Incidence, Causes and Pregnancy Outcomes of Hydrops Fetalis at Srinagarind Hospital, 1996-2005: A 10-Year Review

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Objective: *To identify the incidence and determine causes and pregnancy outcomes of hydrops fetalis at Srinagarind Hospital.*
Study design: *A retrospective descriptive study.*
Setting: *Department of Obstetrics and Gynecology, Faculty of Medicine, Srinagarind Hospital, Khon Kaen University.*
Material and Method: *A retrospective medical record review of all pregnant women and newborns who were diagnosed with hydrops fetalis at all gestational ages and delivered at Srinagarind Hospital between 1996 and 2005.*
Results: *During the period of study, the incidence of hydrops fetalis was 1.80 per 1,000 total births (82 cases of 45,499 total births). Thirty-nine cases (47.56%) were idiopathic, 30 cases (36.58%) were Hb Bart's hydrops fetalis, and three (3.66%) cases were caused by congenital infection. The others 10 cases (12.19%) were achondrogenesis, Turner syndrome, twin-to-twin transfusion syndrome, severe anemia with unknown primary cause, cystic hygroma, multiple congenital anomalies, and Rh isoimmunization. The mortality rate of hydrops fetalis in the present series was 98.78%. One case, caused by Rh isoimmunization, survived. Maternal complications were 30 cases (36.59%) consisting of preeclampsia, preterm labor, disseminated intravascular coagulopathy, placenta previa, and postpartum hemorrhage.*
Conclusion: *The incidence of hydrops fetalis was 1.80 per 1,000 total births. The common known cause was Hb Bart's hydrops fetalis. The mortality rate of hydrops fetalis in the present study was very high.*

Keywords: *Hydrops fetalis, Incidence, Cause, Pregnancy outcomes*

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Hydrops fetalis is one of the severe fetal abnormalities defined as the excessive accumulation of fluids in the interstitial compartment including edema, ascites, pleural and pericardial effusion. A variety of pathogenic mechanisms can lead to hydrops fetali[1,2].

Hydrops fetalis can be classified according to immune and nonimmune causes. The incidence of hydrops fetalis is not frequent, occurring between range from 0.04-6.04 of 1,000 total births in many countries[3-7], 3.95 of 1,000 total births in the North of Thailand[8], and 2.81 of 1,000 total births in the South of Thailand[9]. In Thailand, many studies presented the incidence of Hb Bart's hydrops fetalis, 3.02 of 1,000 total births in the North of Thailand[10], 0.78 of 1,000 total births in the South Thailand[9], 0.69 and 0.61 of 1,000 total births in Siriraj Hospital[11] and Ramathibodi Hospital[12], respectively. Although the incidence of hydrops fetalis is small, it has a high mortality rate. It can cause serious obstetric complications such as pregnancy induced hypertension and postpartum hemorrhage, which lead to the poor maternal and fetal outcomes[13-17]. The early detection can prevent these complications.

The purpose of the present study was to determine the epidemiological information of hydrops

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fetalis at Srinagarind Hospital particularly in the incidence, causes, and pregnancy outcomes.

Material and Method

A retrospective medical record review of all pregnant women and newborns that were diagnosed with hydrops fetalis at all gestational age and delivered at Srinagarind Hospital between 1996 and 2005 was completed. In the present study, hydrops fetalis was defined as fluid accumulation in two cavities or one cavity with skin edema[1].

All cases were reviewed to identify maternal information, laboratory investigation, and pregnancy outcomes. Maternal information included age, places of antenatal care, gravidity, parity, gestational age at time of diagnosis, underlying diseases, previous history of hydrops fetalis, clinical presentations, and obstetric complications.

