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A seven-year retrospective cohort study on non-immune foetal hydrops from a single centre in an LMIC setting

https://doi.org/10.1515/jpm-2024-0518
Received October 30, 2024; accepted March 11, 2025;
published online June 23, 2025

Abstract

Objectives: To study the clinical profile, aetiology and outcomes of foetuses diagnosed with non-immune hydrops (NIHF) at a single centre between 2016 and 2023.
Methods: Pregnancies diagnosed with NIHF were studied retrospectively, using the antenatal records and neonatal electronic database.
Results: Ninety-two foetuses were diagnosed with NIHF including 8 sets of twins. Majority (64 %) were diagnosed in second trimester followed by 25 % in first trimester. One fourth (24 %, n=22) had IUFD (Intrauterine foetal demise) at diagnosis. Congenital anomalies were present in (57 %, 52) most common being cystic hygroma, (10/52) followed by foetal chylothorax and cardiac anomalies. Multiple anomalies were present in 15 % cases. Genetic evaluation, either chromosomal and/or DNA based test was done only in 62 % (57/92). More than one third (39 %, 22) had an abnormal karyotype, most common being 45, XO in 54 %, (12/22) followed by trisomy 21(9/22, 41 %). Twin-to-twin transfusion syndrome (TTTS) was seen in 75 % twins. Overall, most common etiologies were genetic, congenital anomalies, and unknown seen in 30 %, 26 %, and 23 % respectively. Majority of those with unknown aetiology were not/partially evaluated (13/21, 62 %). Recurrent NIHF was seen in 8 women. Two of them were diagnosed to have monogenic disorder while another one was carrier of a balanced chromosomal translocation.
Conclusions: Genetic aetiology was found in one third. The most common cause in twins was TTTS. One fifth had unknown aetiology, mostly due to lack of complete diagnostic work up.

Keywords: non immune hydrops; chylothorax; twin to twin transfusion syndrome; cystic hygroma; aneuploidy

Introduction

Non-immune hydrops foetalis (NIHF) is defined as abnormal foetal fluid collection in ≥ two sites, which is not caused by red cell alloimmunisation [1]. These include ascites; pericardial or pleural effusion and subcutaneous edema >5 mm [2] With the widespread availability and use of anti D globulin, the incidence of Rhesus alloimmunisation leading to foetal immune hydrops is declining. Majority of cases of foetal hydrops, therefore, have a non-immune aetiology, up to as high as 90 % in some studies [3]. The reported prevalence of this condition is 1 in 1,700–3,000 pregnancies [4].

The common pathophysiology is imbalance of fluid movement between the vascular compartment and interstitial space [5]. Common etiologies causing NIHF include cardiovascular; chromosomal; haematologic; foetal infections; twin to twin transfusion syndrome and foetal/placental tumours [1].

Due to the rare incidence and lack of studies from the LMIC (Low- and middle-income countries setting), we did this retrospective analysis of foetuses diagnosed with NIHF at a tertiary care perinatal centre in India.

The primary objectives were to study the clinical profile, and aetiology of NIHF in our cohort. The secondary objective was to study the perinatal outcomes in these pregnancies.

Materials and methods

A retrospective study was done from a prospectively maintained database of the foetal anatomy scans in the Department

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of Obstetrics and Gynecology, at Christian Medical College and Hospital, Vellore from January 2016 to December 2023.

Ethical clearance for the study was obtained from the Institutional Review Board (IRB Min No.10495). Pregnant women with antenatal scans showing foetal hydrops were included in this study. We also included women who were referred to our centre with a diagnosis of foetal hydrops.

NIHF was defined as presence of two or more abnormal fluid collections in foetus such as pericardial effusion, pleural effusion, ascites or generalized subcutaneous edema (>5 mm) as per the Society of Maternal Foetal Medicine (SMFM) clinical guidelines [2]. Women with diagnosis of foetal hydrops were excluded if they had a positive ICT (Indirect Coomb's test).

