MORTALITY RATE OF HUNTINGTON DISEASE IN JAPAN: SECULAR TRENDS, MARITAL STATUS, AND GEOGRAPHICAL VARIATIONS

Yoko Imaizumi

*Institute of Population Problems, Ministry of Health and Welfare,
Chiyoda-ku, Tokyo 100, Japan*

Summary   The death rate from Huntington disease (HD) in Japan was analyzed using Japanese vital statistics for 1969–1985. There was no significant change in the HD death rate over the years. The overall death rate per million population was 0.15 for both sexes. As for marital status, a quarter of the HD deaths was the single group for both sexes. There were remarkable differences in the HD death rates for each sex among the four marital categories. The geographical variations in the HD death rate were observed with the highest death rate in Tokushima prefecture (1.03). The excess of observed than expected numbers of HD deaths was obtained in the occupational category VI (other) of the head of household. The mean age at death in HD was nearly constant during the period, and overall mean age at death was 48 years for both sexes, which value was eight years shorter than that in South Wales.

Key Words   Huntington disease, mortality rate, marital status, geographical variation

INTRODUCTION

The Huntington disease (HD) is an autosomal dominant character. Recently, the HD gene was assigned to chromosome 4 (Gusella *et al.*, 1983). In most Western countries the prevalence rates of HD were between 30 and 70 per million population (McKusick, 1988). On the other hand, the lowest prevalence rate has been found in South African blacks (0.6: Hayden, 1977), Japan (1.1–3.8: Kanazawa, 1983; Kishimoto *et al.*, 1957), and Finland (5: Palo *et al.*, 1987). In Japan, the prevalence rates of HD was three times higher in Aichi (Kishimoto *et al.*, 1957) than in Ibaraki prefecture (Kanazawa, 1983). Therefore it is of interest to know geographical variations in the HD death rate in Japan.

The present study deals with the secular changes in the HD death rate during

the period from 1969 to 1985 and the geographical variations in the HD death rate during the period from 1979 to 1985 in Japan. It also deals with the effects of marital status and occupation of the head of the household on the HD death rate during the period from 1979 to 1985.

MATERIALS AND METHODS

Data consisting of 263 HD deaths reported for 1969–1985 inclusive have been obtained from the death certificate records kept at the Ministry of Health and Welfare, Japan. The International Classification of Diseases in 1968 assigned a code 331.0 for HD in the eight edition and a code 333.4 in the ninth edition in 1979. The certificate includes information on occupation of the head of the household, marital status, sex, place of residence, dates of birth and death, and cause of death.

In computing the HD death rate, the number of deaths from HD in each sex were divided by the population size of each sex during the same period. On the other hand, in computing the regional HD death rate, the average population of the two census years, 1980 and 1985, was used as the denominator in each prefecture.

Table 1. Death rate of Huntington disease by sex during 1969–1985.

Year	Number of deaths			Death rate per million population		
	Males	Females	Total	Males	Females	Total
1969	3	7	10	0.060	0.135	0.098
1970	3	7	10	0.059	0.133	0.097
1971	10	6	16	0.195	0.113	0.153
1972	5	8	13	0.096	0.148	0.123
1973	4	13	17	0.075	0.236	0.157
1974	8	7	15	0.149	0.126	0.137
1975	9	9	18	0.164	0.159	0.162
1976	7	3	10	0.127	0.053	0.089
1977	11	6	17	0.197	0.104	0.150
1978	7	4	11	0.124	0.069	0.096
1979	9	9	18	0.158	0.154	0.156
1980	7	5	12	0.122	0.085	0.103
1981	10	6	16	0.173	0.101	0.137
1982	5	10	15	0.086	0.167	0.127
1983	13	14	27	0.222	0.232	0.227
1984	5	7	12	0.085	0.115	0.100
1985	12	14	26	0.203	0.229	0.216

RESULTS

Secular change in the HD mortality rate

Table 1 shows secular changes in the HD death rates for each sex during the period from 1969 to 1985. The death rate was slightly increased with the year. The linear regression coefficients of the HD death rate on the year (per 100,000 years) were 0.00043 ($\pm$0.00025) for males, 0.00019 ($\pm$0.00027) for females, and 0.00031 ($\pm$0.00019) for total. These values were not significant at the 5% level. The overall HD death rate was 0.15 per million for both sexes.

Age-group specific mortality rate of HD

Table 2 shows the age-group specific HD death rates by sex during the period from 1969 to 1985. In both sexes, the HD death rate was gradually increased up to the 30–34 age group and suddenly increased thereafter up to the 55–59 age group for males and the 50–54 age group for females, and decreased thereafter.

