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A Survey of Late Fetal Deaths in a Japanese Prefecture

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1. Introduction

Vital statistics in Japan show that the fetal death rate at ≥28 weeks gestation was 2.1/1000 live births in 2009 (Table 1), which is the lowest among high-income countries (Mother's & Children's Health & Welfare Association, 2011). Japan started to use 22 weeks instead of 28 weeks as a definition of late fetal death in 1995. Since these statistics started in 1947, the fetal death rate in Japan after 22 weeks gestation has been decreasing, and recently, the rate of decrease has slowed down since 2005. This is a common phenomenon among high-income countries, and especially in the UK, the late fetal death rate after 28 weeks gestation is actually starting to increase in the last few years. This is thought to be related to late child bearing and an increase in multiple births due to assisted reproductive technology in the UK (Confidential Enquiry into Stillbirths and Deaths in Infancy, 2001). Any 'child' expelled or issued forth from its mother after the 24th week of pregnancy that did not breathe or show any other signs of life is registered as a stillbirth in U.K., whereas a stillbirth after the 22nd week of pregnancy is registered as a late fetal death in Japan. Thus, there is a two-week difference in the definition of stillbirth between the U.K. and Japan, and medical interventions have been performed based on these definitions. The WHO general recommendation is 22 weeks of gestation.

Country	Year	Perinatal mortality rate	Fetal death rate at ≥28 weeks	Early neonatal mortality rate at < 7 days of age
Japan	2009	2.9	2.1	0.8
Singapore	2008	3.1	2.2	0.9
Sweden	2008	4.3	3.0	1.3
Italy	2007	4.5	2.8	1.7
Germany	2007	5.6	3.5	2.1
Netherlands	2007	5.8	3.4	2.4
U.S.A.	2003	6.8	3.1	3.7
U.K.	2003	8.5	5.7	2.8
France	2007	10.8	9.2	1.6

Table 1. Perinatal mortality rate in selected countries using fetal death rate at ≥28 weeks for international comparison.

Late fetal deaths at ≥22 weeks have outnumbered early neonatal deaths at < 7 days of age in the last 10 years (2000-2009) in the whole of Japan (77.9-80.7%) and in Wakayama prefecture (75.7-85.7%). Therefore, it is important to study risk factors or causes of late fetal deaths for prevention of these deaths and reduction of perinatal mortality. Obesity, socioeconomic status, and advanced maternal age in pregnancy have been listed as risk factors. Placental abruption, lethal congenital anomalies, infections, birth traumas, and blood type incompatibilities have been described as causes of late fetal death (Fretts, 2005). However, it is difficult to specify the cause of fetal death in a practical clinical setting, and the cause may be unknown in 25 to 60% of cases (Alessandri et al, 1992; Frøen et al, 2001; Huang et al, 2000; Yudkin et al, 1987). Even in a study with a 97% autopsy rate (Fretts, 1992), the causes of fetal death were unknown in 14% of the cases.

Using the new ReCoDe (relevant condition at death) classification, Gardosi et al. (2005) found that intrauterine growth restriction (FGR) was the cause of fetal death in 57.7% of cases classified as due to unknown causes using the conventional classification by Wigglesworth et al. (1980). The ReCoDe classification is based on the relevant condition at death. It does not mean the basic cause of fetal death**.** We surveyed late fetal deaths by means of a questionnaire mailed to obstetricians or midwives in all labor institutes in Wakayama prefecture, one of the 47 administrative divisions of Japan, which has a population of 1.000 million and live births of 7,516 in 2009. Data were examined using the ReCoDe classification, with the goal of obtaining results that will be useful for reducing the perinatal mortality rate in Japan and compensating for the dwindling birthrate in Japan.