Hospital numbers of women with diagnosis of NIHF were obtained from the ADAC (Antenatal Detection of Congenital Anomalies) register kept in the scan room. Clinical details of the patients were obtained from the maternal and neonatal records stored in the Medical Records Department.

Maternal characteristics including age, parity, type of pregnancy, presence of obstetric risk factors or medical comorbidities, perinatal outcomes, details about recurrence and subsequent pregnancies were obtained from the maternal records.

Maternal blood investigations carried out for evaluation such as blood group, ICT, serology for infections such as parvovirus B19 and TORCH (toxoplasmosis, rubella, cytomegalovirus and herpes); Autoimmune work up such as anti SSA/SSB titres and placental biopsy were also noted.

Foetal details noted included the gestational age and trimester of diagnosis; sites of abnormal fluid collection; presence of associated findings such as congenital anomalies; IUFD (Intrauterine foetal demise); placentomegaly and polyhydramnios. Details of invasive prenatal testing including the type of genetic evaluation (such as karyotype/chromosomal microarray and clinical/whole exome sequencing) and foetal interventions and perinatal outcomes were noted. Other diagnostic tests such as foetal autopsy and fetograms were also noted.

Prenatal invasive diagnostic testing in the form of chorionic villus sampling (CVS), amniocentesis or cord blood sampling was offered to all patients, depending upon gestational age at diagnosis. Foetal thoracocentesis followed by biochemical evaluation of pleural fluid for total counts and protein levels were done in cases with suspected chylothorax. Foetal autopsies were offered in all cases of termination of pregnancies. Fetograms were done in cases of suspected skeletal dysplasia. Figure 1 gives a graphical description of diagnostic workflow used in our centre for etiological work up of NIHF.

Maternal and feal details were entered on the Excel sheet and analysed using SPSS Version 25.

Results

Ninety-two foetuses were diagnosed with NIHF during the study period. There were 8 sets of twins in our cohort. Nearly half (46 %) of the study population were primigravidae. The majority (63 %) were diagnosed in second trimester followed by 25 % and 12 % in first and third trimesters respectively (Table 1).

Median maternal age at diagnosis was 24 years (IQR 22–28 years). Median GA (gestational age) at diagnosis was 20.5 weeks (IQR 14–24 weeks).

In our cohort, 50 % (46/92) of affected pregnancies were low risk (Table 1). Previous poor obstetric outcomes, was seen in 26 % of those with risk factors (12/46).

The most consistent scan findings were, a combination of subcutaneous edema and pleural effusion, seen in 42 % (39/92) cases, either alone or in combination with other findings. Twenty-two (24 %) foetuses had fluid collections in pleural, pericardial, and peritoneal cavities. One fourth (24 %, n=22) had IUFD (intrauterine foetal demise) at diagnosis (Table 1).

Maternal evaluation was done only in one third cases (33 %) overall. Of the foetuses who presented with IUFD and hydrops, 45 % (10/22) had undergone maternal evaluation. Maternal evaluation included placental biopsy and maternal blood tests such as indirect Coomb's test; HbA_{1c}, thyroid function test (TFTs), anti SSA/SSB; serology for parvovirus and TORCH (toxoplasmosis; rubella, cytomegalovirus, and herpes) infections.

More than half (57 %, 52) had associated congenital anomalies, most common being cystic hygroma, seen in one fifth (10/52) followed by chylothorax in 15 % (8/52). Cardiac anomalies were detected in 8 % (4/52) including two cases of congenital heart block and suspected cardiomyopathy. Multiple anomalies were present in nearly one third (15/52) cases (Table 2).

Invasive prenatal testing was carried out in 82 % cases (n=75), most common being CVS (chorionic villus sampling), being done in half (51 %, 38/75). Amniocentesis was done in 44 % (33/75) whereas the rest had cordocentesis. A genetics referral was sought in 54 (59 %) cases.

