Hematological Indices of Parents in Non-Immune Hydrops Fetalis Pregnancies


1 Vali-e-Asr Reproductive Health Research Center, Medical Sciences/ University of Tehran, Tehran, Iran
2 Department of Medical Genetics, Medical Sciences, Medical Sciences/ University of Tehran, Tehran, Iran
3 Iranian Fetal Medicine Foundation, Tehran, Iran
4 Gene Clinic, Tehran, Iran
5 Department of Obstetrics and Gynecology, Medical Sciences/ University of Tehran, Tehran, Iran

Received October 2007; Revised and accepted December 2007

Abstract
Objective: To investigate the hematologic indices of mothers in non-immune hydrops fetalis pregnancies and identify the possible causative role of Alpha-Thalassemia among them.

Material and methods: From 2005 to 2007, 11386 hydrops fetalis cases in three major obstetric hospitals affiliated to Tehran University of Medical Sciences were recorded. Indirect coombs test and hematologic indices of maternal samples were assessed.

Results: Among 11386 deliveries, 67 hydrops fetalis cases were detected. Forty-one (62%) cases were immune type and 26 (38%) cases were non-immune hydrops. All the mothers had MCV more than 80 fl and 25 mothers had MCH more than 27 pg, so none of them had Alpha-Thalassemia carrier criteria.

Conclusion: Alpha- Thalassemia is not the major cause of hydrops fetalis in this study and cost-effectiveness of population scaled biochemical and/or molecular screening programs of α-globin gene mutations in Tehran population is under question.

Keywords: Hydrops Fetalis, Alpha-Thalassemia, Iran

Introduction

Hydrops fetalis is a rare but important cause of perinatal morbidity and mortality which is caused by the accumulation of interstitial fluid in the fetus (1). The first case of hydrops fetalis was described by Ballantyne over 100 years ago. There are over 80 conditions known to be associated with this condition (2). Hydrops fetalis can be caused by immune and non-immune mediated mechanisms, among them Alpha-thalassemia is a known cause of non-immune mediated hydrops fetalis (1).

The thalassemias are the most common monogenic diseases and occur mostly in peoples from the Mediterranean to Southeast Asia. Mutations affecting one or more Alpha-globin genes, resulting in decreased or absent production of the Alpha-globin chain, will give rise to Alpha-Thalassemia. The clinical severity of the disease depends on the number of Alpha-globin genes involved. Individuals with the loss of either one (α+ -thal) or two (α0-thalassemia) globin on each of the two chromosomes 16 (in trans, homozygous
Table 1: Frequency of hydrops feta
tis deliveries in three major obstetric hospitals

| Hospital       | Total deliveries (n) | Hydrops feta
tis (n) | Hydrops/1000 deliveries |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mirza</td>
<td>4976</td>
<td>15</td>
<td>3.01</td>
</tr>
<tr>
<td>Vali-e-Asr</td>
<td>3774</td>
<td>40</td>
<td>10.6</td>
</tr>
<tr>
<td>Shariati</td>
<td>2636</td>
<td>12</td>
<td>4.55</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>11386</strong></td>
<td><strong>67</strong></td>
<td><strong>5.88</strong></td>
</tr>
</tbody>
</table>

α^0^-thalassemia) are usually asymptomatic. Some might have borderline anaemia, but most will have hypo
chonic microcytic red blood cells (3).

Homozygous Alpha-thalassemia is the most common cause of hydrops feta
tis in South-East Asia (4) but in
other populations it comprises a minor part of hydrops feta
tis causes (5) or it is not detected to have any role
in this disease (6,7).

Thalassemia is a common disease in Iran. A nation-
wide screening program using RBC indices and Hemoglobin electrophoresis in pre-marriage couples
has been implemented to control the disease. After
rule out of iron deficiency anaemia, individuals with
low mean corpuscular volume (MCV<80fl) and mean
corpuscular hemoglobin (MCH<27pg) and high
HbA2 levels are usually labeled as beta thalassemia
 carriers. However, in couples with low MCV and
MCH and normal HbA2 levels, alpha thalassemia
would be proposed. When both couples are α^-thalassaemia carriers, there is a 25% risk of hydrops
fetalis.

Several studies have been carried out to investi-
gate the frequency of Alpha- Thalassemia in Iranian
population (8,9). However, no data are available
regarding the role of Alpha -Thalassemia carriers in
developing hydrops fetalis in Iran. The present study
was carried out to investigate the parents’ hematol-
ogic indices of non-immune hydrops fetalis and identify
the possible causative role of Alpha- Thala-
ssemia among them.

