

SURVIVAL OF TRISOMY 18 CASES IN JAPAN

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Summary: *Survival of trisomy 18 cases in Japan:* The prognosis of trisomy 18 is lethal, but recently some long-term survival cases have been recognized. We report here the mortality rate of trisomy 18 based on our hospital data and sporadically published reports in Japan. We collected the 7 previously published reports of mortality and 31 cases from our hospital data with trisomy 18. Our data pool comprised a total of 179 cases of trisomy 18 from 8 institutions. The mortality rates within 24 hours, 7, 28, 60, 180, and 365 days from birth were 14.84 % (19/128), 31.01 % (40/129), 56.25 % (72/128), 64.08 % (66/103), 82.17 % (106/129), and 90.90 % (140/154), respectively. Fourteen of the 154 patients (9.09 %) survived for more than 1 year. The Kaplan-Meier survival curves from 78 patients of 5 institutes suggest that trisomy 18 children who have survived over 7 months after birth may have a high probability of long-term survival. We should recognize not only that about 50 % of infants with trisomy 18 die within 1 month after birth, but also that about 10 % of patients survive over 1 year in Japan. These findings comprise Asia's first clinical statistics concerning trisomy 18, in which the data were collected from multiple institutions. This evidence is valuable in order to perform genetic counseling concerning the natural history of trisomy 18 not only in Japan but also in other countries.

Key words: Trisomy 18 - Survival - Japanese - Genetic counseling - Kaplan-Meier

INTRODUCTION

Precise genetic information regarding the prognosis of chromosomal abnormality should be provided in genetic counseling. The incidence of trisomy 18 is as low as 1 in 8000 births, but this is the 2nd highest incidence after trisomy 21 among chromosomal aberrations (9). However, an accurate mortality rate for trisomy 18 has never been reported from industrialized Asian countries. We present here the mortality rate of trisomy 18 based on our data and sporadically published reports in Japan (1, 2, 5, 6, 10, 11, 13). These results may be helpful in order to perform genetic counseling for this syndrome in Japan and other countries.

SUBJECTS AND METHODS

We collected data on mortality in trisomy 18 from 7 institutes in Japan, which were previously reported in literature from 1997 to 2003 (1, 2, 5, 6, 10, 11, 13). Data from a total of 148 cases of trisomy 18 from 7 reports were pooled. In addition, 31 patients with trisomy 18

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were retrospectively diagnosed and admitted to our hospital between 1980 and 2003. All these cases were included in this study: a total of 179 patients of 8 institutions. Regarding all these 179 cases as a population, survival of trisomy 18 patients in Japan was investigated (Table I). Trisomy 18 was definitely diagnosed based on chromosomal analysis in all cases. The karyotype was complete trisomy 18 in 175 cases and in 3 cases. One case had partial trisomy 18 with a karyotype of 46,X,der(Y)t(Y;18)(p11.3;q11.2). Concerning survival, cases were classified into death within 24 hours, 7, 28, 60, 180, and 365 days from birth. Cases of survival longer than 1 year were also summed. Survival curves were prepared by the Kaplan-Meier method. Rare case reports were excluded from this study.

Table I: The number of trisomy 18 cases reported in Japan and the year of publication.

References	Number of cases	Year of publication
1. Kuniba H <i>et al.</i> (6)	15	2003
2. Asanuma H <i>et al.</i> (1)	26	2002
3. Kimura J <i>et al.</i> (5)	50	2001
4. Yamaga H <i>et al.</i> (13)	14	2000
5. Fujii T <i>et al.</i> (2)	25	1999
6. Teraguchi M <i>et al.</i> (11)	12	1998
7. Takita M <i>et al.</i> (10)	6	1997
8. Our data	31	/
Total of 179 cases from 8 institutes		

RESULTS

The mortality rates within 24 hours, 7, 28, 60, 180, and 365 days calculated from the data of the 179 patients were 14.84% (19/128), 31.01% (40/129), 56.25% (72/128), 64.08% (66/103), 82.17% (106/129), and 90.90% (140/154), respectively, and 9.09% of patients (14/154) survived for more than 1 year (Table II).

The longest survival time was set at 365 days in the Kaplan-Meier survival curves prepared from the mortality data of 47 cases collected from 4 institutions (2, 5, 7, 8) and 31 cases of our institution, a total of 78 patients of 5 institutions (Fig. 1), whose dates of death were individually documented in the reports and our data.

Table II: Data on mortality in trisomy 18 from 8 institutes with a total of 179 cases in Japan.

