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Triplets and Higher Order Multiple Births in Japan

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Abstract. Multiple birth rates in entire Japan were analyzed using vital statistics for 1951 to 1988. The triplet rate was nearly constant from 1951 to 1974, where the rate per million births was 58, then increased with the year up to 1982 (104), and decreased up to 1984, and suddenly increased thereafter (109 in 1987). The average rate of quadruplets per million births from 1951 to 1968 was 0.93, then increased with the year up to 1975 (7.5), and decreased until 1984 and suddenly increased thereafter (10.6 in 1987). The rate of quintuplets was 0.77 per million births during the period from 1975 to 1987. The higher multiple birth rate since 1975 was attributed to the higher proportion of mothers treated with ovulation-inducing hormones in Japan. Since 1985, higher multiple birth rates might be partially attributed to in vitro fertilization. The stillbirth rates for male triplets gradually decreased from 1960 to 1978 and thereafter remained constant at a little higher level except in 1988, whereas the rates for females gradually decreased with the year. The overall stillbirth rates decreased to 1/4 for triplets and to 1/5 for quadruplets during the 37-year period from 1951. The overall stillbirth rate of quintuplets was 0.60 (51/85) during the period 1975-1987.

Key words: Triplets, Quadruplets, Quintuplets, Stillbirth rates, Maternal age

INTRODUCTION

In Japan, ovulation-inducing hormones have been used since 1966 [16], and since January 1975 the use of HMG (human menopausal gonadotropin) has been covered by the health insurance system. Bromocriptine has been commercially available since 1979. Imaizumi and Inouye [10] reported the secular trends of the triplet birth rates according to zygosity during the period 1960-1967 and in 1974. Imaizumi [6] also reported the secular trends of the overall rates of triplets and quadruplets during the periods 1951-1968 and 1974-1985, where the higher multiple birth rates since 1974 were attributed to the higher proportion of mothers treated with ovulation-inducing hormones. According to

Allen [2], the rate of triplets in the U.S. white population had nearly doubled by 1983 and in Belgium most triplet pregnancies now result from artificial induction of ovulation.

Imaizumi and Inouye [11,12] and Imaizumi [6] reported the secular trends of the stillbirth rates in triplet and quadruplet births during the periods 1951-1968 and 1974-1985. Imaizumi [7] also reported the stillbirth rate of quintuplet births during the period 1974-1985.

The present study deals with the secular trends of the birth rates and stillbirth rates of triplets, quadruplets and quintuplets in all of Japan, as well as with the effects of maternal age.

MULTIPLE BIRTH DATA

In this analysis data were obtained from vital statistics for the periods 1951-1968 and 1974-1988 [13]. Vital statistics data on multiple births have also been available in computer files since 1968, and in this study the computerized data between 1975 and 1985 were analysed. Another source of data is the "Survey on Socio-Economic Aspects of Vital Events - Plural Births in 1975" [14], the details of which were reported elsewhere [8,9].

RESULTS

Secular Changes of Multiple Birth Rate

Table 1 shows the secular changes in the overall rate of triplet births during the periods 1951-1968 and 1974-1988. The triplet rate was nearly constant up to 1974, where the rate per million births was 58.3. The rate gradually increased with the year up to 1980 (76.2), rapidly increased up to 1982 (103.8), and decreased up to 1984, and suddenly increased thereafter (109.2 in 1987). Fig. 1 shows the secular changes in the rate of triplets according to zygosity during the period 1955-1967 and in 1974 [10]. Frequencies of monozygotic, dizygotic and trizygotic triplet sets were estimated by Allen's method [1]. Monozygotic rate was slightly decreased with the year, but dizygotic rate as estimated from monozygotic and dizygotic twinning rates was decreased with the year. Trizygotic rate was increased with the year and particularly higher in 1974. Estimated rates of mono-, di-, and trizygotic triplet deliveries per million were 32.3, 17.7, and 4.2, respectively, during the period 1960-1967 and in 1974 [10].

Table 2 shows the secular changes in the overall rate of quadruplet births during the periods 1951-1968 and 1974-1988. The average rate per million from 1951 to 1968 was 0.93, then increased to 3.27 in 1974 and 7.49 in 1975, decreased until 1984, and suddenly increased thereafter (10.63 in 1987). According to Imaizumi and Inouye [12], estimated rates of mono-, di-, tri- and tetrazygotic quadruplet deliveries per million were 0.78, 0.19, 0.04, and 0.23, respectively, during the period 1955-1967 and in 1974.