However, genetic evaluation, either chromosomal test (karyotype/QFPCR/prenatal microarray) and/or exome sequencing, was carried out in 76 % (57/75) of foetal samples. The ramaining 18 cases had foetal DNA banked but no further test was done on them. Following discussion of the clinical scenario with the geneticist, either Foetal karyotype

(n=17) or exome sequencing (n=10) or combination of both KT and DNA banking was done (n=30). In 5 foetuses, the DNA sample was obtained from cord blood or foetal skin, at birth.

Out of those undergoing prenatal genetic testing, 54 % (31/57) had congenital anomalies. Nearly 60 % (31/52) of foetuses with congenital anomalies had genetic testing while the rest didn't.

Foetal interventions done included thoracentesis (n= 8); paracentesis (n= 1); pleuroamniotic shunt placement (n=1), amniodrainage (n=1) and intrauterine transfusion (n=1). Thoracentesis was done in cases of foetal hydrothorax for evaluation of pleural fluid. Pleuroamniotic shunt placement was done in a foetus with chylothorax.

Most common etiologies were genetic, congenital anomalies, and unknown seen in 29 %, 26 %, and 24 % respectively (Table 3). Genetic causes included chromosomal abnormaliites (n=22) and single gene disorders (N=5) (Table 3).

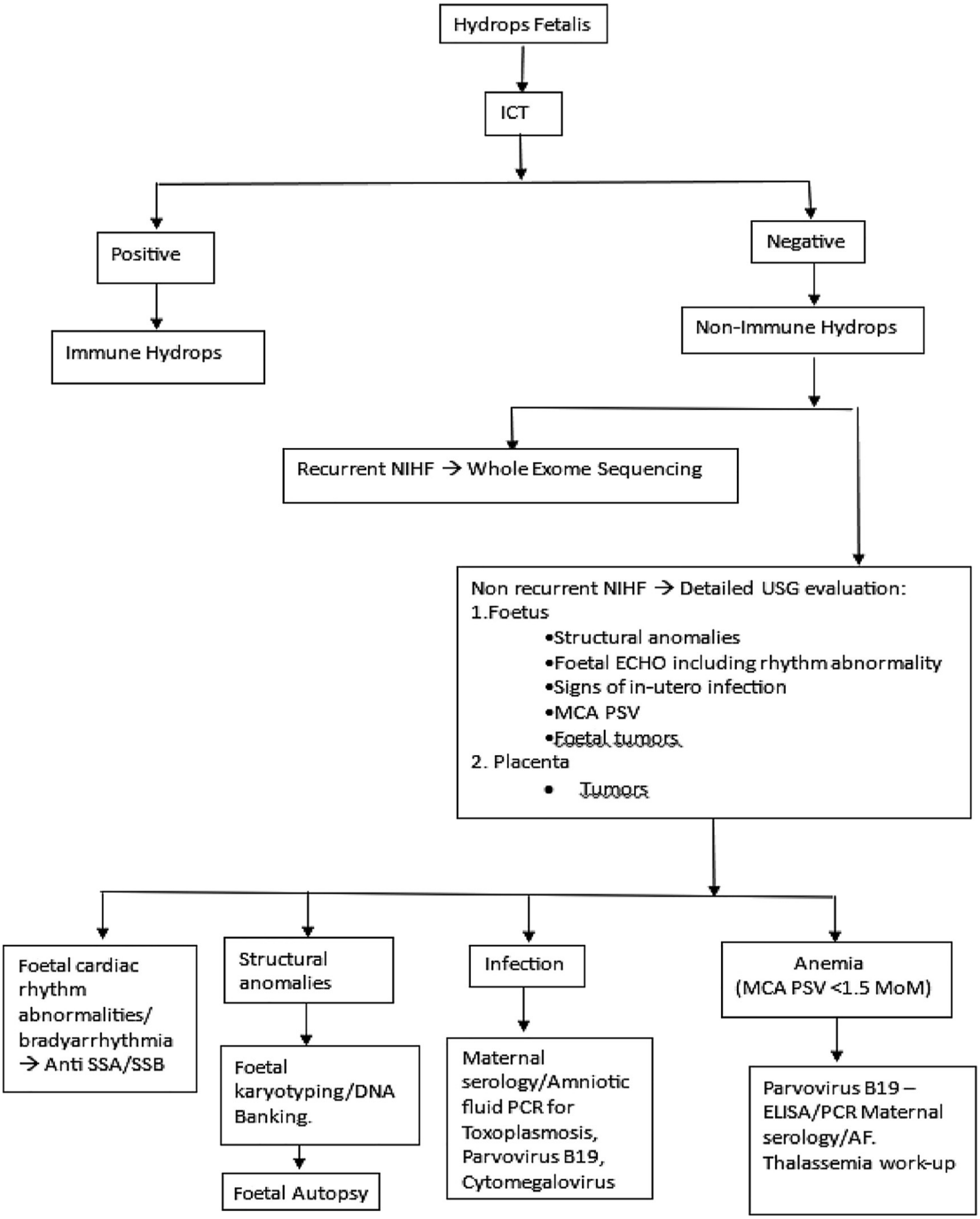

Figure 1: A simplified diagnostic algorithm for non-immune hydrops foetalis. MCA PSV, middle cerebral artery peak systolic value; ELISA, enzyme linked immuno sorbent assay; PCR, polymerase chain reaction; AF, amniotic fluid.

Table 1: Baseline characteristics of pregnancies affected with NIHF (n=92).

Characteristics	n	Percentage
Parity		
Primi	42	46 %
Multi	50	54 %
Type of pregnancy		
Singleton	84	91 %
Twins	8	9 %
Obstetric risk factors		
Diabetes	5	5 %