Laboratory investigations of mothers included complete blood count, RBC indices, Hb typing, blood group, indirect Coomb's test, TORCH titers, and VDRL. Their couples were evaluated for complete blood count, RBC indices, Hb typing, and blood group. All fetuses were evaluated the same as the mothers, in addition to direct Coomb's test and fetal karyotype by individual methods as umbilical cord blood sampling, venepuncture at neonatal unit or postmortem heart blood sampling. The authors collected all ultrasonographic findings including fetal parameters, fetal abnormalities, placental thickness and amniotic fluid volume.

At postmortem period, the authors confirmed the diagnosis and causes by autopsy especially in the last 5 years. These performed by fetal pathologist in our department.

Regarding the etiologic diagnosis, hydrops fetalis was classified in the following categories: Hb Bart's hydrops fetalis, congenital infections, congenital anomalies, blood group incompatibility, chromosomal abnormalities and finally, after extremely finding out all investigations, unknown cause or idiopathic hydrops fetalis.

All data were calculated by frequency, percentage and mean and analyzed by the statistical data SPSS 14. The present study was approved by the Human Research Ethics Committee of Khon Kaen University.

Results

During the 10-year period study, there were 45,499 total births at Srinagarind Hospital. In this population, the diagnosis of hydrops fetalis was made in 82 cases. The incidence was 1.80 per 1,000 total births and varied from 0.91-4.67 per 1,000 total births in each year (Table 1).

The causes of hydrops fetalis were determined in 43 of the 82 cases (52.44%). The unknown cause was accounted in 39 of the 82 cases (47.56%). The most common cause was Hb Bart's hydrops fetalis, which accounted for 30 of the 82 cases (36.59%) in which the incidence was 0.66 per 1,000 total births. Three of 43 cases (3.66%) were congenital infections, which consisted of two cases of CMV infections and one case of parvovirus B19. The other 10 cases of the 82 cases (12.19%), two each of Turner syndrome (45, XO), twin-to-twin transfusion syndrome, and severe anemia with unknown primary cause and one each of achondrogenesis, multiple anomalies, cystic hygroma, and Rh isoimunization (Table 2).

The mean maternal age was 26 years. Most of them were in the range between 21-30 years. Regarding the gestational age at detection of hydrops fetalis, ranged from 16-40 weeks. Mean gestational age at detection was 25 weeks. In first five years (1996-2000), the pregnant women who attended the antenatal clinic at Srinagarind Hospital, three cases could be detected before 28 weeks and five cases were detected after 28 weeks. For the last five years (2001-2005), the detection was earlier. Similarly as in the cases referred from other hospitals, 11 cases were detected before 28 weeks in the first five years and increased to 17 cases in the last five years.

Of the 82 cases, 40 cases were fetal death (48.78%), five cases (6.10%) of stillbirth, and 36 cases (43.90%) of early neonatal death. Only one case (1.21%)

Table 1. Incidence of hydrops fetalis

Year	Total births	Hydrops fetalis	Incidence (1,000 total births)
1996	5,835	8	1.37
1997	6,974	15	2.15
1998	4,386	4	0.91
1999	4,034	5	1.24
2000	4,090	5	1.22
2001	3,617	5	1.38
2002	3,545	13	3.67
2003	2,900	8	2.76
2004	2,783	13	4.67
2005	2,677	6	2.24
Total	45,499	82	1.80

Table 2. Causes of hydrops fetalis

Year	Hb Bart's hydrops fetalis		Infection		Unknown		Others	Total
	n	%	n	%	n	%		
1996	3	3.66	0	0	3	3.66	2 - (Achondrogenesis) - (Turner syndrome)	8
1997	8	9.76	2*[a]	2.44	5	6.0	-	15
1998	1	1.22	0	0.00	3	3.66	-	4
1999	2	2.44	0	0	2	2.44	1 - (Severe anemia, unknown cause)	5
2000	1	1.22	0	0	3	3.66	1 - (Turner syndrome)	5
2001	3	3.66	0	0	1	1.22	1 - (Cystic hygroma)	5
2002	3	3.66	0	0	9	10.97	1 - (Rh isoimmunization)	13
2003	4	4.88	0	0	3	3.66	1 - (Twin to twin transfusion syndrome)	8
2004	3	3.66	1*[b]	1.22	8	9.76	1 - (Severe anemia, unknown cause)	13
2005	2	2.43	0	0	2	2.44	2 - (Twin to twin transfusion syndrome) - (Multiple anomalies)	6
Total	30	36.58	3	3.66	39	47.56	10	82