Table 3 shows sex compositions and survival states in 17 quintuplet pregnancies during the period 1975-1987. The rate of quintuplets per million births was 0.77.

Table 1 - Secular change of triplet births and stillbirth rates, 1951-1968 and 1974-1988

Year	Live births		Fetal deaths		Total ^a	Triplet rate per million births	Stillbirth rate		χ ²
	M	F	M	F			M	F	
1951	-	-	-	-	408	58.13	-	-	0.532
1952	-	-	-	-	375	56.95	-	-	0.560
1953	-	-	-	-	273	44.43	-	-	0.491
1954	-	-	-	-	309	52.99	-	-	0.608
1955	-	-	-	-	390	68.00	-	-	0.505
1956	-	-	-	-	306	55.67	-	-	0.592
1957	-	-	-	-	288	55.44	-	-	0.545
1958	-	-	-	-	327	59.67	-	-	0.606
1959	-	-	-	-	285	52.89	-	-	0.607
1960	53	63	77	68	264	49.61	0.592	0.519	1.14
1961	55	56	104	91	309	58.60	0.654	0.619	0.27
1962	64	72	77	88	303	56.60	0.546	0.550	0.002
1963	78	75	76	82	315	57.59	0.494	0.522	0.16
1964	67	81	67	64	279	49.67	0.500	0.441	0.74
1965	78	95	64	81	321	54.24	0.451	0.460	0.003
1966	62	80	55	70	273	60.70	0.470	0.487	0.005
1967	85	97	58	84	330	53.10	0.406	0.464	0.89
1968	-	-	-	-	351	58.43	-	-	-
1974	98	133	65	61	372	58.30	0.399	0.314	2.40
1975	114	160	68	50	396	65.89	0.374	0.238	7.88*
1976	125	147	42	62	388	66.84	0.252	0.297	0.73*
1977	136	146	56	41	392	70.64	0.292	0.219	2.24
1978	145	172	32	29	386	71.66	0.181	0.144	0.68
1979	131	153	51	46	386	74.59	0.280	0.231	0.96
1980	148	141	43	38	378	76.16	0.225	0.212	0.03
1981	170	191	38	51	463	95.94	0.183	0.211	0.39
1982	183	180	68	52	496	103.75	0.271	0.224	1.17
1983	157	165	46	37	430	90.68	0.227	0.183	0.92
1984	156	162	47	31	408	87.06	0.232	0.161	2.71
1985	133	174	37	32	394	87.52	0.218	0.155	2.02
1986	139	169	60	17	393	90.43	0.302	0.091	25.23*
1987	165	195	57	36	462	109.18	0.257	0.156	6.46*
1988	175	211	30	18	451	109.43	0.146	0.079	4.38*

^a Including unknown sexes. * Significant at the 5% level.

Table 2 - Secular change of quadruplet births and stillbirth rates, 1951-1968 and 1974-1988

Year	Live births		Fetal deaths		Total ^a	Quadruplet rate per million births	Stillbirth rate
	M	F	M	F			
1951	-	-	-	-	0	0	-
1952	-	-	-	-	8 ^b	0.91	0.500
1953	-	-	-	-	0	0	-
1954	-	-	-	-	8	1.02	1.000
1955	2	0	7	11	20	2.61	0.900
1956	2	0	4	6	12	1.63	0.833
1957	0	0	4	8	12	1.72	1.000
1958	0	0	4	4	8	1.09	1.000
1959	0	0	0	0	0	0	-
1960	0	0	0	0	4	0.56	1.000
1961	4	0	4	0	8	1.13	0.500
1962	0	3	0	1	4	0.56	0.250
1963	0	0	0	0	0	0	-
1964	6	0	6	8	20	2.65	0.700
1965	0	0	4	0	4	0.50	1.000
1966	0	0	8	0	8	1.33	1.000
1967	0	4	4	0	8	0.96	0.500
1968	3	1	0	0	4	0.50	0
Subtotal	-	-	-	-	28	0.93	0.773
1974	7	4	9	4	28	3.27	0.607
1975	17	24	5	6	60	7.49	0.212
1976	5	3	10	5	38	4.91	0.652
1977	1	0	2	2	20	2.70	0.800
1978	9	13	4	4	30	4.18	0.267
1979	14	14	0	0	32	4.64	0.125
1980	4	4	4	4	16	2.42	0.500
1981	7	9	3	1	20	3.11	0.200
1982	11	15	0	5	31	4.86	0.161
1983	8	8	0	0	16	2.53	0
1984	8	3	0	1	16	2.56	0.313
1985	12	17	8	7	48	8.00	0.396
1986	13	22	2	3	48	8.28	0.271
1987	23	24	1	4	60	10.63	0.217
1988	23	20	3	2	48	8.74	0.104

^a Including unknown sexes.^b 4 live births and 4 fetal deaths.

