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Twins in Sibships with Klinefelter's Syndrome and the XYY Syndrome

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SUMMARY

The frequency of twins and triplets was significantly higher than expected among 56 patients with Klinefelter's syndrome (7.1%), compared with 1.58% in the population (P<0.001), and the frequency of multiple births in the 56 sibships (4.08%) was also significantly higher than expected (P<0.01).

One of 15 patients with the XYY syndrome was a twin, and there were 2 twin births among the 53 births in the 15 sibships.

The study of twins and triplets in the sibships of 18 patients with Klinefelter's syndrome published by Nielsen (1966, 1968) have been extended to comprise 56 patients with Klinefelter's syndrome and 15 patients with the XYY syndrome.

The patients have been found in surveys of patients in psychiatric, neurological and medical institutions. The diagnoses have been made by sex chromatin analysis on Feulgen stained buccal smear and chromosome analysis on leucocyte cultures.

Results

The results of the study of the frequency of twins in the sibships of the 56 patients with Klinefelter's syndrome and the 15 with the XYY syndrome are shown in Tab. I.

Three of the 56 patients with Klinefelter's syndrome were twins and one was a triplet, giving a total frequency of 7.1% being a twin or a triplet; this is a significantly higher frequency than the 1.58% of multiple births in Denmark from 1921 to 1925 ($\chi^2 = 11.159$, P < 0.001).

A total of 11 twin births and one triplet birth was found among the 294 births in the 56 sibships of the patients with Klinefelter's syndrome, giving a frequency of 4.08%; this is a significantly higher frequency than the expected frequency of 1.58% ($\chi^2 = 7.865$, P < 0.01).

Two of the 53 births in the 15 sibships of the patients with the XYY syndrome were twin births, giving a frequency of 3.77%; one of the 15 patients with the XYY syndrome was a twin himself as seen in Tab. I. There were further two half-siblings to one of the patients with the XYY syndrome who were twins (Fig. 1).

The zygosity and sex of the twins and triplets in the 14 multiple births are seen in Tab. II and the pedigrees are seen in Fig. 1.

**Tab. I. Patients with Klinefelter's syndrome and the XYY syndrome.
Distribution by karyotype and number of multiple births**

Karyotype	Number of patients	Twins or triplets with Klinefelter's syndrome or XYY syndrome		Total births in the sibships	Multiple births in the sibships	
		Total	%		Total	%
47, XXY	45	4*	8.9	244	10*	4.10
48, XXXY	2	—	—	6	—	—
46, XX	1	—	—	2	—	—
46, XY/47, XXY	8	—	—	42	2	4.76
Total	56	4	7.1	294	12	4.08
47, XYY	15	1	6.7	53	2	3.77

* One of the births was a triplet birth.

**Tab. II. Maternal age at the time of the multiple births,
sex and zygosity of the twins and triplets**

Case number	Karyotype	Maternal age	Zygosity and sex of twins and triplets
2	47,XXY	44	DZ, ♀♀
6	47,XXY	35	DZ, ♀♂
		37	? Z, ♂♂
9	47,XXY	43	*TZ, ♂♂♂
11	47,XXY	23	*DZ, ♂♂
13	47,XXY	34	*DZ, ♂♂
17	47,XXY	27	DZ, ♂♀
39	47,XXY	48	*? Z, ♂♂
47	47,XXY	40	? Z, ♂♂
58	47,XXY	35	DZ, ♀♀
23	46,XY/47,XXY	38	DZ, ♀♂
24	46,XY/47,XXY	31	DZ, ♀♂
Mean and SD:		36.3 ± 7.1	
40	47,XYY	44	DZ, ♂♀
91	47,XYY	26	*DZ, ♂♂

* The patient with Klinefelter's syndrome or XYY syndrome is a twin or triplet.
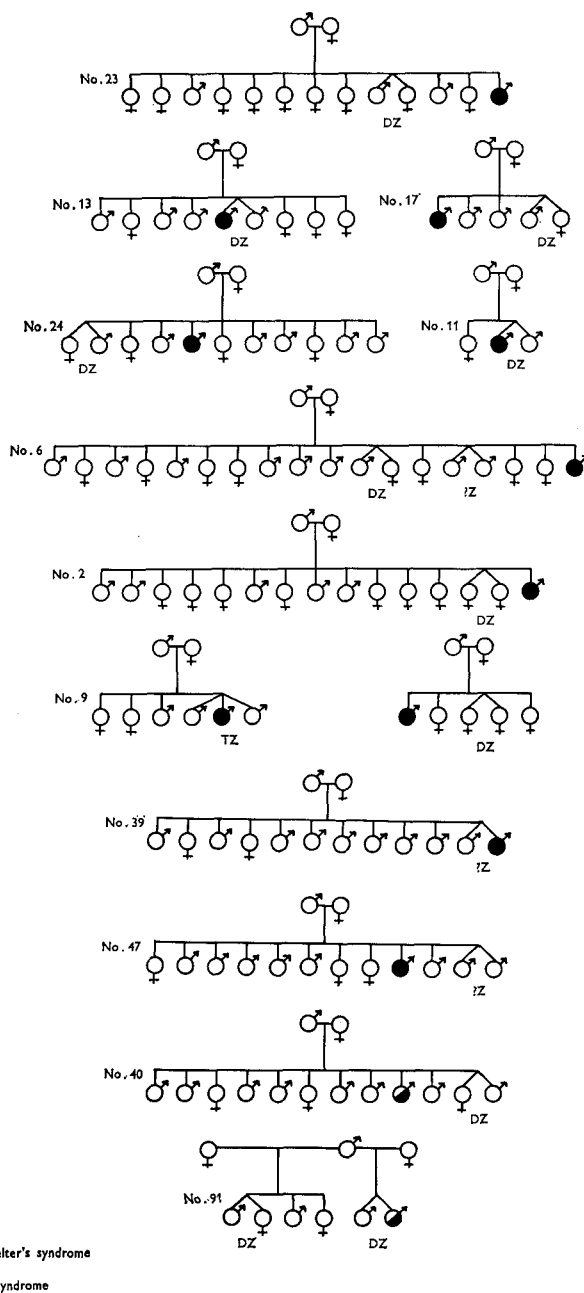
Fig. 1. Pedigrees of sibships which include patients with Klinefelter's syndrome or XYY syndrome as well as twins or triplets