2. Methods

We surveyed late fetal deaths, which were defined as stillbirths after 22 weeks of gestation, every year from 2001 to 2010 in Wakayama prefecture using a questionnaire mailed to obstetricians or midwives in all labor institutes in the prefecture. We mailed the questionnaire in March or April every year and requested a report on late fetal deaths in the previous year, including data and conditions that the obstetrician or midwife in charge considered to be most relevant to stillbirth. The requested data included the date of delivery, gestational age, the baby's birth weight and sex, maternal characteristics, and pregnancy details. The questionnaire collection was completed by the end of June. The cases were classified according to the ReCoDe classification using the data of the questionnaire obtained from the obstetrician or midwife in charge of them who reviewed the case record. The ReCoDe classification system seeks to establish what went wrong, but not necessarily why. The hierarchy of classification starts from conditions affecting the fetus and moves outwards in simple anatomical groups to those affecting umbilical cord, placenta, amniotic fluid, uterus, mother, intrapartum, trauma, and unclassified, which are subdivided into pathophysiological conditions, with the primary condition being the first on the list that is applicable to a given case. More than one category can be coded if the information is available. Intrauterine growth restriction is included as the last category in group A (A7): a fetus below the 10th percentile is assigned this classification only if no other specific fetal conditions are present (Committee of Neonate, Japan Pediatric Society, 2010). All cases were divided into groups of primipara and multipara pregnancies and the relationships between the parity and the relevant conditions for fetal death were compared by Fisher's direct method.

3. Results

Sixteen to 35 late fetal deaths (stillbirths after 22 weeks of gestation) per year from 2001 to 2010 were reported from 27-30 facilities in Wakayama prefecture. The total was 240 cases in the 10-year period. The mean response rate for the questionnaires mailed yearly to obstetricians and midwives in all labor institutes in the prefecture was 0.843 (0.743-0.933). There were 81425 live births and 303 late fetal deaths in Wakayama prefecture during the 10 years from 2001 to 2010, according to the vital statistics based on residence (Vital statistics in Japan, Tokyo: Ministry of Health, Labor and Welfare, 2010).

In the ReCoDe classification, the most frequent condition associated with late fetal death was intrauterine growth restriction (FGR) (A7) (n=73, 30.4%); followed by umbilical cord abnormalities excluding prolapse, entanglement, knot, and velamentous insertion (n=29, 12.1%); unexplained antepartum stillbirths (n=27, 11.2%); lethal congenital anomaly (n=27, 11.2%); placental abruption (n=26, 10.8%); intrapartum asphyxia (n=15, 6.3%); and twin-twin transfusion (n=15, 6.3%) (Table 2).

Primary ReCoDe classification		Year	01-05	06-10	01-10	%
A,	1. Lethal congenital anomaly	A1	16	11	27	11.3
Fetus	2. Infection, 2.1 Chronic	A2.1			0	0
	2.2 Acute	A2.2	1	1	2	0.8
	3. Non-immune hydrops	A3		2	2	0.8
	4. Isoimmunisation	A4			0	0
	5. Fetomaternal transfusion	A5			0	0
	6. Twin-twin transfusion	A6	7	8	15	6.3
	7. Fetal growth restriction	A7	35	38	73	30.4
B,	1. Prolapse	B1	2	2	4	1.7
Umbilical	2, Constricting loop or knot	B2	2	2	4	1.7
cord	3. Veramentous insertion	B3	1		1	0.4
	4. Umbilical cord-other	B4	13	16	29	12.1
C,	1. Abruptio	C1	11	15	26	10.8
Placenta	2. Previa	C2	1		1	0.4
	3. Vasa previa	C3	1		1	0.4
	4. Placental insufficiency	C4			0	0
	5. Placenta-other	C5		1	1	0.4
D,	1. Chorioamnionitis	D1		1	1	0.4
Amniotic	2. Oligohydramnios	D2		1	1	0.4
fluid	3. Polyhydramnios	D3		1	1	0.4
E,	1. Rupture	E1	3		3	1.3
Uterus	2. Uterine anomalies	E2			0	0
	3. Uterus-other	E3		1	1	0.4