*[a] = CMV infection, *[b] = parvovirus B 19 infection

Table 3. Maternal complications

Maternal complications	No. of patients	%
Preeclampsia	17	20.73
Preterm labor	9	10.97
Disseminated intravascular coagulopathy	2	2.44
Placenta previa	1	1.22
Postpartum hemorrhage	1	1.22
No complication	52	63.42
Total	82	100.00

with Rh isoimmunization survived due to emergency cesarean section at 34 weeks and promptly performed blood transfusion after birth. The overall mortality rate was 98.78%.

Maternal clinical presentations were 18 cases of decreased or loss of quickening (21.95%), nine of preterm labor (10.98%), eight of edema and hypertension (9.76%), seven of large for date (8.54%), and three of term labor (3.66%). However, most of the cases, 36 of the 82 (43.90%), had no clinical symptoms and were detected by ultrasound screening.

Maternal complications, 30 of 82 cases, were preeclampsia in 17 cases (20.73%), preterm labor in nine cases (10.97%), disseminated intravascular coagulopathy in two cases (2.44%), and one case each (1.22%) of placenta previa and postpartum hemorrhage (Table 3).

The comparison of maternal complications in Hb Bart's hydrops fetalis group and non-Hb Bart's hydrops fetalis group, the authors found that, preeclampsia had significantly higher in the Hb Bart's hydrops fetalis group than in the non-Hb Bart's hydrops fetalis group (33.33% and 13.46%, p-value < 0.05), respectively.

Discussion

From the result of the present study, the incidence of hydrops fetalis at Srinagarind Hospital,

the Northeastern region of Thailand, was 1.80 per 1,000 total births. The trend of the incidence up to 10 years was increasing. This is probably because the Fetal Diagnosis and Therapy Division was established in our department in 1999 and our hospital is the tertiary center. When other hospitals suspected hydropic signs in ultrasound screening, which was widely performed in many hospitals nowadays, the patients were referred to our hospital for confirmed diagnosis and performed proper managements. However, the incidence was less than the report in the Northern region of Thailand[8] due to high incidence of Hb Bart's hydrops fetalis in that area[10].

The most common known cause was Hb Bart's hydrops fetalis accounted in 0.66 per 1,000 total births. The incidence of Hb Bart's hydrops fetalis was less than the report of 3.02 per 1,000 total births from Maharaj Nakorn Chiang Mai Hospital, the Northern region of Thailand[10], but found the similar incidence rate reported in the South of Thailand, Central part of Thailand from Siriraj Hospital[11] and Ramathibodi Hospital[12], which were 0.78, 0.69 and 0.61 per 1,000 total births, respectively. This is possibly, because the epidemic area of alpha-thalassemia 1 was high in the North of Thailand but it was the same rate in other regions[18-21].

The incidence of unknown cause of hydrops fetalis in the present study is rather high when compared with other studies[2-8]. This might be the limitation of laboratory investigations to determine these causes of hydrops fetalis such as fetal echo-cardiography and fetal autopsy, especially in the first five-year period study, due to strong association between nonimmune hydrops and cardiac abnormalities, some inborn error of metabolism disease, viral infections, and genetic syndromes.

The mean maternal age in the present study showed that hydrops fetalis was not related to advanced maternal age. On the contrary, the authors found the higher rate in early age group below 30 years.

As the result, for the last five years, the detection was earlier. The development of antenatal care has been increasing in the Northeastern part of Thailand and obstetricians could detect hydrops fetalis in earlier gestational age due to ultrasound screening.

