ANALYSIS OF MULTIPLE BIRTH RATES IN JAPAN

III. SECULAR TREND, MATERNAL AGE EFFECT AND GEOGRAPHICAL VARIATION IN TRIPLET RATES

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Summary Over-all triplet birth rate in Japan was decreased during 1955 to 1967 and 1974. 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 high in 1974.

Monozygotic rate was slightly increased up to the maternal 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. Analysis of secular change during the period from 1960 to 1967 indicated a clear decrease of monozygotic rate in the older maternal age groups. The maternal age effect on the increase of trizygotic rate is less clear.

The highest monozygotic rate was seen in the northeast Hokkaido District (56 per million). On the other hand, dizygotic rate was slightly higher in the northeast than in the southwest. As to trizygotic rate, the highest rate was seen in the southwest Kyushu District (10 per million). Heterogeneity of geographical variation was indicated in monozygotic and trizygotic rates, but not in dizygotic rate.

Underrepresentation of unlike-sexed triplet sets was suggested in two districts. After excluding the two districts, corrected monozygotic rate is 30, and dizygotic and trizygotic rates are 18 and 7 per million, respectively.

INTRODUCTION

The rates of triplet births in Japan were reported previously by Komai and Fukuoka (1936), based upon population statistics, midwives' records and hospital records. The figures varied from 2.6 to 18.4 per million. In 1948 the forms of birth and stillbirth certificates were revised, and since then the reports on the number of

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children per delivery have been legally required. Inouye (1957) reported the rate was 35.4 per million in three cities of Japan, based upon revised legal reports.

According to Bulmer (1970) the rates in England and Wales, U.S.A. and Italy are 109, 110 and 148 per million, respectively. Studies on secular change in the rates of triplet births have been reported in the United States (Jeanneret and MacMahon, 1962), Poland (Rola-Janicki, 1974) and Australia (Brackenridge, 1978). Brackenridge (1978) also studied the effect of maternal age on triplet rates.

The present study deals with the overall triplet birth rate and the rate for each zygosity during or a part of the period of 1955–1967 and in 1974 in all of Japan. Data on fetal deaths are after the beginning of 4th month of fetal life in Japan. Secular changes and geographical variations were also analysed. It also deals with the effect of maternal age on the rate of triplet births.

MATERIALS AND METHODS

The first source of data is annual volumes of "Vital Statistics of Japan for the Years 1951–1968 and 1974" (Health and Welfare Statistics and Information Department, Ministry of Health and Welfare). The statistics from 1955 to 1967 and for 1974 list the sex of the children, and they were used for estimating the triplet rate according to zygosity. Maternal age is given in the statistics from 1960 to 1967 and for 1974, and the statistics from 1951 to 1959 and 1974 provide the numbers of multiple births for each prefecture. Second source is "Survey on Socio-Economic Aspects of Vital Events-Plural Births," from which data on administration of ovulation-inducing hormone to the mothers of triplets in 1974 were taken for analysis.

RESULTS

Secular changes of triplet birth rate

Table 1 shows the number of total triplet births in each year. Also shown in Table 1 are the numbers of the births according to sex composition. From these figures numbers and frequencies of monozygotic, dizygotic and trizygotic triplet sets were estimated by Allen's method (1960) (Table 2, Fig. 1). In applying this method, triplet sets with unknown sex in one or more children were excluded. Monozygotic triplet birth rate is slightly decreased with the year, but not significant at the 5% level. The lowest rate was 27.8 per million deliveries in 1964. On the other hand, dizygotic triplet birth rate, estimated by $2Da$ where D is dizygotic and a is monozygotic twinning rate, is decreased with the year, which was statistically significant at the 1% level. Trizygotic triplet birth rate is increased with the year, and it was particularly high in 1974 (12.22 per million deliveries), but the increase is not significant at the 5% level.

Table 1. Sex composition of Japanese triplets, 1955-1967 and 1974.