No.	Article	Reference number	Number of cases	>24 hours	>7 days	>28 days	>60 days	>180 days	>1 year	1 year<
1	Kuniba <i>et al.</i>	6	15	1	4	9	10	11	12	3
2	Asanuma <i>et al.</i>	1	26	-	5	-	-	18	24	2
3	Kimura <i>et al.</i>	5	50	8	-	32	-	-	45	5
4	Yamaga <i>et al.</i>	13	14	1	5	7	8	13	14	0
5	Fujiu <i>et al.</i>	2	25	-	10	-	15	21	-	-
6	Teraguchi <i>et al.</i>	11	12	1	2	3	6	10	10	2
7	Takita <i>et al.</i>	10	6	4	6	6	6	6	6	0
8	our data	-	31	4	8	15	21	27	29	2
	Total (%)		179	19/128 (14.84%)	40/129 (31.01%)	72/128 (56.25%)	66/103 (64.08%)	106/129 (82.17%)	140/154 (90.90%)	14/154 (9.09%)

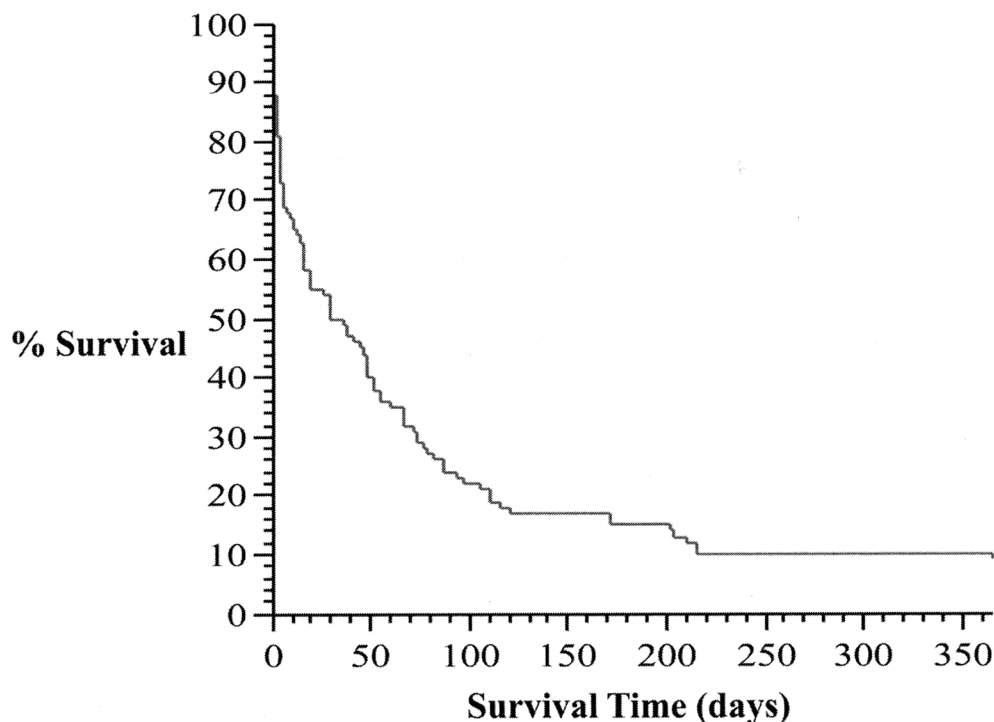


Figure 1: Kaplan-Meier survival curves for patients with trisomy 18 in Japan. This data comprised a total population of 78 patients with trisomy 18 from 5 centers. The vertical and horizontal axes represent % survival and survival time (days), respectively, setting the longest survival time at 365 days.

DISCUSSION

Complete autosomal trisomies frequently result in non-implantation or miscarriage, and chromosomal abnormality cases which can survive after birth are mostly trisomies 21, 18, and 13 (1). Trisomy 21 patients have a relatively long-term survival. The natural history and life prognosis of trisomy 21 have been statistically clarified, and it is now possible to provide the families of patients with sufficient medical information for genetic counseling and medical management.

On the other hand, cases of trisomies 18 and 13 have a poor prognosis and short survival; most of these patients die during the neonatal period or infancy (4, 12). Recently, the natural history and life prognosis of the 2 trisomies have been studied in the United states of America (8). However, there are no reports of large-scale statistics combining data from multiple medical centers for mortality statistics of trisomy 18 in Japan. Therefore, genetic counseling has been provided in Japan based on statistics from countries with different racial backgrounds and different medical health care environments.

To our knowledge, the prognosis of trisomy 18 is lethal (7), but some cases with long-term survival have been reported (4, 12). Our results were characterized by a mortality rate within 1 year of less than 90 %

and a higher rate of long-term survival. Our data are similar to those in previously reported literature on the mortality rate of trisomy 18 (3, 8). We suggest that the mortality rate of trisomy 18 is not affected by racial differences.

The Kaplan-Meier survival curves for 78 patients showed that all patients who survived for more than 210 days after birth had a long-term survival of more than 365 days, suggesting that trisomy 18 children who have survived over 7 months after birth may have a high probability of long-term survival in Japan.

In counseling for prenatally or postnatally diagnosed trisomy 18, or for patients with long-term survival, health care professionals and the families of patients should fully recognize not only that 30-50 % of infants with trisomy 18 die within 1 month after birth, but also that about 10 % of patients survive over 1 year in the medical care environment, and that a few cases of longer survival have been reported (4, 12). Since the details of fatal complications that frequently develop in trisomy 18, such as congenital heart diseases, esophageal atresia, and malformation of the digestive tract and brain, were unclear, the names of fatal diseases in individual cases and the presence or absence of complications in long-term survival cases could not be analyzed. However, these findings comprise Asia's first clinical statistics concerning the survival of patients with trisomy 18 covering multiple institutions based on Japanese data. These data are helpful to facilitate genetic counseling regarding trisomy 18 not only in Japan but also in other countries.

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