Gestational hypertension	5	5 %
Previous poor obstetric outcomes	12	13 %
Twins	8	9 %
Others	16	17 %
None	46	50 %
Trimester at diagnosis		
First	23	25 %
Second	58	63 %
Third	11	12 %
Invasive tests		
Chorionic villus sampling	38	41 %
Amniocentesis	33	36 %
Cordocentesis	4	4.3 %
Not done	17	19 %
IUFD[a] at diagnosis		
Yes	22	24 %
No	70	76 %
Congenital anomalies		
Present	52	57 %
Absent	39	43 %
Associated findings on scan		
Congenital anomalies	52	57 %
Placentomegaly	10	11 %
Polyhydramnios	2	2 %
Combination of findings	5	6 %
None	23	24 %
Perinatal outomes (n=100)[b]		
Abortus	74	74 %
Stillborn	20	20 %
END[c]	1	1 %
Liveborn	3	3 %
Not known	2	2 %

[a]Intrauterine foetal demise. [b]Perinatal outcomes were available for 100 foetuses including eight sets of twins. [c]Early neonatal death.

Table 2: Types of associated congenital anomalies (n=52).

Type of anomalies	n	Percentage
Lymphatic system	18	35 %
Cystic hygroma	10	
Chylothorax	8	
Multiple anomalies	15	29 %
Cardiac anomalies	4	8 %
CHB[a]	2	
AVSD[b]	1	
Cardiomyopathy	1	
CNS[c]	3	6 %
Dandy Walker malformation	1	
Hydrocephalous	1	
Frontal encephalocoele	1	
Others	10	19 %
Foetal akinesia	3	
Skeletal dysplasia	2	
CDH[d]	1	
Gastroschisis	1	
Facial malformations	2	
Genitourinary	1	
Information not available	2	4 %

[a]Congenital heart block. [b]Atrioventricular septal defect. [c]Central nervous system. [d]Congenital diaphragmatic hernia.

Table 3: Aetiology of NIHF (n=92).

Cause	n	Percentage
Genetic causes	27	29 %
Chromosomal	22	
Single gene disorders	5	
Twin complications	8	9 %
TTTS[a]	6	
Discordant anomalies	2	
Chylothorax	8	9 %
Congenital anomalies	24	26 %
Foetal anemia	2	2 %
Parvovirus infection	1	
Suspected haemoglobinopathy	1	
Suspected teratogenesis	1	2 %
Not known	21	23 %

[a]Twin-twin transfusion syndrome.