Primary ReCoDe classification		Year	01-05	06-10	01-10	%
F,	1. Diabetes	F1	1		1	0.4
Mother	2. Thyroid diseases	F2			0	0
	3. Essential hypertension	F3			0	0
	4. Hypertensive diseases in pregnancy	F4	2		2	0.8
	5. Lupus or antiphospholipid syndrome	F5			0	0
	6. Chorestasis	F6			0	0
	7. Drug misuse	F7			0	0
	8. Other maternal condition	F8		2	2	0.8
G,	1. Asphyxia	G1	9	6	15	6.3
Intrapartum	2. Birth trauma	G2			0	0
H,	1. External	H1			0	0
Trauma	2. Iatrogenic	H2			0	0
I,	1. No relevant condition identified	I1	13	14	27	11.3
Unclassified	2. No information available	I2			0	0
	Total		118	122	240	100.0

Table 2. Primary ReCoDe classification for 240 late fetal deaths in 2001-2010 in Wakayama prefecture.

There was no major change in the number of each primary ReCoDe classification between the first 5 years (total 118) and the latter 5 years (total 122) during the 10 years form 2001 to 2010.

A second ReCoDe class was found in 86 cases (35.8%). Among 73 cases whose primary ReCoDe classification was FGR (since FGR was the first on the list), 48 (65.8%) had a second category, with umbilical cord-other (B4) (n=21) and placental abruption (C1) (n=10) being the most frequent second ReCoDe category for FGR (A7) (Table 3). FGR was the second ReCoDe category in 19 (70.4%) of the 27 cases of lethal congenital anomalies (A1), 1 of 2 acute infections (A2.2), 1 of 2 non-immune hydrops (A3), and 6 (40%) of 15 twin-twin transfusions.

(A7) FGR	n=73
(A7) alone	n=25
(A7) with 2nd ReCoDe	n=48
(B2) Constricting loop or knot	3
(B3) Veramentous insertion	1
(B4) Umbilical cord-other	21
(C1) Placental abruption	10
(C2) Placenta previa	3
(C4) Placental insufficiency	1
(D3) Polyhydramnios	2
(E3) Uterus-other	1
(F4) Hypertensive diseases	2
(F8) Other maternal condition	1
(G1) Intrapartum aspyhxia	3

Table 3. Second ReCoDe categories in cases with FGR as the primary ReCoDe class.

The time of stillbirth was divided into 7 groups at three weeks intervals. The number of late fetal deaths was highest in weeks 22-24 of gestation, decreased gradually in weeks 25 to 30, and increased again in weeks 34 to 39. Late fetal death due to placental abruption occurred most often from 34 to 36 weeks of gestation (Fig. 1).