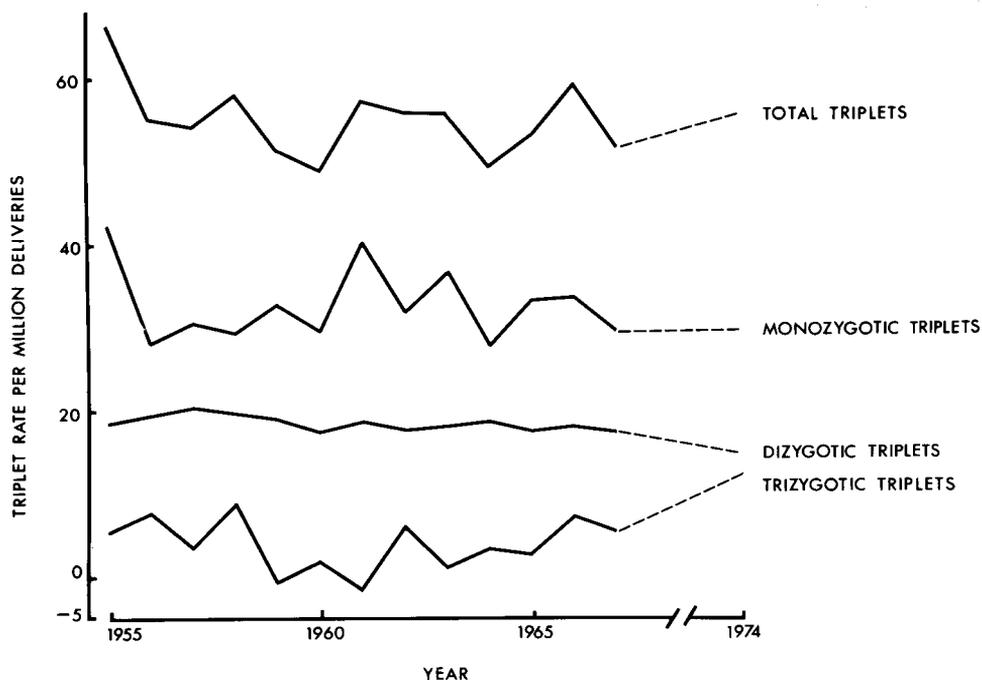


Fig. 1. Secular change of total, mono-, di- and trizygotic triplet rates during 1955-1967 and 1974 (from Imaizumi and Inouye [10]).

Effect of Maternal Age on Multiple Birth Rates

Fig. 2 shows the rates of triplet births according to zygosity and maternal age groups during the period 1960-1967 and in 1974 [10]. Monozygotic triplet rate is slightly increased up to the age group of 35-39 years and decreased thereafter. Similar but more marked pattern is seen for dizygotic rate, whereas trizygotic rate seems to be independent of maternal age. Table 4 shows the numbers and the rates of triplet births according to maternal age group during the period 1975-1985. Fig. 3 shows the overall rates of triplet births according to maternal age group during two periods: 1960-1968 and in 1974, and 1975-1985. The triplet rate in the former period increased up to the age group of 35-39 years and decreased thereafter, whereas the rate in the latter period increased up to the age group of 30-34 years and decreased thereafter. Then the maternal age pattern in the latter was different from that in the former period. In addition, the rate in the latter period was about 1.5 times higher than that in the former period in each maternal age group.

