

## Evaluation of Causes, Frequency and Prognosis of Hydrops Fetalis: A Case- Series Study at a Referral Hospital in Tehran, Iran

Elahe Amini<sup>1</sup>, Zahra Farahani<sup>1</sup>, Parvin Akbari Asbagh<sup>1</sup>, Tahere Esmaili nia<sup>1</sup>, Sedighe Borna<sup>1</sup>,  
Saiid Mohammad-ali Poor Kenari<sup>1</sup>, \*Mohaddese Fallahi<sup>1,2</sup>

<sup>1</sup>Maternal \_ Fetal & Neonatal Research Center, Tehran University of Medical Sciences (TUMS), Tehran, Iran.

<sup>2</sup>Breast Feeding Research Centre, Tehran University of Medical Sciences (TUMS), Tehran, Iran.

### **Abstract**

#### **Introduction**

Hydrops Fetalis is a serious condition in fetal period, characterized by the presence of serous fluid accumulation in at least two potential spaces in fetus including pleural effusion, pericardial effusion, and ascites. The incidence of hydrops fetalis is one per 2500-3000 pregnancies. This condition is followed by different diseases. Fetal hemolytic anemia and its hypoxemia due to hydrops fetalis are potentially life or function threatening. Mortality rate is 50-90%; this poor prognosis is improving with advances in prenatal and medical treatment.

#### **Methods and Materials**

This study performed on patients' records with hydrops fetalis diagnosis in one of the neonatal referral and academic center, Vali-e-Asr Hospital Tehran, the capital of Iran from 2003 to 2010. Etiology, prognosis, and frequency of Hydrops fetalis in newborns were evaluated.

#### **Results**

Out of 10878 cases, 0.35% was born with hydrops fetalis: 18.42% immune [Rh incompatibility (%85.71), Kell antigen system(% 14.29) ] and 81.58% non-immune.

#### **Conclusion**

The rate of hydrops due to Rh incompatibility is significant in our center (85.71%), however, it is unusual in most of medical centers all over the world.

**Key words:** Immune causes, Hydrops fetalis, Non- immune causes.

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#### **\*Corresponding Author:**

Dr. Mohaddese Fallahi , 2<sup>nd</sup> Floor, Breast feeding research centre, Vali-Asr Hospital, Imam Khomeini Hospital, Bagher Khan Ave. Tehran – Iran.

E-mail: [dr.fallahi2020@yahoo.com](mailto:dr.fallahi2020@yahoo.com)

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## Introduction

The incidence of hydrops fetalis is one per 2500-3000 pregnancies. Hydrops is not considered a disease, but it is a common end stage for over 100 different processes. This condition is related to an imbalance in fluid hemostasis where fluid accumulates in interstitial space of fetal systems abnormally. It accounts for up to %3 all prenatal mortality (1). Hydrops fetalis is divided in two categories: Immune hydrops fetalis (IHF) that refers to hydrops due to maternal alloimmunization to red cell antigens (more than 50Ag) (2), and Non-immune hydrops fetalis (NIHF) that includes hydrops due to each disease process other than alloimmunization.

Although Rh blood group, D antigen (RhD) was once the major etiology of fetal and neonatal hemolytic disease, the widespread injection of antenatal and postpartum Rhesus immune globulin has resulted in a marked decrease in prevalence of alloimmunization to the RhD antigen in pregnancy. Non-immune hydrops fetalis (NIHF) is followed by cardiovascular abnormalities, chromosomal defects, infections, Twin-twin transfusion syndrome (TTTS), anemia, chylothorax, genitourinary anomalies, tumors, and idiopathic causes(1, 3).

Liver and cardiac failure, volume overload, lymphatic disorders lead to low oncotic pressure, high central venous pressure, and decreased lymphatic flow cause neonatal mortality due to hydrops. The changes in capillary permeability have confirmed by leakage of amino acid into amniotic fluid in NIHF fetuses (4).

Evaluating the fetus with hydrops would be sophisticated and potentially invasive. The least complex test is family history taking that followed by maternal laboratory evaluation, a detailed sonography,

echocardiography, fetal blood sampling and doppler monitoring (1). Fetal intravascular transfusion became the treatment of choice due to reduction in prenatal mortality, neonatal morbidity, and preterm delivery rates. In addition some investigations were distinguished the long-term neurodevelopmental and neuropsychological outcomes of fetuses with intravascular transfusion would be better (4).

Treatment of a fetus with hydrops fetalis constrains a great budget on health services. Furthermore, even hydrops survivors, would be at high risk for neurodevelopmental disorders (5). This study was performed for evaluation of frequency, etiology, and prognosis of this high-incidence and serious disease in our center.