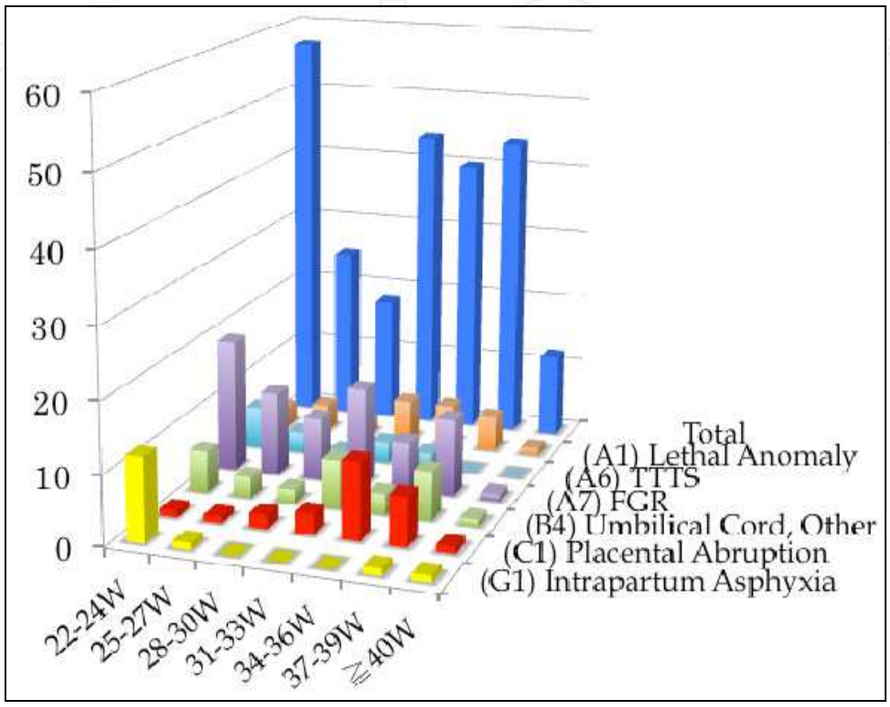


Fig. 1. Frequency of major ReCoDe categories according to gestational age.

A comparison of the causes of late fetal death in multipara and primipara cases showed that placental abruption was a more frequent cause in multipara cases (OR 3.64 [95%CI 1.47-9.02]), whereas FGR was a less frequent cause in multipara cases (OR 0.43 [95%CI 0.24-0.77]) (Table 4). Hypercoiled cord was most frequent in the umbilical cord-other category in the ReCoDe classification (15/29) (Table 5).

	Primipara n=129	Multipara n=111	Odds ratio	95% Confidence limit
(A1) Anomaly	18	9	0.54	[0.23-1.27]
(A6) TTTS	8	7	1.02	[0.36-2.90]
(A7) FGR	49	24	0.45	[0.25-0.80]
(B4) Umbilical cord-other	15	14	1.10	[0.50-2.39]
(C1) Abruptio	7	19	3.60	[1.45-8.92]
(G1) Asphyxia	5	10	2.46	[0.81-7.41]

Table 4. Odds ratio for major ReCoDe categories in multipara cases compared to primipara cases.

(B4) Umbilical cord-other	n=29
Hypercoiled	13
Stricture	5(1)
Torsion	2(1)[1]
Single Umbilical Artery	2
Umbilical Vein Thrombosis	1
Umbilical Cord Ulcer	1
Short Umbilical Cord	1
Unspecified	4

( ): number of cases combined with hypercoiled cord
[ ]: number of cases combined with single umbilical artery

Table 5. Items in the umbilical cord-other category.

Intrapartum asphyxia in babies from 22 to 23 weeks of gestation was the highest in the intrapartum asphyxia group (12/15) (Table 6). Unspecified multiple anomalies were most frequent and 18 trisomy was the second most common condition in the congenital lethal anomaly category (Table 7).

(G1) Intrapartum asphyxia	n=15
vaginal delivery at 22, 23 weeks gestation	12
vaginal delivery at 25 weeks gestation	1
Shoulder dystocia	1
Transverse lie	1

Table 6. Items in the intrapartum asphyxia category.

(A1) Lethal congenital anomaly	n=27
Unspedified multiple anomalies	10
18 trisomy	7
13 trisomy	3
Cardiac anomalies	3
Anencephaly	2
Other	2

Table 7. Items in the lethal congenital anomaly category.

There were 51 cases (21.3%) of advanced maternal age in pregnancy (≥35 years old) and the causes of late fetal deaths were FGR (n=12, 23.5%), placental abruption (n=9, 17.6%), umbilical cord-other (n=7, 13.7%), lethal anomaly (n=4, 7.8%) and unclassified (n=9, 17.6%).