Table 4 also shows the numbers and the rates of quadruplet births according to maternal age group during the period 1975-1985. Fig. 4 shows the overall rate of quadruplet births according to maternal age group during two periods: 1960-1968 and in 1974, and 1975-1985. The quadruplet rates in each maternal age group was higher in the

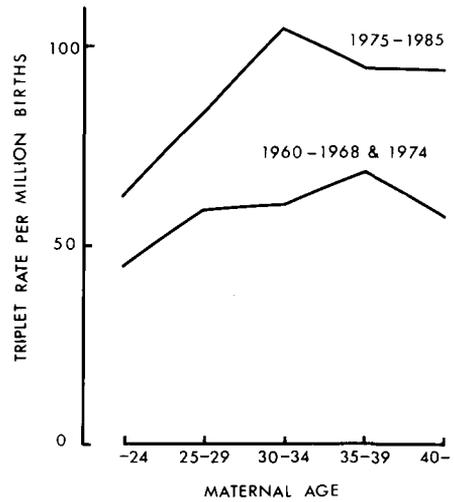
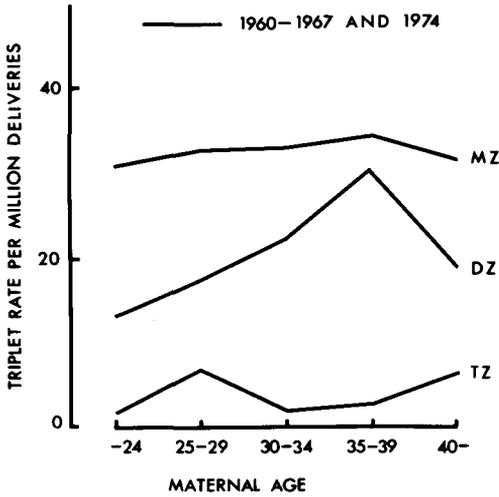


Fig. 2. Birth rates of triplets by zygosity and maternal age during 1960-1967 and in 1974 (from Imaizumi and Inouye [10]).

Fig. 3. Birth rates of triplets by maternal age during 1960-1968 and in 1974, and 1975-1985.

Table 3 - Sex compositions and survival states in quintuplet births, 1975-1987

Year	Sex composition	Survival states at birth
1975	MFFMF	LLLSS
	MMMFF	SSSSS
1976	MMFFF	LLLLL
	MUUUU	SSSSS
1977	MMMMF	LLSSS
	MMFFF	SSSSS
	MMMFF	SSSSS
1979	MMFFF	LLLLS
1980	MMFFF	LLLLL
	MFMMF	LLSSS
1981	MMMFF	LLLLL
	MMMFF	SSSSS
1982	MFFFF	SSSSS
	MFFFF	SSSSS
1983	MMFMF	LLLSS
1986	MFMMF	LLLLL
1987	UMMUM	SSSSS

L = Liveborn; S = Stillborn; U = Sex unknown.

Table 4 - Multiple births and stillbirth rates by maternal age, 1975-1985

Multiple births	Maternal age					Total
	<25	25-29	30-34	35-39	>40	
Triplets						
Number of livebirths	507	1,784	949	141	8	3,389
Number of fetal deaths	194	545	300	72	17	1,128
Total	701	2,329	1,249	213	25	4,517
Birth rate (per million)	62.30	83.45	104.04	94.91	93.80	84.15
Stillbirth rate	0.277	0.234	0.240	0.338	0.680	0.250
Quadruplets						
Number of livebirths	30	100	71	5	0	206
Number of fetal deaths	13	51	15	4	0	83
Total	43	151	86	9	0	289
Birth rate (per million)	2.87	4.06	5.37	3.01	0	4.04
Stillbirth rate	0.302	0.338	0.174	0.444	0	0.287
Quintuplets						
Number of livebirths	0	12	17	0	0	29
Number of fetal deaths	0	23	18	5	0	46
Total	0	35	35	5	0	75
Birth rate (per million)	0	0.73	1.67	1.20	0	0.80
Stillbirth rate	0	0.657	0.514	1.000	0	0.613

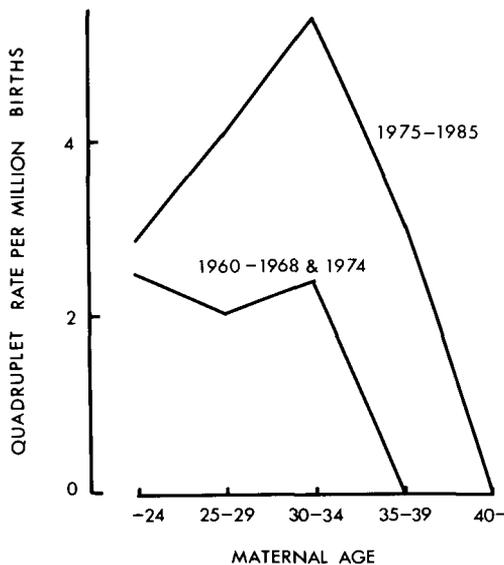


Fig. 4. Birth rates of quadruplets by maternal age during 1960-1968 and 1974, and 1975-1985.

latter than the former period. In the former period, the rates of quadruplet deliveries per million were 1.49, 1.03, 1.40 and 0, from the youngest to the oldest maternal age groups in this order, and a clear maternal age effect was not indicated [12]. The corresponding rates in the latter period were 2.87, 4.06, 5.37 and 3.01, respectively, where the rate increased up to the age group of 30-34 years and decreased thereafter.