Of the 47 foetuses who underwent chromosomal tests, 47 % (22) had an abnormal result (Table 3) The commonest aneuploidy detected was 45, XO seen in 54 %, (12/22) followed by trisomy 21(9/22, 41 %). One foetus were diagnosed to have chromosomal structural rearrangements. Majority (95 %) of foetuses with abnormal karyotypes had diagnosis of hydrops in the first or second trimesters.

There were eight cases (9 %) of chylothorax resulting in foetal hydrops. Diagnosis of chylothorax was made on biochemical evaluation of foetal pleural fluid obtained on thoracentesis, and which showed lymphocyte predominance (>80 % of cells were lymphocytes).

There were six monochorionic and two dichorionic twins in our cohort (Table 1). TTTS (twin to twin transfusion syndrome) was the cause for hydrops in all monochorionic pregnancies whereas the presence of anomalies in one of the twins was the cause in the dichorionic twins (Table 3).

Five out of six monochorionic twins presented with either Quintero stage IV or V TTTS (hydrops/IUFD in one or

both twins) at <24 weeks. Four women underwent termination of pregnancy. The fifth pregnancy was also complicated by s FGR (selective foetal growth restriction) and was treated with selective foetal reduction of the smaller twin. The woman went on to deliver at 35 + 4 weeks a single liveborn weighing 1.5 kgs.

One of the monochorionic pregnancies presented with TTTS at 27 weeks. Following detailed counselling, the couple opted for serial amnioreduction as therapy. She, however, went into preterm labour at 28 weeks following amnioreduction and delivered two liveborn weighing 880 g and 990 g. The long-term follow up of these babies, however, is not available. Both the dichorionic pregnancies had one twin affected with NIHF secondary to presence of cardiac anomalies. While one was lost to follow up, the other pregnancy resulted in a liveborn and END at 30 weeks.

There was one case of foetal parvovirus infection with positive maternal serology. Other causes included one case of congenital anemia due to suspected haemoglobinopathy and one case of suspected teratogenesis (Table 3) The latter was a patient of systemic lupus erythematosus (SLE) with class II lupus nephritis, who had conceived while on Methotrexate. Her anomaly scan revealed foetal hydrops with absence of limb buds. Fetal genetic evaluation was normal in this case.

Majority of those with unknown aetiology were not/partially evaluated (13/21, 62 %).

Moreover, 40 % (21/52) of foetuses with congenital anomalies did not have any genetic evaluation.

Perinatal outcomes were available for 100 babies (including twins). Three fourths (74 %) of foetuses were aborted, including four sets of monochorionic twins. One fifth resulted in stillbirths (20 %). Three per cent had livebirths ; 1% ended in END and perinatal outcomes were not known in 2%. Two twin pregnancies resulted in three livebirths (Table 1). One of these was dichorionic pregnancy, discordant for foetal anomalies and hydrops in one of twins, resulting in livebirth of the normal twin. The other one was a monochorionic pair with late onset TTTS and delivered two liveborn following preterm labour.

Subsequent pregnancies resulted in live and healthy newborns in 28 cases (30 %); miscarriage/stillborn in 20 (22 %); 2 had ongoing pregnancies. However, no information about subsequent pregnancies was available in 42 (46 %).

Eight women had a history of recurrent hydrops (Table 4). Two women (Cases 2 and 5, Table 4) had had four pregnancies affected by foetal hydrops. CES (Clinical exome sequencing) in foetal DNA, in case 5, was suggestive of (lysosomal storage disorder). The other couple had foetal DNA banked but did not go ahead with genetic evaluation.

Case 6 had history of two missed miscarriages and two foetuses affected with cystic hygroma and hydrops. In the last pregnancy, foetus was evaluated and found to have an unbalanced chromosomal translocation. Parental evaluation detected a balanced translocation in the mother (Table 4).

Foetal karyotype (KT) was done in 7 pregnancies in 5 women. One woman (Case 7) had had foetal KT done twice and chromosomal microarray done once, in three different pregnancies. Two of her babies had presented with structural cardiac anomalies, one with normal KT and one with low level mosaicism for trisomy 9. Another foetus who had presented with cystic hygroma and hydrops in the first trimester, was found to have Turner's syndrome on CMA (chromosomal microarray).