Materials and methods

Between July 2005 and July 2007, all hydrops fetalis
cases in three major obstetric hospitals (Imam
Khomeini hospital, Mirza Koochak Khan hospital,
Shariati hospital) affiliated to Tehran University of
Medical Sciences were recorded. Hydrops fetalis
diagnosis was made according to either ultrasound
findings during pregnancy or pathological findings
after autopsy.

Presence of two or more of the following ultra-
sound findings: skin edema (skin thickness more than
5mm), pericardial effusion, pleural effusion, ascitis
were diagnostic of hydrops fetalis. Moreover, patho-
logic features of paleness, generalized edema, pericar-
dial effusion, pleural effusion, ascitis or cardiomegaly
were also classified as positive findings.

Indirect coombs test was performed for all maternal
samples to distinguish between immune and non-
immune hydrops fetalis cases. Maternal samples with
positive indirect coombs results were enrolled in the
present study and hematological indices were measu-
red.

Results

Between July 2005 and July 2007, 11386 deliv-
erys were recorded in three major obstetric hospitals in
Tehran. Among them, 67 hydrops fetalis cases were
detected according to the mentioned criteria (table 1). Forty-one (62%) cases were immune type and 26
(38%) cases were non-immune (table 2).

None of the evaluated mothers had Alpha- Thala-
ssemia carrier criteria. All mothers had MCV more
than 80pg among them 8 cases had MCV of higher
than 90pg. Twenty-five mothers had MCH more than
27 pg. In one case, the mother had low MCH (MCH= 26.6) but normal MCV and HbA2 level. Evaluating
the hematologic indices of the fetus showed no
anaemia (hemoglobin=12.2) and therefore Alpha-Tha-
lassemia as the leading cause of hydrops fetalis was
ruled out. Details of the findings are shown in (table
3).

Discussion

Thalassemias are the most common and clinically
significant single gene disorders in the world and
occur mostly in peoples from the Mediterranean to
Southeast Asia (1). There are four clinically different
types of Alpha-Thalassemia depending on the number
of α-globin genes involved. When both couples are
α^-thalassaemia, there is a 25% risk of hydrops fetalis.
The frequency of α^-thalassaemia is very low in
Iranian population but no study has been carried out
to examine the possible role of α^-thalassaemia hydrops
fetalis in Iran. The frequency of non-immune hydrops
fetalis was 1 in 438 in this study. Various studies
have reported this frequency from 1 in 500 (in Southeast Asian countries in which Alpha-Thalassemia is common) to 1 in 4000 (2). Despite the high frequency of non-immune hydrops fetalis which was found in this study, no hematologic findings supportive of Alpha-Thalassemia were detected in the parents.

While the frequency of immune type hydrops fetalis has decreased to 13% in developed countries due to preventive programs (2), this figure was 62% of all cases in the present study. This significant difference may be the result of the low rate of anti-Rh antibody therapy in at risk pregnancies. Moreover, this hospital-based study was done in three referral centers for high risk pregnancies, so these results may not be representative of actual population.

Differential diagnosis and causes of non-immune hydrops fetalis have been evaluated in many studies that the results vary and for the majority of cases the leading cause can not be found (5). In a recent study, Abrams et al. evaluated all hydrops fetalis cases among neonates admitted for neonatal intensive care unit. In 598 cases with confirmed hydrops diagnosis, the common causes were congenital heart problems, twin-to-twin transfusion, congenital anomalies, chromosomal abnormalities, congenital viral infection and congenital anemia which are the least common cause. Two other retrospective studies on hydrops fetalis revealed that the common underlying causes are the same as previous study but no hydropic fetus was detected due to Alpha-Thalassemia (6,7).

However, Alpha-Thalassemia is very common in Southeast Asians and homozygosity for α-thalassemia genotype (α/-α-) is the major cause of hydrops fetalis in this population (10). Different studies on this population have reported Alpha-Thalassemia as the most important cause of hydrops fetalis and have recommended antenatal screening of alpha thalassemia to reduce the occurrence of hydrops fetalis (11, 12). In the present study, no alpha thalassemia carrier was detected among mothers of hydrops fetalis fetuses, so it seems that these results are compatible with other studies except Southeast Asian population.

The aim of this study was to identify the possible role of alpha thalassemia as a cause of hydrops fetalis and to elucidate the necessity of molecular study on alpha thalassemia carriers to prevent this fatal disorder. As previously described, the frequency of α⁺ thalassemia in Iranian patients is very low (8,9), and therefore, alpha thalassemia is not a major cause for hydrops fetalis in Tehran population.

These findings questions the cost-effectiveness of population scaled detailed biochemical and/or molecular screening programs of α-globin gene mutations in Iranian population.

Acknowledgement
This work was a project funded by Medical Sciences/University of Tehran.

References
4. Lam YH, Ghosh A, Tang MH, Lee CP, Sin SY. Second-