Table 4 also shows the numbers and the rates of quintuplet births according to maternal age group during the period 1975-1985. The rate of quintuplets increased up to the age group of 30-34 years and decreased thereafter.

Secular Changes of Stillbirth Rate of Multiple Births

Table 1 also shows the secular changes in the stillbirth rate of triplets according to sexes during the periods 1960-1967 and 1974-1988. The rates for male triplets gradually decreased up to 1978 and thereafter remained constant at a little higher level except in 1988. On the other hand, the rates for female triplets gradually decreased with the year. The rates for male and female triplets were roughly the same up to 1981 and the rates were higher in males than in females thereafter, where the rates are significantly higher in male than in female triplets in 1975 and after 1986. The overall rates gradually decreased to 1/4 during the 37-year period from 1951. Fig. 5 shows the secular changes of the stillbirth rates of like- and unlike-sexed triplets during the period 1955-1967 and



Fig. 5. Secular change of stillbirth rates of like- and unlike-sexed triplets during 1955-1967 and 1974 (from Imaizumi and Inouye [11]).

in 1974. Stillbirth rate of like-sexed triplets increased slightly up to 1961 and decreased thereafter, and the figure in 1974 was 67% (0.33) of that in 1955 (0.50). On the other hand, the stillbirth rate of unlike-sexed triplets remained almost constant for the entire period, and the figure in 1974 was 88% (0.40) of that in 1955 (0.45). For the entire period 1955-1967 and in 1974, the difference between stillbirth rates of like- and unlike-sexed triplets is statistically significant at the 0.1% level, the rate being higher in like-sexed (0.53) than unlike-sexed (0.45) triplets [11].

Table 2 also shows the secular changes of the stillbirth rate of quadruplets during the periods 1951-1968 and 1974-1988. The overall rates decreased to 1/5 during the 36-year period from 1952. The stillbirth rates of quadruplet births were 0.73 for males and 0.83 for females during the period 1955-1968. The corresponding rates were 0.24 and 0.21, respectively, during the period 1974-1988. The difference between stillbirth rates of male and female quadruplets is not statistically significant at the 5% level.

As shown in Table 3, the stillbirth rates of quintuplet births were 0.55 (22/40) for males, 0.59 (23/39) for females, and 0.60 (51/85) overall, during the period 1975-1987.

Effect of Maternal Age on Stillbirth Rate of Multiple Births

Table 4 and Fig. 6 show the stillbirth rates of triplets and higher order multiple births according to maternal age group during the period 1975-1985. The lowest stillbirth rate of triplets is seen in the age group of 25-29 years, and increased with maternal age. Ac-

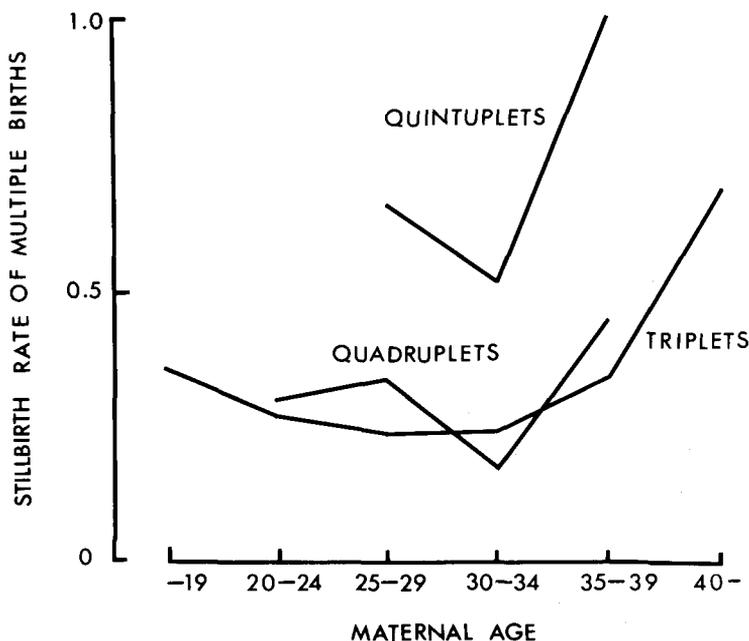


Fig. 6. Stillbirth rates of triplets and higher order multiple births by maternal age, 1975-1985.