## Material and methods

This was a case-series study performed on patients' records with hydrops fetalis diagnosis in one of the neonatal referral and academic center Vali-e-Asr Hospital, Tehran (the capital of Iran), Iran from 2003 to 2010.

The beginning step of evaluation was filling up questionnaires by expert staff. All important maternal and fetal information were considered. Extracted information included: Maternal age, maternal disease (Diabetes-Hypertension-Epilepsy-Hepatitis-Thalassemia), maternal and neonatal blood group, Coombs test result, gestational age, birth weight, ultrasound findings, echocardiography findings, G6pd activity state, final diagnosis, kind of treatment, family history of hydrops, parent consanguinity, fetal and neonatal mortality(as poor prognosis cases). Finally all data analyzed with SPSS-13 (descriptive statistics) software.

## Result

From 10878 newborn infants, hydrops fetalis has been confirmed in 38 records (%0.35). We classified hydrops fetalis on

basis interference immunity system and subgroups (Table.1).

**Table 1:** Etiology frequency in 38 cases with hydrops fetalis

Immune hydrops fetalis: 7 (%18.42)	Rh incompatibility 6 (%85.71) Kell antigen system 1 (% 14.29)
Non immune hydrops fetalis: 31 (%81.58)	- Cystic hygroma 8 (%25.8) - Chromosomal anomaly 5 (%16.13) - Chylothorax, pulmonary hypoplasia, lymphangiectasis 4 (%12.9) - Myocarditis, congenital heart disease, *SVT 5 (%16.13) - TORCH 2 (%6.45) - $\alpha$ thalassemia 1 (%3.2) - Unknown 6 (%19.3)

\*Supraventricular tachycardia

The most Rhesus (Rh) factor state in immune hydrops cases was Rh negative. 34% of mothers were < 25 years old and 66% were >25 years. Just 1 case (3%) had Rh0 (D) immune globulin (RhoGAM) injection. Only one of them had a positive obstetric history of hydrops. 44.7% of mothers had positive past medical history of diabetes, hypertension, epilepsy, hepatitis, and thalassemia, totally. 10 cases (26%) had positive family history of repeated hydrops. Among 38 hydrops cases 47% were male. Mean birth weight and mean gestational age were 2910 gr and 29 weeks, respectively. Most common ultrasonic finding was cystic hygroma (18%). Echocardiography in 15% of hydrops babies showed Tricuspid regurgitation (TR). There were 44% intrauterine deaths and 22% early neonatal deaths.

It was noticeable that, there was a significant difference between Coombs test and immune hydrops. Also there was a descriptive correlation between mother and fetal's blood group (P=0.019). Positive relation between mother's blood group and

type of hydrops was notable (P=0.018). Eventually, an inverse correlation between RhoGAM injection and hydrops fetalis was observed (P = 0.03).

No significant relation between type of hydrops and time of fetal death was seen. In addition there was not any relation between familial history and kind of hydrops. The correlation between Coombs and RhoGAM injection was not statistically significant. No difference between maternal age and type of hydrops was seen. Finally no significant relation between type of hydrops with gestational age and neonatal weight was reported.

## Discussion

When we compared our data with former published statistics we found that hydrops frequency in our study (0.35%) was similar to Sohank's report (1/1000\_1/3000) (6, 7).

Mortality rate in NIHF was 22 out of 31 cases that no significant difference was seen

with Maccoy's report (6, 7). Prematurity, myocardial failure due to anemia and hypoxia, liver disease, nephropathy, and other organ dysfunction would be responsible for fetal and neonatal death.

It is not expected to see the Rh incompatibility with such a high frequency as a hydrops cause (6 cases) because of RhoGAM availability. This incidence is much higher than other investigations. Newest studies show that only 4.5% of all cases are immune hydrops (8), but we found that the incidence of immune hydrops is 18.42% and about 85.7% of immune group was Rh incompatibility. It means that we should warn parents against this problem before pregnancy and administration of RhoGAM during prenatal care.

Before 1995 cardiovascular disease and arrhythmia were responsible for 30% of hydrops. Today it decreases to 13% due to early chromosomal abnormalities diagnosis. In our study 13.15% comprising 5 cases of all hydrops cases were diagnosed by congenital cardiovascular disease, too. The frequency of cystic hygroma in our finding was 25%, that all of them expired. We also saw this poor prognosis in Thamson & Moore reports (9). In Kumar's report, Bart hemoglobinopathy and  $\alpha$ -thalassemia were expressed as a common cause in NIHF. Also some studies indicate that  $\alpha$ -thalassemia is the most common cause of NIHF among Asian, however, in our investigation we found just one case.