The mortality rate of hydrops fetalis was nearly 100%, of which only one case with Rh isoimmunization survived. This case was detected at 34 weeks gestation. After the cause was identified, the authors counseled the mother about termination of pregnancy by cesarean section to save the baby's life and promptly transfused blood components after birth. This baby is still alive after follow up in 2-year period.

Maternal complications were found about two in three of all cases, which was a higher rate. If obstetricians ignore these complications, this can lead to poor maternal and fetal outcomes[10-17]. When the authors compared the maternal complications between Hb Bart's hydrops fetalis group and non-Hb Bart's hydrops fetalis group, the authors found the occurrence of preeclampsia was significantly higher in Hb Bart's hydrops fetalis group. This finding is very important in clinical practice because once obstetricians found hydrops fetalis with preeclampsia, obstetricians should intend to find out Hb Bart's hydrops fetalis due to it being the most common cause of fetal hydrops in Thailand[8-12].

Early identification of causes of fetal hydrops, especially Hb Bart's hydrops fetalis, which could help the parents choose the optimal modalities of management before numerous serious maternal and fetal complications occurred.

As the advance of fetal therapy, in utero fetal intravascular blood transfusion to hydropic fetus due to idiopathic fetal anemia is progressively performed in many centers[22,23]. Our institute reported the first case of Thailand in 1999 by this therapy in non-hydropic fetus with Rh isoimmunization[24]. This therapy leads to the improvement of fetal outcome.

The benefit of the present study is to apply these findings to counsel pregnant women with hydrops fetalis about the investigation, prognosis of disease, as well as the optimal modalities of management.

The present study was a retrospective study, some informations and laboratory investigation could not be completely collected. However, future studies should be made prospectively for complete information and extensive laboratory investigation.

Conclusion

The incidence of hydrops fetalis was 1.8 per 1,000 total births. The most common known cause was Hb Bart's hydrops fetalis. Nearly one hundred percent of perinatal mortality and severe maternal complications were seen. Early diagnosis, early treatment in treatable cases, or early termination of pregnancy will avoid these complications.

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ผลการศึกษา: *จากการศึกษา พบภาวะทารกบวมน้ำ 82 ราย จากการคลอดทั้งหมด 45,499 ราย คิดเป็นอุบัติการณ์ 1.80 ต่อ การคลอดทั้งหมด 1,000 ราย 39 ราย (47.56%) ไม่ทราบสาเหตุ พบสาเหตุจากภาวะฮีโมโกลบิน บาร์ทส์ ไฮดรอพส์ ฟีทาลีส 30 ราย (36.59%) การติดเชื้อแต่กำเนิด 3 ราย (3.66%) และสาเหตุอื่น ๆ 10 ราย (12.19%) ได้แก่ achondrogenesis, Turner syndrome, twin to twin transfusion syndrome ภาวะซีดไม่ทราบสาเหตุ cystic hygroma ความพิการแต่กำเนิดหลายชนิด และ Rh isoimmunization อัตราตายของภาวะทารกบวมน้ำสูงถึง ร้อยละ 98.78 มีเพียง 1 รายที่รอดชีวิต จากสาเหตุ Rh isoimmunization ภาวะแทรกซ้อนในมารดาพบ 30 ราย (36.59%) ประกอบด้วย ภาวะครรภ์เป็นพิษ การเจ็บครรภ์คลอดก่อนกำหนด ภาวะการเกิดลิ่มเลือดกระจายทั่วไปในหลอดเลือด รกเกาะต่ำ และตกเลือดหลังคลอด*
สรุป: *อุบัติการณ์ภาวะทารกบวมน้ำ 1.80 ต่อ การคลอดทั้งหมด 1,000 ราย สาเหตุที่พบมากที่สุด คือ ภาวะฮีโมโกลบินบาร์ทส์ ไฮดรอพส์ ฟีทาลีส พบอัตราตายของภาวะทารกบวมน้ำสูง*