There were 20 cases (8.5%) of pregnancies with assisted reproductive technology (ART). The mean maternal age in these cases was 35.0 years old, compared to 29.9 years old for non-ART pregnancies. ART included IVF-ET (n=12), AIH + ovulation inducer (n=4), AIH (n=2) and unspecified (n=2). The causes of late fetal deaths were FGR (n=9, 45%), lethal anomaly (n=3, 15%), uterus rupture (n=2, 10%), velamentous insertion (n=1, 5%), placental abruption (n=1, 5%), umbilical cord-other (n=1, 5%), and unclassified (n=3, 15%). Two of the 3 cases of uterus rupture (E1) involved pregnancies with ART, including one with AIH and one with an unspecified technique.

4. Discussion

A retrospective review of records is often a weak design due to lack of information recorded. In order to reduce this risk, this study was based on the yearly surveys obtained from the doctors or midwives in charge of the late fetal deaths who reviewed the previous year's records. The mothers were residents in Wakayama prefecture in 220 of the 240 cases of late fetal deaths reported in our survey. The custom of home-return for delivery, in which pregnant women give delivery in their home town where their parents can support them and care for their baby, is still partially alive in Japan, and this is the main reason why data from delivery institutes in a certain area do not coincide with the vital statistics in that area. However, the results of our survey are presumed to reflect the actual conditions of fetal deaths in Wakayama prefecture because we identified 220 (72.6%) of the 303 fetal deaths reported in the vital statistics.

We classified late fetal deaths according to the newly developed ReCoDe system (Gordosi et al, 2005) and found that the most frequent cause of late fetal death was FGR. This result is similar to that in a population-based cohort study performed in 1997-2003 in the West Midlands, U.K. (Gordosi et al, 2005).

The second most frequent cause of late fetal death in our survey was clearly an umbilical cord abnormality, excluding prolapse, constricting loop or knot, and velamentous insertion (B4), and these cases mainly involved a hypercoiled cord. There was no definition of hypercoiled cord in the questionnaire used in the survey. The obstetrician or midwife in charge reported conditions that they considered the most relevant to stillbirth and B4 ranked as the second most frequent cause of late fetal death. This is consistent with a report in Japan that 45% late fetal deaths are related to umbilical cord abnormality and that more than half of these cases involved a hypercoiled cord (Hasegawa et al, 2008). A hypercoiled cord has also been related to fetal death, fetal distress, meconium staining, and FGR in other studies (de Laat et al, 2007; Kashanian et al, 2005; Strong et al, 1994). Umbilical cord-other (n = 21) and placental abruption (n = 10) were the most common of the 48 second ReCoDes for FGR. To assess umbilical coiling, the umbilical coiling index (UCI) can be measured by ultrasound (Degani et al, 1995), but the sensitivity of the UCI for detection of hypercoiled cord at birth is only 17.3-25.4% (Quin et al, 2002; Predanic et al, 2005) and this method requires further development before it can be reliably used clinically to assess hypercoiled cord in utero.

Placental abruption is a serious emergency for both mother and child and is also highly unpredictable (Gordosi et al, 2005). The incidence of labor with placental abruption is highest at around 39 weeks of pregnancy, which is slightly earlier than for pregnancies without this complication (Ananth et al, 2001). The incidence of stillbirth with placental abruption peaked at 34-35 weeks of gestation in our survey, 4-5 weeks earlier than 39 weeks of gestation. We could not find any information that explained this difference in this survey. Overall, these results suggest that placental abruption may develop frequently from 34 to 39 weeks gestation, but perhaps in different ways in cases of late fetal death and live birth. In addition, multipara cases were more frequently associated with late fetal death due to placental abruption, compared to primipara cases. This does not necessarily mean that multipara pregnancies have a higher risk for placental abruption, since this study was based only on cases of late fetal death. Cohort studies and case controlled studies (Ananth et al, 1996. Kramer et al, 1997.

Sanchez et al, 2006) have been conducted in this regard, but these have produced different results for the risk of placental abruption with higher parity, with some showing no difference in the incidence of placental abruption between primipara and multipara pregnancies. Therefore, further studies are needed to reach a conclusion on this issue.