Parental KT was done in three cases. Indications for doing parental KT were: foetuses with monosomy XO (Turner's syndrome) and unbalanced translocation (Case 6, 7 Table 4) and pregnancy termination due to foetal anomalies suggestive of chromosomal abnormality but foetal KT was not done. (Case 2, Table 4).

DNA based testing to rule out single gene disorders was done in 4 pregnancies. This included clinical exome sequencing (n=2) and one whole exome sequencing (Table 4). Exome sequencing picked up pathogenic variants which can explain foetal phenotype in cases 5 and 7 and no pathogenic variants in one case (Case 4) (Table 4).

Case 7 had three pregnancies affected with foetal hydrops. In the first and third pregnancies, foetuses had cardiac structural anomalies whereas in the second pregnancy, foetus had hydrops and cystic hygroma in the first trimester. Karyotype was normal in first pregnancy but showed low level mosaicism for trisomy 9 in third pregnancy (5 metaphases). CMA of foetus in the second pregnancy was suggestive of monosomy XO. Maternal KT showed low level mosaicism for trisomy X (2 metaphases) (Table 4).

In view of recurrence, WES was done in third pregnancy and showed foetus to be heterozygous for cardiomyopathy, left ventricular compaction (AD) and father was the carrier for same variant.

Table 4: Clinical presentation, evaluation and results in pregnancies affected with recurrent NIHF. Some of the pregnancies occurred prior to the study period.

Case	Clinical presentation	Genetic tests	Results
Case 1	G1: IUD and hydrops at 29 weeks	DNA banking	DNA analysis not done.
	G2: IUFD and hydrops at 29 + 3 weeks. Foetus with large ears; long philtrum; tapering fingers and hydrocoele	Foetal karyotype	KT: 46, inv (sex chromosome) [20]
Case 2	G1-G3: Foetal hydrops diagnosed at anomaly scan.	DNA banking	DNA analysis not done.
	G4: IUD at 27 + 2 weeks. Foetal hydrops; cystic hygroma; hypoplastic lungs and thymus; hypertelorism	Parental KT	Parental KT: 46, XX and 46XY
Case 3	G1: Mid trimester IUD. Foetus had facial dysmorphism and hydrops.	Foetal KT	Karyotype normal.
	G2: IUD at 22 + 1 weeks	DNA banked	Not evaluated
Case 4	G1: TOP at 12 + 3 weeks. Foetus with cystic hygroma.; Cleft lip and palate and gastroschisis	Foetal KT	Normal
	G2: Hydrops at anomaly scan. No structural anomalies.	CES	CES: No pathogenic or likely pathogenic variants
Case 5	G1: IUD and hydrops at 21 weeks	CES	CES: Homozygous for pathogenic variant in ASAH1 gene, causing Farber lipogranulomatosis (Lysosomal storage disorder)
	G2: IUD and hydrops at 24 weeks		
	G3: IUD and hydrops at 22 weeks		
	G4: Hydrops at 19 weeks. No structural anomalies.		
Case 6	G1: Missed miscarriage at 8 weeks.	Foetal Karyotype	Foetal KT: 46, der (6) [23]
	G2: TOP for cystic hygroma and hydrops at 13 weeks	Parental Karyotype	Mother:46, XX, t(1, 6)(q42;q25) [20]
	G3: Missed miscarriage at 8 weeks.		Father: 46XY
	G4: Cystic hygroma and hydrops at 16 + 4 weeks		
Case 7	G1: Anomaly scan at 21 weeks showed foetal hydrops, tricuspid atresia, VSD with hypoplastic right heart.	Foetal KT	KT: normal
	G2: Hydrops at 12 + 3 weeks	Foetal CMA	CMA: Turner's
		Maternal KT	Maternal KT:47, XXX [2]/46XX [48]
	G3: TOP at 20 weeks for foetal hydrops; hypoplastic left heart and single outflow	Foetal KT	mos 47, –, +9[5]/46, –[45]
		WES	Heterozygous for cardiomyopathy/left ventricular non compaction. Likely pathogenic (Parents heterozygous for the same variant)

IUD, intrauterine demise; TOP, termination of pregnancy; KT, karyotype; CES, clinical exome sequencing; WES, whole exome sequencing; VSD, ventricular septal defect; CMA, chromosomal microarray; VOUS, variants of uncertain significance.

