers who had gone through a trying pregnancy with a fetus with hydrops to meet the neonatal teams early, so that early rapport could be established. All these were possible through the combined efforts of both the obstetric and neonatal teams in our centre.

We demonstrated good long-term outcome in our centre, having 84.6% of the neonates surviving to at least 1 year of age with no neurological impairment. This is encouraging, and goes to show how good immediate outcome can have a pivoting role in determining the prognosis for the fetuses with hydrops. Antenatal interventions in-utero may contribute to this and do not negatively impact on the eventual neurological outcome of the child.[15]

Despite the encouraging rates that our retrospective study showed, a major limitation of our study was the small number of cases we gathered in these 8 years, which limited the

statistical power of our results, limiting our comparisons of the in-utero interventions given. The cases of Bart's hydrops terminated were also significant at 56.7%, which again limited the actual number of cases being studied till perinatal period. In addition, as this was a retrospective study, the interventions were not randomised to determine its efficacy. In any case, as some of these antenatal interventions are life-saving, randomisation may not be feasible due to ethical reasons.

Another limitation affecting the survival rates in non-immune hydrops is related to the variable aetiologies in each study.[16] Our study consisted of mainly cases of chylothorax, which were not the predominant cause of non-immune hydrops in the other 2 centres that Takci S et al[1] and Ng et al[2] studied about. The specific aetiologies of hydrops are an important prognostic factor for survival,[9] and hence that was a significant limiting factor in our efforts to compare the survival rates of different studies.

As such, we hope to continue to evaluate more cases of hydrops in future studies, which would capture a broader range of aetiologies, with the aim of studying the benefit of each antenatal intervention in the management of fetal hydrops, as well as to follow-up in more detail the long-term neurodevelopmental outcomes of these surviving infants. Hydrops fetalis is a serious condition, yet it can be very amenable to antenatal and perinatal interventions that can alter the outcome of a child with such a condition. Much can be done to further improve practices that can alter the mortality and morbidity rates for these fetuses.

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