Year	Total	MMM	MMF	MFF	FFF	Unknown*
1955	130	39	13	12	62	4
1956	102	39	11	17	34	1
1957	96	35	15	7	37	2
1958	109	43	12	18	33	3
1959	95	40	7	9	36	3
1960	88	35	7	11	34	1
1961	103	46	5	9	41	2
1962	101	36	9	15	40	1
1963	105	42	8	10	42	3
1964	93	34	10	12	37	0
1965	107	37	9	12	47	2
1966	91	29	8	14	38	2
1967	110	35	12	14	47	2
⋮						
1974	124	36	20	15	48	5
Total	1,454	526	146	175	576	31

*Sex of the one or more of the triplets is unknown.

Fig. 1. Estimated number of total, mono-, di- and tri-zygotic triplet rates in Japan.

Effect of maternal age on triplet birth rates

Table 3 shows the number of triplet births according to sex composition and maternal age group in the pooled data of 1960-1967 and 1974. Here again were excluded the sets with unknown sex in one or more of the triplets. Table 4 and Fig. 2 show the numbers and the rates of triplet births according to zygosity and maternal age group. Monozygotic triplet rate is slightly increased up to the age group of 35-39 years and decreased thereafter, while dizygotic triplet rate as esti-

Table 2. Triplet rates per million deliveries according to zygosity, 1955–1967 and 1974.

Year	Triplet deliveries				Triplet rate per million deliveries			
	Total	Monozygotic	Dizygotic	Trizygotic	Total	Monozygotic	Dizygotic	Trizygotic
1955	126	81	35	10	66.26	42.37	18.31	5.23
1956	101	52	35	14	55.12	28.38	19.10	7.64
1957	94	53	35	6	54.29	30.61	20.21	3.47
1958	106	54	36	16	58.03	29.56	19.71	8.76
1959	92	59	34	—1	51.22	32.85	18.93	—0.56
1960	87	53	31	3	49.04	29.88	17.47	1.69
1961	101	71	33	—3	57.46	40.39	18.77	—1.71
1962	100	57	32	11	56.04	31.94	17.93	6.16
1963	102	67	33	2	55.95	36.75	18.10	1.10
1964	93	52	35	6	49.67	27.77	18.69	3.20
1965	105	66	34	5	53.22	33.45	17.23	2.53
1966	89	51	27	11	59.37	34.02	18.01	7.34
1967	108	61	36	11	52.13	29.45	17.38	5.31
⋮								
1974	119	62	31	26	55.95	29.15	14.57	12.22

Table 3. Sex composition of Japanese triplets according to maternal age, 1960–1967 and 1974.

Maternal age	MMM	MMF	MFF	FFF	Total
Under 25	84	17	21	99	221
25–29	146	42	65	188	441
30–34	81	22	18	61	182
35–39	25	6	7	13	51
Over 40	3	1	1	4	9
Total	339	88	112	365	904

Table 4. Triplet rates per million deliveries according to maternal age and zygosity, 1960–1967 and 1974.

Maternal age	Triplet deliveries			Triplet rate per million deliveries		
	Monozygotic	Dizygotic	Trizygotic	Monozygotic	Dizygotic	Trizygotic
Under 25	157	39	25	32.52	8.08	5.18
25–29	253	135	53	32.63	17.41	6.84
30–34	105	71	6	32.99	22.31	1.89
35–39	26	23	2	34.30	30.34	2.64
Over 40	5	3	1	31.36	18.81	6.27
Total	539	295	70	32.31	17.68	4.20

mated from twinning rates markedly increased up to the age group of 35–39 years and decreased thereafter. Trizygotic triplet rate seems to be not dependent on maternal age.

Table 5 shows the expected numbers of like- and unlike-sexed triplet sets accord-

Fig. 2. Mono-, di- and tri-zygotic triplet rates according to maternal age, 1960-1967 and 1974.

Table 5. Prediction of sex-concordance in triplet sets and expected triplet rates according to maternal age, 1960-1967 and 1974.