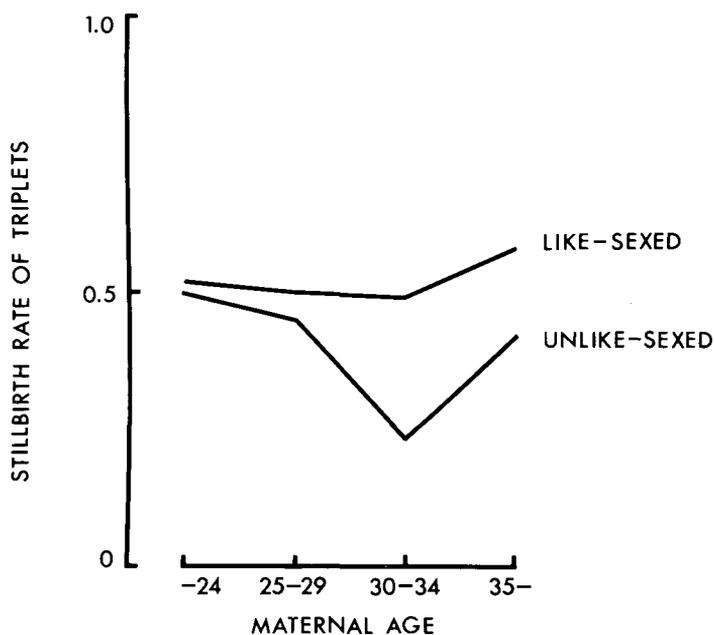


Fig. 7. Stillbirth rates of like- and unlike-sexed triplets according to maternal age during the entire period of 1960-1967 and in 1974 (from Imaizumi and Inouye [11]).

According to Imaizumi and Inouye [11], the stillbirth rate in like-sexed triplets decreased from the youngest maternal age group to maternal age group of 30-34 years, then markedly increased thereafter (Fig. 7). The pattern is similar but more marked in unlike-sexed triplets. As for the stillbirth rates of quadruplets and quintuplets, the lowest rate is seen in the age group of 30-34 years and the highest rate in the group aged 35 years or more.

DISCUSSION

With respect to racial differences in triplet rates according to zygosity, monozygotic triplet rates in England and Wales (1938-62), USA (1922-54), Italy (1933-54) [5], and Australia (1920-69) [4] were 13, 21, 21 and 24 per million deliveries, respectively. The rate in Japan was 32 per million deliveries during the period 1955-1967 and in 1974 [10]. Then the monozygotic triplet rate in Japan was around two times higher than the former four countries. Dizygotic triplet rates per million deliveries in the former four countries were 62, 58, 75, 52, respectively, whereas the rate in Japan was 18, 3 to 4 times lower than in the other countries. Trizygotic triplet rates per million deliveries were 34, 31, 52, 24 in the former four countries, respectively, and 4 in Japan, 6 to 13 times lower than in the other countries. Low dizygotic and trizygotic triplet rates are the characteristic features of Japanese.

According to Bulmer [5], the estimated rates of mono-, di-, tri- and tetrazygotic quadruplet deliveries per million were 0.29, 0.43, 0.42 and 0.56, respectively, for the combined data from England and Wales, USA, France and Italy. The monozygotic quadruplet rate was 2.7 times higher in Japan than in Europe and USA, the dizygotic and tetrazygotic quadruplet rates of the former were a half of the latter, and the trizygotic quadruplet rate of the former was one tenth of the latter. Therefore, Imaizumi and Inouye [12] concluded that a characteristic feature of multiple birth rate in Japan is higher rates of triplets and quadruplets of polyembryonic origin and lower rates of those of polyovulational origin than in Caucasian populations.