Chylothorax, pulmonary hyperplasia and lymphangiectasia were 12.9 % of NIHF cases. These data are compatible with Sohank, Ismail, and Swain by 15.6%, 14.5% and 17.5%, respectively. Though, in other studies thorax disorders vary from 3.7% to 10.2% (10).

It is noticeable that mean maternal age in our study was 28.3 years old meanwhile in

Harper study, this criterion was reported 29 $\pm$ 5 years old(4).

The mean gestational age was 29 weeks, although in Boutall research the mean gestational age at presentation was 25.7(11).

The idiopathic causes in this study was 19.3%, however in other studies were reported 3%-6.9%. It is significant that in well – equipped centers this was reported up to 1/3 of all cases (12). Prognosis in idiopathic, cystic hygroma, and chromosomal abnormalities in our study were compatible with Moore's finding (13).

Fetal infection [Toxoplasmosis Other (syphilis) Rubella Cytomegalovirus (CMV) Herpes simplex virus (HSV)] (TORCH) accounted for 2 (6.45%), which was lesser than other result (14%) (11). It was considered that Rubella vaccination had a great role.

The best prognosis in our study is possessed to arrhythmia, chylothorax and lymphangiectasia, that our profiles are the same as others.

Since Bukowski et al. in 2000 have shown associations between NIHF and multiple pterygium syndrome, arthrogryposis, skeletal dysplasias, and several mucopolysaccharidoses in their studies (5). We also suggest that because of high frequency of repeated hydrops in our cases, parents' human leukocyte antigen (HLA) assay, placental pathological evaluation and attention to metabolic disorders like mucopolysaccharidoses and quasher would be beneficial. However, future prospective studies are needed to reassess these findings

Although Rh incompatibility is eradicated or unusual in most of medical centers all over the world, unfortunately in this study rate of Rh incompatibility is significant that

reminds necessity of announcement and instruction of parents and enough prescription of medicines on the other hand. In our study like other studies, the prognosis was dependent on etiology so that patients with chylothorax, pulmonary lymphangiectasia and SVT had best prognosis.

**Conflict of interests:** None

### **Acknowledgment**

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### **References**

1. Leslie A. Parker RNC, MSN,NNP. Hydrops fetalis. *Newborn and infant Nursing review* 2006;16(3): 1-8.
2. Kenneth J Moise. Fetal anemia due to non-Rhesus-D red-cell alloimmunization.Seminar in fetal and neonatal medicine 2008;13: 207-214.
3. Su R.M, Yu CH ,Chang CH,Yang HB,Chang FM. Prenatal diagnosis of twin-twin transfusion syndrome complicated with hydrops fetalis at 14 weeks of gestation.*International J Gynecology & obstetrics* 2001; 73:151-4.
4. Dennis C. Harper HM, Swingle CP. Weiner DJ. Bonthius GP. Long term neurodevelopmental outcome and brain volume after treatment for hydrops fetalis by in utero intravascular transfusion. *American J of Ob- Gyn* 2006;195:192-200.
5. Bukowski R, Saade G. Hydrops fetalis. *Clinics in perinatology* 2000; 27:1007-1027.
6. Sohan K, Carroll SG, De La Fuente S, Soothill P, Kyle P. Analysis of outcome in hydrops fetalis in relation to gestational age at diagnosis and treatment, aet a abstet *Gynecol scand* 2001; 80(8):726-30.
7. Maccoy Mc. NIHF after 20m weeks gestation. *OBGynecol* 1995; 85:578.
8. Ratanasiri T, Komwilaisak R. Incidence, causes and outcomes of hydrops fetalis at Strin Agarined Hospital1996-2005:a 10 year review. *J Med Assoc Thai* 2009; 92(5):594.
9. Wolf RB, Moore TR. Amniotic fluid and non immune hydrops. *Fanaroffs martin neonatal perinatal medicine* 2011; 22:377-97.
10. Ismail KM, Marin WL. Etiology and outcome of hydrops fetalis. *J mater fetal med*2001; 10(3):175.
11. Boutall A, Urban M, Stewart Ch. Diagnosis, etiology, and outcome of fetal ascites in south Africa hospital. *International J of GYN & OB* 2011;115:148-52.
12. Watson J, Campbel S. Antenatal evaluation and management in no immune hydrops fetalis, *OB Gynecol* 1986;67:589.
13. Wolf R, Moore T. Amniotic fluid and non immune hydrops fetalis. *Fanaroff martins neonatal perinatal medicine* 2011; 22:377-97.