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Antenatal shunting and outcomes in fetuses with non-immune hydrops fetalis

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Abstract

Objectives: Hydrops fetalis is associated with high morbidity and perinatal mortality. The aim of our study was to compare the outcomes of infants who had non-immune hydrops fetalis (NIHF) who did or did not undergo antenatal shunting.

Methods: Between January 2014 and June 2023, 20 infants with the diagnosis of NIHF were admitted to the neonatal intensive care unit (NICU) at King's College Hospital NHS Foundation Trust. The criteria for antenatal shunt placement were development of hydrops fetalis, polyhydramnios due to oesophageal compression by a pleural effusion that would likely result in preterm labour or a large pleural effusion (no hydrops at presentation) resulting in likely inferior vena cava compression and significant risk of development of hydrops.

Results: The 20 infants had a median gestational age of 34 (27–40) weeks of gestation at delivery and were diagnosed at a median gestational age of 29 (17–40) weeks. Eight infants had a shunt inserted antenatally (six pleuro amniotic and two abdominal amniotic) and they delivered at a significantly later median gestational age (36 vs. 32.5 weeks, p=0.025). After adjustment for gestational age at delivery and antenatal severity, those who had a shunt placed were not more likely to be oxygen dependent at 36 weeks post menstrual age (PMA) and had a lower length of stay (23 vs. 95 days, p=0.019).

Conclusions: Infants who had NIHF and had antenatal shunting had favourable outcomes compared to those who did not, despite a more severe antenatal presentation.

Keywords: neonatal; perinatal; hydrops; antenatal intervention; shunt

Introduction

Hydrops Fetalis is diagnosed when there is excessive fluid accumulation in the foetus in two or more body compartments. It can be subdivided into immune hydrops fetalis (IHF), caused by red blood cell alloimmunization and nonimmune hydrops fetalis (NIHF) which encompasses all other aetiologies [1]. It has a prevalence of one in 1700–3000 pregnancies with an estimate in live born infants of one in 4000 [2]. It is associated with high morbidity and a perinatal mortality ranging from 35 to 98 % depending on the cause [2]. The causes of NIHF are varied (including cardiac, hematologic, infectious, neoplastic and chromosomal), but up to 20 % of cases are idiopathic. Fluid regulation in the fetus is disrupted by increased hydrostatic capillary pressure, reduction in plasma oncotic pressure, obstruction of lymphatic flow and/or increased capillary permeability [2]. The diagnosis is usually made antenatally by ultrasound. Management will depend on the cause and severity of the hydrops and can be treated with pleuroamniotic and abdominal shunt placements [3]. Thoracocentesis may be useful in diagnosing the aetiology of the hydrops and resulting in initial decompression of the lungs, but there is a high risk that the fluid will reaccumulate [4]. Studies have demonstrated significant advantages of pleuroamniotic shunt placements, particularly in reducing the risk of pulmonary hypoplasia and serious postnatal respiratory problems [5].

Some effusions may resolve spontaneously. Hydrops Fetalis, however, is associated with effusions that increase over time leading to oesophageal compression, polyhydramnios and a risk of preterm birth [4]. One study reported the outcomes of 88 fetuses with pleural effusions who underwent pleuroamniotic shunting. Sixty seven percent of the fetuses were hydropic; 71.4 % of fetuses whose hydrops resolved survived compared to only 35.5 % survival in those

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whose hydrops did not resolve. Those results indicate that resolution of hydrops, similar to increased gestational age at birth, is a significant predictor of survival [6]. A retrospective review of 132 fetuses with pleural effusions who underwent shunt insertion also demonstrated improved survival rates, with 65 % survival compared to only 12 % in untreated cases who developed hydrops [7]. Another study on the outcomes of fetal pleural effusions treated by pleuroamniotic shunting in 21 fetuses reported a 44 % survival rate among the 16 fetuses with hydrops;three of the five fetuses without associated hydrops survived [8]. In total, there were eight intrauterine deaths and three neonatal deaths. All 10 survivors were born after 32 weeks of pregnancy, indicating extension of the time spent in the uterus might be another benefit of pleuroamniotic shunting [8]. Four survivors, however, required chest drains postnatally and two of the 11 deaths were due to shunt complications [8]. It is, therefore, important to further determine if the placement of antenatal shunts does improve outcomes in hydropic fetuses. The aim of our study, thus, was to compare the outcomes of infants who had been hydropic *in utero* and did or did not undergo "shunting".

Methods

Between January 2014 and June 2023, 20 infants with the diagnosis of NIHF were admitted to the neonatal intensive care unit at King's College Hospital NHS Foundation Trust. Using the NIHR tool, this project was defined as an audit. The project was registered as an audit with King's College Hospital (Ref: CH197). The fetuses were diagnosed with NIHF if they had two or more of the following findings on antenatal ultrasound examination or at birth: ascites, pleural effusion, pericardial effusion and/or skin oedema.