Discussion

NIHF is often the result of diverse underlying pathologies. The differential diagnosis is often extensive and success in elucidating the cause requires extensive diagnostic work up, which may not be possible in limited resource settings. Recent studies, including a systematic review, have reported that in 60 % cases, aetiology could be determined prenatally and in 85 % cases when postnatal detection was added [6, 7].

The most common etiologies for NIHF described in literature include cardiovascular anomalies; chromosomal defects and haemoglobinopathies [1]. The most common aetiology in our cohort, however, was genetic, responsible for nearly one third cases. These included 22 foetuses with chromosomal aberrations, both numerical and structural, and 5 foetuses with single gene disorders (Table 3).

Karyotyping was performed as first line test in foetuses with hydrops and associated structural malformations on scan, or as second line test, in foetuses with normal morphology, after other common causes such as infections were ruled out. The standard recommendations advise karyotype assessment for all foetuses irrespective of presence/absence of congenital anomalies [1]. However, in a low resource setting like ours where genetic tests are not government funded and patient has to bear the expenses, following these recommendations may not be practically feasible.

In our cohort, Karyotype abnormalities were seen in 23.9 % (22/92) and genetic syndromes were diagnosed in 5.4 % (5/92) cases. Bellini et al. reported karyotype abnormalities in 9 % and genetic syndromes in 5 % [7]. The difference in aneuploidy rates in our study is because majority of our cases (88 %) presented in early pregnancy (first and early second trimester) where likelihood of chromosomal anomalies is much higher.

The most common foetal karyotype abnormalities in our cohort were Monosomy X and Trisomy 21. This is

similar to the observation in a large systematic review [7]. Majority of the aneuploid foetuses (95 %) were detected to have hydrops in early pregnancy, similar to findings by others [4, 6].

Cardiovascular abnormalities have been reported to be a cause of NIHF in 20.1 % cases [7]. In contrast, we found only 9 % foetal hydrops cases attributed to either structural or functional cardiac defects. This might be because we did not include cardiac anomalies which were part of multi-system involvement; chromosomal or single gene disorders as these have been classified separately (Table 2).

We found cardiac causes in about 9 % (8/92) of foetal hydrops.: these included cardiac structural anomalies; CHB (congenital heart block) in two cases and cardiomyopathy in one foetus. Four structural anomalies were found in foetuses with multiple anomalies. In the two pregnancies complicated with CHB, women were found to have elevated titres of maternal anti SSA/SSB antibodies, confirming the diagnosis of Sjogren's syndrome.

Foetal thoracic abnormalities have also been reported to be one of the common causes of NIHF, accounting for 6 % cases [1] These includes the presence of lung masses such as CPAM (congenital pulmonary airway malformation), CDH (congenital diaphragmatic hernia) and chylothorax. Large effusions or masses cause mediastinal shift, impairing venous return and cardiac output, thereby resulting in hydrops. Esophageal compression, an associated finding in such cases, often leads to polyhydramnios.

In our series, we had eight cases of chylothorax and one case of CDH causing NIHF (Tables 2 and 3). These accounted for 10 % cases. However, only one foetus underwent pleuroamniotic shunting but had foetal demise after two days.

Although the contribution of foetal infections to NIHF has been reported as 5–10 % [6], we had only one case of foetal infection by parvovirus B19, confirmed by positive maternal serology. This woman had presented at 28 weeks with IUFD and foetal hydrops.

Parvovirus B19 causes foetal anemia by inhibiting the erythroid progenitor cells and suppressing erythropoiesis [8, 9]. It is also known to be one of the treatable causes of NIHF, amenable to intrauterine transfusion [10]. Other foetal infections include Toxoplasmosis; CMV and syphilis [1].