Twelve of 15 intrapartum asphyxias occurred in weeks 22-23 of gestation. Mortality in infants born at 22-23 weeks gestation has recently decreased in Japan, but the rate of major handicaps such as neurodevelopmental delay, cerebral palsy, visual impairment and hearing impairment are yet to improve (Hintz et al, 2005. Lorentz et al, 1998).

There are different policies on how to resuscitate babies born at 22-23 weeks gestation among delivery facilities in Japan. Babies with at least 24 weeks gestation are resuscitated at perinatal centers. If resuscitation at 22-23 weeks gestation becomes widely accepted in the near future in Japan, these fetal deaths will disappear or change to neonatal death. Intrapartum asphyxia at 22-23 weeks gestation may also affect the rate of late fetal death. Therefore, evaluation of the yearly change in late fetal death requires careful observation of the number of babies at 22-23 weeks gestation included in the sample population. We were unable to evaluate the extent of the risk of each abnormal condition because our survey was not performed as a cohort study that included all pregnancies in Wakayama or as a case controlled study with live births. However, this study does provide useful information for understanding the causes of late fetal deaths and for developing approaches for future prevention of these deaths.

5. Conclusion

Our data suggest that clinical follow up is important for placental abruption in multiparous pregnancy during weeks 34 and 36, for cord abnormalities (especially a hypercoiled cord) after 22 weeks gestation, and for primiparous pregnancy with FGR in order to decrease the late fetal deaths.

6. Summary

We surveyed late fetal deaths, defined as stillbirths after 22 weeks of gestation, from 2001 to 2010 in Wakayama prefecture using a questionnaire mailed to obstetricians and midwives in all labor institutes in the prefecture, one of the 47 administrative divisions of Japan. In the ten-year period, 240 stillbirths occurred and they were categorized using the ReCoDe (relevant condition at death) classification. The most common condition was intrauterine growth restriction (FGR) (n=73, 30.4%); followed by umbilical cord abnormalities such as a hypercoiled cord, excluding prolapse, entanglement, knot, and velamentous insertion (n=29, 12.1%); unexplained antepartum stillbirths (n=27, 11.3%); lethal congenital anomaly (n=27, 11.3 %); placental abruption (n=26, 10.9%); intrapartum asphyxia (n=15, 6.3%); and twin-twin transfusion (n=15, 6.3 %). A hypercoiled cord (n=15/29, 51.7%) was the most frequent condition in the umbilical cord category. Twelve of 15 stillbirths with intrapartum asphyxia occurred from 22 to 23 weeks gestation. The number of stillbirths with placental abruption peaked in the period from 34 to 36 gestational weeks (n=11/26, 42.3%). Multiparous women had a higher rate of placental abruption as the relevant condition at fetal death compared to primiparous women (OR 3.60 [1.45-8.92]), whereas fetal growth restriction was less common in multiparous women (OR 0.45 [0.25-0.80]).

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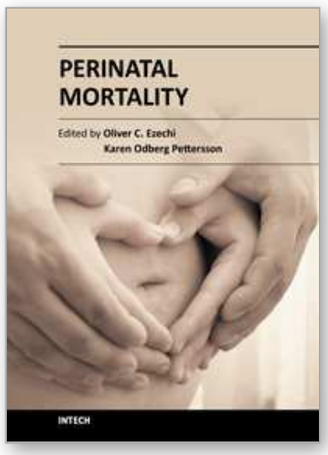
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This book is a compendium of important topics related to perinatal mortality. It has been written for anyone who is interested in perinatal medicine and wishes to be part of the global strategy for prevention and control of perinatal mortality. It covers variety of subjects using simple language that can easily be understood by most health workers and those interested in quality health care. Postgraduate students in midwifery, obstetrics and paediatrics will also find it a very useful companion.

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