The criteria for antenatal shunt placement were assessed subjectively by ultrasound as follows:

- Hydrops defined as accumulation of fluid in more than one cavity.
- Polyhydramnios due to oesophageal compression by the pleural effusion that would likely result in preterm labour. Polyhydramnios was defined as a deepest pool>8 cm (mild polyhydramnios 8–11 cm, moderate 12–15 cm, severe>16 cm). If polyhydramnios was mild 8–11 cm and the cervix was long and closed the ultrasound examination was repeated in a week to see progression before shunting. If the deepest pool was>11 cm then a shunt was inserted.
- Severe pleural effusion (no hydrops at presentation) or peritoneal ascities resulting in likely inferior vena cava compression and significant risk of development of hydrops. The severity was defined based on the lung compression and/or mediastinal shift.

All patients who had shunts placed had hydrops prior to delivery.

Antenatal data were collected from the maternal records and included demographic details, ultrasound reports, gestational age at diagnosis and which fetuses underwent shunt placements. To determine the severity of the hydrops, the number of body compartments with fluid accumulation was documented; severity was diagnosed if there were more than two compartments affected. Any genetic abnormalities and if a diagnosis regarding the aetiology of the hydrops was made before birth were documented. Complications were recorded (technical issue at the time of insertion, antenatal dislodgement/migration, premature rupture of membranes). Shunts were silicone double pigtailed shunts inserted under ultrasound guidance.

Postnatal data were obtained from the neonatal case records from which information on birth weight, whether surfactant was administered and the duration of invasive ventilation and supplementary oxygen support was obtained. The use of inotropes, the number of transfusions and the placement of drains postnatally were also documented. The length of hospital stay, corrected age and weight at discharge, as well as mortality rates and oxygen requirement at 28 days after birth and 36 weeks postmenstrual age (PMA) were also recorded.

Statistical analysis

The data were tested for normality using the Shapiro-Wilk test and were found to be non-normally distributed. The Mann Whitney U test and Chi-Squared test, therefore, were used to assess if differences were statistically significant. The significance level was set as $p<0.05$. Multiple regression analysis was used to adjust for demographic differences and confounding factors. Data were analysed using SPSS version 29.0.1.0.

Results

Twenty consecutive infants with NIHF were admitted to the neonatal unit. They had a median gestational age of 34 (27–40) weeks of gestation at delivery and were diagnosed at a median gestational age of 29 (17–40) weeks. Eight infants had antenatal shunts inserted (six pleuro amniotic and two abdominal amniotic) and they delivered at a significantly later gestational age ($p=0.025$) (Table 1). After adjustment for gestational age at delivery and antenatal severity, those who had a shunt placed had a lower LOS ($p=0.019$) (Table 2).

Table 1: Antenatal data of those who did and did not have a shunt inserted.

	Shunt inserted	No shunt inserted	p-Value
n	8	12	
Male, n	4 (50)	7 (58)	0.714
Maternal age, years	34 (24–46)	29 (20–44)	0.181
Antenatally diagnosed, yes	8 (100)	10 (83)	0.224
More than two systems involved antenatally	5 (63)	3 (25)	0.317
Antenatal intervention, any[a]	8 (100)	5 (42)	0.007
Antenatal transfusion	1 (13)	2 (17)	0.798
Antenatal steroids given	6 (75)	9 (75)	1.000
Genetic abnormalities	4 (50)	4 (33)	0.456
No diagnosis found	4 (50)	5 (42)	0.361

Data are demonstrated as n (%) or median (range) [a]shunt, amniocentesis, amnio drainage.

Antenatal complications occurred in three of the eight infants who had antenatal drains inserted. Three infants had a drain that dislodged and in one case the drain had migrated into the chest cavity. Two patients had repeat procedures due to those complications. There were no incidences of premature rupture of membranes or premature delivery associated with the procedure.

Genetic abnormalities were detected in eight of the 20 patients. These were Noonans sydrome (two patients), Trisomy 21, Mucopolysaccaridosis, PTPN11 related RASopathy and non-specific genetic abnormalities (three patients). Two patient had infections identified (parvovirus and syphilis), two had hepatic arteriovenous malformations. No patients had underlying structural lung malformations.

Discussion

We have demonstrated that infants with NIHF who required antenatal shunting, despite a more severe antenatal presentation, had a more favourable outcome compared to those who did not receive shunting. Whilst this was not a randomised trial, the infants who underwent shunting in this cohort delivered at a later gestational age and required a shorter length of stay and had no significantly increased risk of postnatal problems.