Both twins were girls in two pairs, both were boys in six pairs, and a boy and a girl were found in five pairs. The triplets were boys. Distribution according to sex, compared with the distribution of twins born in Denmark from 1921 to 1925, is seen in Tab. III.

The mean maternal age was 36.3 ± 7.1 for the 12 multiple births in the sibships of the patients with Klinefelter's syndrome and the maternal age for the two multiple births in the sibships of the patients with the XYY syndrome was 44 and 26, respectively.

The frequency of twin births in relation to maternal age for the total number of births cannot be calculated, as the maternal age was not known for all births in the sibships of patients with Klinefelter's syndrome and the XYY syndrome, but the distribution of maternal age for the total number of twins born in Denmark from 1921 to 1925 is seen in Tab. IV. There is no significant difference in the maternal age distribution between the two groups.

Tab. III. Sex of twins

	Twins born in Denmark 1921-1925		Twins in sibships with Klinefelter's syndrome and the XYY syndrome	
	Total	%	Total	%
♂♂	1897	32	6	46
♂♀	2198	37	5	38
♀♀	1772	30	2	15
Total	5867	99	13	99

Tab. IV. Maternal age. Distribution by mothers with multiple births in Denmark (1921-1925) and in sibships with Klinefelter's syndrome

Maternal age	Mothers with multiple births			
	In Denmark (1921-1925)		Sibships with Klinefelter's syndrome	
	Total	%	Total	%
< 20	127	2	1	8
20-24	957	16	1	8
25-29	1610	27	2	17
30-34	1619	27	4	33
35-39	1198	20	3	25
40-44	334	6	1	8
45 <	15	1	0	0
Unknown	80	1	0	0
Total	5940	100	12	99

There were multiple births in other near relatives in 9 of the 56 patients with Klinefelter's syndrome and 6 of the 15 patients with the XYY syndrome; this appears to be a comparatively high frequency, but the total frequency of twin births among near relatives cannot be calculated as the total number of births among near relatives is unknown.

Discussion

There was, thus, a significantly higher frequency (7.1%) of twins or triplets among the patients with Klinefelter's syndrome than expected (P<0.001); this correlates with the findings by Soltan (1968) of 8.8% twins among 34 patients with Klinefelter's syndrome, and with the results of a survey of 202 previously published cases of Klinefelter's syndrome by Ferguson-Smith (1966), who found that 5.4% of these patients were twins.

We also found a significantly higher frequency of multiple births among the 294 births in the 56 sibships with Klinefelter's syndrome, 4.08%, compared with the frequency of 1.58% in the population (P<0.01). Soltan (1968) found a frequency of 2.0% twin births in 200 births in 34 sibships of patients with Klinefelter's syndrome.

Our finding indicates that there is a relationship between the risk of nondisjunction, resulting in a surplus of X chromosome material, and multiple births.

The finding of 1 twin among 15 patients with the XYY syndrome and 2 twin births among 53 births in the 15 sibships of patients with the XYY syndrome indicates that there also might be a higher frequency of multiple births among patients with the XYY syndrome, as well as among the siblings, than expected in the general population. More studies of multiple births in the sibships of patients with the XYY syndrome as well as of patients with Klinefelter's syndrome are, however, needed.

References

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RIASSUNTO

La frequenza di gemelli e trigemini in 56 pazienti di sindrome di Klinefelter (7.1%), e nelle 56 fratrie rispettive (4.08%) si è rivelata significativamente più alta di quella attesa in base alla frequenza dell'1.58% nella popolazione generale (P<0.001 e P<0.01, rispettivamente). Uno dei 15 pazienti con sindrome XYY era gemello e, sulle 53 nascite delle 15 fratrie, 2 erano gemellari.

RÉSUMÉ

La fréquence de jumeaux et triplettes chez 56 patients atteints de syndrome de Klinefelter (7.1%) et leurs souches respectives (4.08%) s'est révélée significativement plus élevée de celle attendue sur la base de la fréquence de 1.58% dans la population générale (P<0.001 et P<0.01, respectivement). Un des 15 patients avec syndrome XYY était jumeau et, sur 53 naissances dans les 15 souches, 2 étaient gémellaires.

ZUSAMMENFASSUNG

Das Vorkommen von Zwillingen und Drillingen war bei 56 Patienten mit Klinefelter-Syndrom (7.1%) und den zugehörigen 56 Sippschaften (4.08%) bedeutsam höher als aufgrund der Frequenz von 1.58% in der Gesamtbevölkerung (P<0.001 bzw. P<0.01) theoretisch zu erwarten wäre. Einer der 15 Patienten mit XYY-Syndrom war ein Zwilling und auf 53 Geburten in den dazugehörigen 15 Sippen fielen 2 Zwillingsgeburten.

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