Inborn errors of metabolism (IEM) are known to be responsible for 1–2 % cases, lysosomal storage disorders (LSD) being the most common cause [11]. These are important causes of recurrent NIHF as they are AR (autosomal recessive) with 25 % chances of recurrence in each pregnancy [1].

One of the women in our cohort, had four pregnancies, complicated by mid trimester detection of hydrops and IUFD in structurally normal foetuses (Case 5, Table 4). She presented at 19 weeks in her fourth pregnancy with foetal hydrops. At autopsy, the foetal liver was sent for biopsy and was suggestive of metabolic storage disorder. CES of the banked foetal DNA showed homozygous status for pathogenic variant in ASAH1 gene which causes Farber's lipogranulomatosis, and the parents were found to be carriers of the pathogenic variant (Table 4). Following this, she had PND (prenatal diagnosis) in her subsequent pregnancy and had a successful outcome.

TTTS is the most common cause of NIHF among twins and is the result of vascular anastomoses between the two foetuses. It is known to complicate 10 % of monochorionic pregnancies and presence of foetal hydrops carries poor prognosis in the absence of treatment. Laser ablation of the vascular anastomoses has been shown to improve foetal outcomes [12]. In our cohort, only one patient could afford definitive therapy and had a good outcome.

Prognosis of NIHF depends upon the underlying aetiology; gestational age at diagnosis and the genetic association. Early diagnosis is mostly associated with chromosomal abnormalities and, therefore, have a poor prognosis. Moreover, in the absence of aneuploidies, the overall survival was found to be <50 % [3].

It is reasonable to offer termination of pregnancy in case the diagnosis is made prior to period of viability (1). Neonatal mortality among the liveborn has been shown to be 60 % [13]. Although treatable causes of NIHF include foetal arrhythmias and Parvovirus infection, long term morbidity has been described in the survivors [14, 15].

In our series, the overall perinatal outcomes were poor. There were only three livebirths and nearly 75 % foetuses were aborted and rest resulted in stillbirths/END (Table 1). This could be because of several factors: 22 % foetuses had IUFD at presentation; majority of the diagnoses was in early pregnancy, prior to viability thereby prompting terminations; lack of finances for undergoing treatment for treatable causes such as TTTS; and a lack of awareness among the couples.

The limitation of our study is that it is retrospective in nature and data has been obtained from clinician's notes. The strength of our study is that it has a large sample size and one of the few studies from the LMIC setting. We have also included cases of recurrent hydrops and discussed their aetiology.

Conclusions

The most common aetiology of NIHF was genetic followed by congenital anomalies. In, 24 % cases, aetiology was unknown, mostly due to incomplete diagnostic workup. TTTS was the most frequent cause among twins. Among those with recurrent NIHF, single gene disorders were picked up in two cases and chromosomal structural rearrangements in one. Overall perinatal outcomes were poor in our setup.

Acknowledgments: We thank Paramasivam, Jency, Jaya Prabha, Technical Staffs Department of Medical Genetics, CMC Vellore Tamil Nadu. Ms Narayani, Scan Technician Department of Obstetrics and Gynecology CMC Vellore Tamil Nadu for their contribution.

Research ethics: IRB Min No: 10495 and the Ethics Committee of Christian Medical College and Hospital Vellore.

Informed consent: Informed consent was not applicable as it was a retrospective study. However, both informed and written consent were obtained from the patients prior to genetic testing/procedures.

Author contributions: All authors have accepted responsibility for the entire content of this manuscript and approved its submission. VND and MB conceptualized the study. Data collection was done with assistance of VND, LSJ, PN, SR, SD and MPC. The manuscript was prepared by VND and MB. VND is the first author and MB is the corresponding author.

Use of Large Language Models, AI and Machine Learning Tools: None decalred.

Conflict of interest: The authors state no conflict of interest.

Research funding: None declared.

Data availability: All data underlying the results are available as part of the article and no additional source data is required.

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