We have previously reported that following pleuroamniotic shunting, the majority of babies had lung volumes within the normal range at follow-up [5]. This suggests that by effective drainage of the pleural effusion and hence prevention of chronic antenatal intrathoracic compression impairment of antenatal lung growth was avoided. The present findings of no significant differences in oxygen dependency at 28 days or 36 weeks PMA between those who did and did not require shunts are consistent with those results. Similarly, in one study, the outcomes of 132 fetuses who underwent pleuroamniotic shunting. After birth, 65 % of the 87 survivors experienced some respiratory or cardiovascular morbidity leading to long hospital stays. Despite this, 88 % of survivors had no long-term pulmonary issues. The remaining 12 % were predominantly reported to have to manageable asthma suggesting an overall benefit to shunting [7].

Table 2: Postnatal outcomes of those who did and did not have a shunt inserted.

	Shunt inserted	No shunt inserted	p-Value	p-Value adjusted for gestational age and antenatal severity
n	8	12		
Gestational age at birth, weeks	36 (32.3–38.1)	32.5 (27.3-40-2)	0.025	
Birthweight, g	2758 (2300–4536)	2254 (1000–4018)	0.238	
Surfactant given	2 (25)	5 (42)	0.444	0.529
Intubation	6 (75)	11 (92)	0.306	0.501
Invasive ventilation, days	3 (0–48)	23 (7–105)	0.072	0.480
Invasive or non-invasive support, days	11 (0–60)	32 (8–107)	0.094	0.981
Oxygen requirement at 28 days	3 (38)	8 (67)	0.199	0.958
Oxygen requirement at 36 weeks CGA	2 (25)	7 (58)	0.142	0.931
Total oxygen, days	18 (1–74)	64 (9–148)	0.072	0.937
Inotropes	2 (25)	10 (83)	0.009	0.093
Transfusions	3 (38)	12 (100)	0.002	0.999
Chest or abdominal drain placementt	2 (25)	8 (67)	0.068	0.999
Pneumothorax	3 (38)	4 (33)	0.848	0.911
Pulmonary haemorrhage	0 (0)	3 (25)	0.125	0.999
Length of stay, days	23 (9–85)	95 (36–214)	0.009	0.019
Corrected age at discharge, weeks	40.3 (37.2-46-4)	46.9 (36.1–67.1)	0.072	0.023
Discharge weight, g	2600 (2224–4144)	4094 (2274–5170)	0.121	0.732
Died	1 (13)	4 (33)	0.292	0.257
Death/Oxygen requirement at 28 days	3 (38)	10 (83)	0.035	0.138

Data are demonstrated as n (%) or median (range).

A study which evaluated the outcomes of 39 infants who received pleuroamniotic shunting, 51 % of whom were hydropic reported a live birth rate of 97 % with 74 % surviving the neonatal period. Hydrops resolved in 65 % of affected cases. Thirty-three percent of the 57 procedures, however, were technically difficult and linked to complications including chorioamniotic separation, chorioamnionitis, membrane rupture and shunt dislocation [9]. In the current series only three of the eight infants had complications due to the shunt insertion and this was in all cases due to shunt dislodgement.

Two infants in our series had abdominal amniotic shunts to relieve intrathoracic pressure. Whilst there is limited evidence supporting the use of abdominal amniotic shunts, this approach has been used by others to good effect when the abdomen was the predominant body compartment affected [10] or when pleuroamniotic shunting was unsuccessful [11].

The infants who had undergone antenatal shunting delivered at a later gestational age, as has been previously noted [8]. This likely explains their more favourable outcome regarding length of stay on the neonatal unit. In addition, despite being more severely affected antenatally they did not suffer more postnatal complications.

This study has strengths and some limitations. We report a consecutive series of infants with NIHF and compared those who did and did not receive antenatal shunting, of which there is limited evidence. Two of eight had abdominal shuts to relieve the pressure on the thoracic cavity but due to the small number, it was not possible to compare abdominal vs. pleuroamniotic shunt outcomes. We do not report a randomised trial, as antenatal shunting was undertaken because of clinical need. We did, however, undertake multiple regression analysis to adjust for demographic differences and confounding factors and demonstrated that those who underwent antenatal shunting had more favourable outcomes than those who did not. Our sample size was relatively small, but we did detect significant differences between the groups regarding timing of delivery and length of stay.

In conclusion, amongst infants who had NIHF, we found that those who had undergone antenatal shunting had a more favourable outcome on the neonatal unit. Whether the long term results at follow-up of such infants is improved merits testing.

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Research ethics: The NIHR toolkit was used that confirmed that this project did not require Ethical Approval.

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