Marital status

Table 3 shows the age-group specific HD death rates by sex and marital status during the period from 1979 to 1985. To compute the age-group specific HD death rate by sex and marital status during the period, the average population at 15 years and over for the two census years, 1980 and 1985, was used as the denominator. The HD death rate in each age category was higher in the single than in the married group for both sexes, except over 65 years of age for males and over 55 years of age for females.

Table 4 illustrates average annual age-adjusted HD death rates by sex and matiral status which were computed using age-group specific HD death rates in each marital status for 1979–1985 (Table 3) and the size of the population at 15 years and over. The lowest age-adjusted death rate per million was seen in the widowed group for males (0) and in the married group for female (0.12). On the other hand, the highest death rate for males was seen in the divorced (1.03), followed in order by the single (0.63) and the married group (0.13), whereas the highest death rate for females was seen in the single (0.47) followed in order by the divorced (0.45) and the widowed group (0.43).

Geographical variation

Table 5 shows the HD death rate by prefecture during the period from 1979 to 1985. The overall HD death rate was 0.15 per million. The highest death rate was seen in Tokushima prefecture (1.03), followed by Yamagata (0.80), and Wakayama (0.53) prefectures. Therefore, the HD death rate in Tokushima prefecture was seven times as high as the overall HD death rate in Japan. On the other hand, the lowest death rate (0) was seen in 13 prefectures (see Table 5). Second lowest HD death rate was seen in Saitama prefecture (0.05).

Table 2. Deaths and average annual death rates for Huntington disease (HD) by age and sex, 1969–1985.

Age	Male	Female	Total
	Number of deaths with Huntington disease		
Total	128	135	263
Under 4	0	0	0
5– 9	1	1	2
10–14	2	2	4
15–19	0	3	3
20–24	4	2	6
25–29	8	6	14
30–34	6	8	14
35–39	12	11	23
40–44	16	23	39
45–49	20	18	38
50–54	16	20	36
55–59	16	14	30
60–64	11	10	21
65–69	9	8	17
70–74	5	4	9
Over 75	2	5	7
	Average annual death rate of HD per million population		
Total	0.136	0.139	0.138
Under 4	0	0	0
5–9	0.013	0.013	0.013
10–14	0.027	0.028	0.027
15–19	0	0.043	0.021
20–24	0.052	0.027	0.040
25–29	0.102	0.077	0.089
30–34	0.075	0.100	0.087
35–39	0.159	0.146	0.153
40–44	0.229	0.329	0.279
45–49	0.325	0.281	0.303
50–54	0.314	0.354	0.335
55–59	0.391	0.289	0.335
60–64	0.333	0.244	0.284
65–69	0.330	0.237	0.279
70–74	0.243	0.152	0.192
Over 75	0.093	0.150	0.128

Table 3. Deaths and average annual death rates for Huntington disease (HD)
by age, sex and marital status, 1979–1985.

Age	Male				Female			
	Single	Married	Widowed	Divorced	Single	Married	Widowed	Divorced
Number of deaths with Huntington disease								
Total	16	38	0	7	16	30	12	6
Under 15	2	—	—	—	1	—	—	—
15–24	2	0	0	0	4	0	0	0
25–34	3	0	0	0	5	0	0	0
35–44	6	5	0	6	3	9	2	1
45–54	2	13	0	1	3	11	0	2
55–64	1	14	0	0	0	8	2	3
Over 65	0	6	0	0	0	2	8	0
Average annual death rate of HD per million population								
Total	0.176[a]	0.181	0	1.561	0.226[a]	0.143	0.288	0.660
Under 15	0.000	—	—	—	0.000	—	—	—
15–24	0.035	0	0	0	0.078	0	0	0
25–34	0.117	0	0	0	0.444	0	0	0
35–44	1.013	0.086	0	4.264	0.842	0.154	1.827	0.403
45–54	1.116	0.256	0	0.772	1.235	0.233	0	0.873
55–64	1.672	0.420	0	0	0	0.260	0.231	1.717
Over 65	0	0.220	0	0	0	0.117	0.284	0

[a] Including number of deaths with HD under 15 years old.

Table 4. Average annual age-adjusted death rates for Huntington disease, by
age, sex, and marital status, 1979–1985.