According to Baba [3], only 4 quintuplet pregnancies had been reported in Japan during the period from 1900 to 1974. However, 17 pregnancies occurred during the period from 1975 to 1987, and the rate of quintuplets per million births was 0.77. As Imaizumi [6] suggested, the higher multiple birth rate since 1974 was attributed to the higher proportion of mothers treated with ovulation-inducing hormones in Japan. But it seems that higher multiple birth rates since 1985 may be attributed to other causes. In Japan, the first in vitro fertilized baby was born in 1983. A survey of in vitro fertilization was conducted in December 1986 through questionnaires by Mori [15]. Among 142 in vitro fertilized pregnancies, 11 (7.7%) were multiple pregnancies. Therefore, the increase since 1985 may also be partially attributed to in vitro fertilization.

The stillbirth rate of twins was significantly higher in males than females in each year during the periods 1960-1967 and 1974-1985 [6]. In the present study, the stillbirth rate of triplets was only significantly higher in males than females in 1975 and after 1986 (Table 1), and the stillbirth rates of quadruplets and quintuplets were roughly the same for both sexes.

The effect of maternal age on stillbirth rate of triplets was similar to that in twins [9], but to a lesser degree. According to Imaizumi and Inouye [12], maternal age effect on stillbirth rate of quadruplets was not indicated during the period 1960-1968 and in 1974. In the present study, the lowest stillbirth rate is seen in the age group of 30-34 years (0.17) and the highest rate in the age group of 35-39 years (0.44), where the difference is not significant at the 5% level. Similarly, the corresponding stillbirth rates of quintuplets were 0.51 and 1.00, respectively. On the other hand, the lowest stillbirth rates for twins and triplets are seen in the age group of 25-29 years.

REFERENCES

1. Allen G (1960): A differential method for estimation of type frequencies in triplets and quadruplets. *Am J Hum Genet* 12:210-224.
2. Allen G (1988): Frequency of triplets and triplet zygotity types among U.S. births, 1964. *Acta Genet Med Gemellol* 37:299-306.
3. Baba K (1978): Quintuplet births in the world (in Japanese). *Nihon Taishitsugaku Zashi* 43:863-869.
4. Brackenridge CJ (1978): Aspects of the increasing triplet rate in Australia. *J Biosoc Sci* 10:183-188.

5. Bulmer MG (1970): *The Biology of Twinning in Man*. Oxford: Clarendon Press.
6. Imaizumi Y (1987): The recent trends in multiple births and stillbirth rates in Japan. *Acta Genet Med Gemellol* 36:325-334.
7. Imaizumi Y (1989): Stillbirth rate and weight at birth of quintuplets in Japan. *Acta Genet Med Gemellol* 38:65-69.
8. Imaizumi Y, Inouye E (1979): Analysis of multiple birth rates in Japan. I. Secular trend, maternal age effect, and geographical variation in twinning rates. *Acta Genet Med Gemellol* 28:107-124.
9. Imaizumi Y, Asaka A, Inouye E (1980): Analysis of multiple birth rates in Japan. II. Secular trend and effect of birth order, maternal age, and gestational age in stillbirth rate of twins. *Acta Genet Med Gemellol* 29: 223-231.
10. Imaizumi Y, Inouye E (1980): Analysis of multiple birth rates in Japan. III. Secular trend, maternal age effect, and geographical variation in triplet rates. *Jpn J Hum Genet* 25:73-81.
11. Imaizumi Y, Inouye E (1980): Analysis of multiple birth rates in Japan. IV. Secular trend, effect of maternal age and gestational age in stillbirth rates of triplets. *Jpn J Hum Genet* 25:219-227.
12. Imaizumi Y, Inouye E (1982): Analysis of multiple birth rates in Japan. VI. Quadruplets: Birth and stillbirth rates. *Jpn J Hum Genet* 27:227-234.
13. Japan, Ministry of Health and Welfare: *Vital Statistics. Health and Welfare Statistics and Information Department, Ministry of Health and Welfare, Tokyo. Annual. 1951-1968 and 1974-1988.*
14. Japan, Ministry of Health and Welfare: *Survey on Socio-Economic Aspects of Vital Events – Plural Births in 1975. Health and Welfare Statistics and Information Department, Ministry of Health and Welfare, Tokyo, 1977.*
15. Mori T.(1987): Progress in reproductive and medical technology (in Japanese). *Sanfujinkano Sekai* 39:963-966.
16. Sawazaki C, Tsubata H (1976): Statistics of multiple births in Japan (in Japanese). *Sanka to Fujinka* 43:863-869.

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