Maternal age	Like-sexed		Unlike-sexed		χ^2	Expected triplet rate per million deliveries		
	Observed	Expected*	Observed	Expected*		Monozygotic	Dizygotic*	Trizygotic
Under 25	183	181	38	40	0.12	32.11	8.08	5.59
25-29	334	346	107	95	1.93	34.69	17.41	4.77
30-34	142	138	40	45	0.74	30.79	22.31	4.08
35-39	38	36	13	15	0.38	30.34	30.34	6.60
Over 40	7	7	2	2	0	31.36	18.81	6.27

* Expected value was computed by the method of Allen and Firschein (1957), where expected dizygotic triplet rate is equal to observed value because of the model.

ing to maternal age group in which expected values were computed by the method of Allen and Firschein (1957). In all maternal age groups, χ^2 -value between the observed and the expected values is not significant at the 5% level. Also shown in Table 5 are rates of the expected mono-, di- and tri-zygotic triplets, according to maternal age group. Here is seen the effect of maternal age also on trizygotic triplet rates. With respect to the agreement between observed and expected rates, dizygotic triplet rates are same to "observed" rates in Table 4, since expected and "observed" rates are both estimated by $2Da$. In monozygotic triplets the difference between the observed and expected rates is not significant ($\chi^2=1.9$, $df=4$, $0.75 < p < 0.90$), while it is significant in trizygotic triplets ($\chi^2=12.6$, $df=4$, $0.025 < p < 0.01$).

Geographical variation of triplet rates

Table 6 shows sex composition of triplets according to district in the pooled

Table 6. Monozygotic, dizygotic and trizygotic triplet rates per million deliveries according to district, 1955–1959 and 1974.

District	Triplet deliveries				Triplet rates			
	MMM	FFF	MMF	MFF	Monozygotic	Dizygotic	Trizygotic	Total
Hokkaido	24	18	5	0	56.32	20.34	−3.13	75.09
Tohoku	28	31	7	11	34.67	24.19	3.22	63.69
Kanto	63	68	25	17	37.05	18.53	8.52	65.95
Chubu	25	44	14	16	24.17	18.51	8.23	53.48
Kinki	30	32	14	9	25.96	16.15	6.92	49.03
Chugoku	16	12	1	9	25.27	17.69	5.05	48.01
Shikoku	13	11	1	1	44.18	14.73	−4.21	61.01
Kyushu	33	34	11	15	29.40	16.20	10.20	55.79

Fig. 3. Total, mono-, di- and tri-zygotic triplet rates in eight districts, 1955–1959 and 1974.

data of 1955–1959 and 1974, from which monozygotic, dizygotic, and trizygotic triplet rates were computed in each district. The highest monozygotic triplet rate is seen in Hokkaido District (56 per million), and the lowest in Chubu District (24 per million) (Fig. 3). On the other hand, dizygotic triplet rate estimated by $2Da$ is slightly higher in the northeast (Hokkaido and Tohoku) than in the southwest (Shikoku and Kyushu). As to trizygotic triplet rate, the highest rate is seen in Kyushu District (10 per million) whereas the lowest value in Hokkaido and Shikoku districts. Heterogeneity of geographical variation was indicated in monozygotic (χ^2 -value between observed and expected values was 22.96) and trizygotic ($\chi^2=25.70$) triplet rates, but not in dizygotic triplet rates ($\chi^2=3.47$).

Triplet rates in 1974 in urban and rural areas were 60.32 and 49.02 per million, respectively, but the difference is not significant at the 5% level.

DISCUSSION

Over-all rate of triplet births in Japan was decreased during the period under study. The decrease was also seen in the United States from 1922 to 1958 (Jeanneret and MacMahon, 1962), and in Poland from 1949 to 1971 (Rola-Janicki, 1974). In Australia, however, the rate increased from 1920 to 1969 (Brackenridge, 1978). The secular change in Japan seems to be mainly due to decline of dizygotic triplet rate, since the correlation between the dizygotic rate and the year was significant. As to trizygotic triplet rate a slight increase was noted, but not significant. Brackenridge (1978) reported that if dizygotic and trizygotic triplets are combined, an increase rather than decrease was noted in Australia in the period under study.

In 1974, the rate of trizygotic triplet births was particularly high (Table 2, Fig. 1). According to Imaizumi and Inouye (1979), the proportion of mothers treated with ovulation inducing hormone was 17 percent among all mothers gave birth to triplets. In Japan ovulation-inducing hormone has been used since 1966 (Sawazaki and Tsubata, 1976). However, the rate of the DZ twinning was not increased in 1974 compared to the preceding years (Imaizumi and Inouye, 1979), and the proportion of mothers treated with ovulation-inducing hormone was 5 percent among mothers who gave birth to twins as opposed to 17 percent among mothers who gave births to triplets. Accordingly administration of ovulation-inducing hormone may have resulted particularly in the high trizygotic triplet rate in 1974.

With respect to racial difference of triplet rates according to zygosity, monozygotic triplet rates in England and Wales (1938-62), U.S.A. (1922-54), Italy (1933-54) (Bulmer, 1970), and Australia (1920-69) (Brackenridge, 1978) were 13, 21, 21, and 24 per million deliveries, respectively. The rate in the present study was 32 per million deliveries from Table 4. Dizygotic triplet rates per million deliveries in the former four countries were 62, 58, 75, 52, respectively, whereas the rate in Japan was 18, from one third to one fourth of the rate in the other countries, and trizygotic triplet rates per million deliveries were 34, 31, 52, 24 in the former four countries and 4 in Japan from one sixth to one thirteenth of the other countries. Low dizygotic and trizygotic triplet rates are the characteristic features of Japanese.

Dizygotic triplet rate estimated from twinning rates indicated a clear maternal age effect (Table 4, Fig. 2). To an extent of lesser degrees monozygotic triplet rate also indicated a maternal age effect. On the other hand, trizygotic triplet rate did not indicate such effect in disagreement with Brackenridge (1978), who has shown the trizygotic triplet rate increased with maternal age up to the group of 35-39 years and decreased thereafter. However, the estimated number of trizygotic triplet births is only 70 in the present data, which does not permit to draw a definite conclusion. Analysis of the secular changes of triplet birth rates ac-

Fig. 4. Secular change of mono- and tri-zygotic triplet rates according to maternal age during 1960-1967.

cording to maternal age and zygoty during the period from 1960 to 1967 (Fig. 4) indicated a clear decrease of monozygotic triplet births, particularly in the older maternal age groups. In this figure the increase of trizygotic triplets is also seen, but the maternal age effect is less clear.

It was indicated that geographical variation of triplet birth rate was significant in monozygotic and trizygotic triplets. However, as is seen in Table 6 the estimated trizygotic triplet rates in Hokkaido and Shikoku districts bear minus sign, which may be due to underrepresentation of unlike-sexed sets. The χ^2 -values between the observed and expected numbers of trizygotic triplets are 9 and 8 for the two districts. The low estimated trizygotic triplet rates can result in high estimated monozygotic triplet rates in the two districts. The χ^2 -values between observed and expected monozygotic triplet rates are 10.71 and 2.40 for the two districts. These analyses suggest a possible inaccuracy of the reports of triplet births in the two districts. If the two districts were excluded, monozygotic triplet rate tends to decrease from northeastern Tohoku to southwestern Kyushu districts as is seen in Fig. 3. Also seen in Fig. 3 is a tendency that trizygotic triplet rate tends to increase from north-eastern to southwestern districts. Such geographical cline of multiple birth rates in Japan was also seen in dizygotic twinning rates, which was higher in the north-east than in the southeast (Imaizumi and Inouye, 1979).

Milham (1964) suggested a relation between gonadotropins and dizygotic twinning rate; a high twinning rate is related to a high blood gonadotropin level (Nylander, 1973). Soma *et al.* (1975) reported significantly lower plasma gonado-

tropin levels in Japanese women than in Nigerian women, who, as reported by Nylander (1973), had a high frequency of twinning. Soma *et al.* (1975) suggested that the low dizygotic twinning rate in Japanese women might be related to their low output of gonadotropin. Same may be applied to a relation between gonadotropins levels and dizygotic and trizygotic triplet rates. However, as was suggested in the above discussion, if the geographical cline of trizygotic triplet rates in Japan is present to the opposite direction to that of dizygotic twinning rates, the effects of gonadotropin level in women and/or locality on the polyovulation are yet to be studied.

As to a high monozygotic triplet rate (32 per million deliveries) compared to other countries, it might be due to overestimation of the monozygotic triplet rates in Hokkaido and Shikoku districts. The corrected figure by excluding the two districts is 30 per million deliveries for monozygotic, and 7 per million deliveries for trizygotic triplets. Still monozygotic triplet rate is higher, and trizygotic rate is lower in Japan than in Europe and USA.

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