Marital status	Age-adjusted death rate per million population more than 14 years of age		
	Male	Female	Male/Female
Single	0.628	0.471	1.33
Married	0.134	0.120	1.12
Widowed	0	0.431	0
Divorced	1.025	0.447	2.29

It is called a city or town and village according to whether the population size
of the administrative unit is over 30,000 or not. The census districts were divided
into two groups: urban (city) and rural (town and village) areas. The HD death
rate during the period from 1979 to 1985 was slightly higher in the former areas

Table 5.   Death rate of Huntington disease per million population in each prefecture, 1979–1985.

Prefecture	Number of deaths	Death rate	Prefecture	Number of deaths	Death rate
Whole of Japan	126	0. 151			
Hokkaido	5	0. 127	Shiga	1	0. 128
Aomori	0	0. 000	Kyoto	4	0. 223
Iwate	1	0. 100	Osaka	9	0. 150
Miyagi	3	0. 201	Hyogo	3	0. 082
Akita	3	0. 341	Nara	1	0. 114
Yamagata	7	0. 796	Wakayama	4	0. 526
Fukushima	2	0. 139	Tottori	0	0. 000
Ibaraki	0	0. 000	Shimane	1	0. 181
Tochigi	2	0. 156	Okayama	1	0. 075
Gunma	0	0. 000	Hiroshima	4	0. 206
Saitama	2	0. 051	Yamaguchi	0	0. 000
Chiba	6	0. 173	Tokushima	6	1. 033
Tokyo	12	0. 146	Kagawa	0	0. 000
Kanagawa	6	0. 119	Ehime	3	0. 282
Niigata	1	0. 058	Kochi	0	0. 000
Toyama	1	0. 129	Fukuoka	8	0. 247
Ishikawa	1	0. 126	Saga	2	0. 327
Fukui	0	0. 000	Nagasaki	0	0. 000
Yamanashi	1	0. 175	Kumamoto	0	0. 000
Nagano	3	0. 203	Oita	2	0. 231
Gifu	4	0. 287	Miyazaki	0	0. 000
Shizuoka	3	0. 122	Kagoshima	0	0. 000
Aichi	9	0. 203	Okinawa	0	0. 000
Mie	4	0. 333	Unknown	1	—

(0.16 per million) than the latter (0.12), where the number of HD deaths were 102 and 24, respectively.

Occupation

Table 6 shows the number of HD deaths by occupation of the head of the household. These occupations were classified into six categories according to the classification in the certificate records: I (agriculture only), II (agriculture with other work), III (self employed), IV (white collar), V (blue collar) and VI (other). Expected numbers of deaths in Table 5 were calculated based on the total numbers of HD deaths for 1979–1985 and the rate of each occupation of the head of the household in total number of deaths for 1979–1985. The number of HD deaths was

Table 6.   Observed and expected numbers of deaths from Huntington disease (HD) by occupation of the head of the household, 1979–1985.

	Occupation	Number of HD		χ^2
I	Agriculture only	Obs.	8	
		Exp.	13	1.92
II	Agriculture with other works	Obs.	10	
		Exp.	17	2.88
III	Self employed	Obs.	12	
		Exp.	17	1.47
IV	Employee (white collar)	Obs.	11	
		Exp.	18	2.72
V	Employee (blue collar)	Obs.	25	
		Exp.	19	1.89
VI	Other	Obs.	60	
		Exp.	42	7.71*

* Significant at the 1% level.
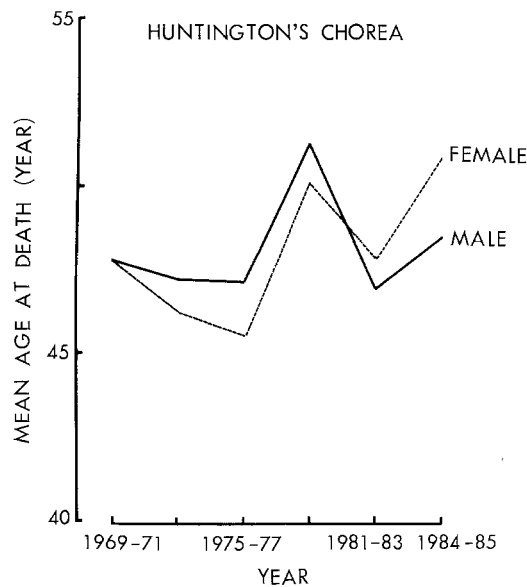
Fig. 1.   Trends of mean age at death of Huntington disease by sex, during 1969–1985.

higher in the observed than in the expected values for categories V and VI, whereas the opposite tendency was seen in categories I through IV.   The difference between the observed and the expected numbers of HD deaths was statistically significant in category VI.

Mean age at death
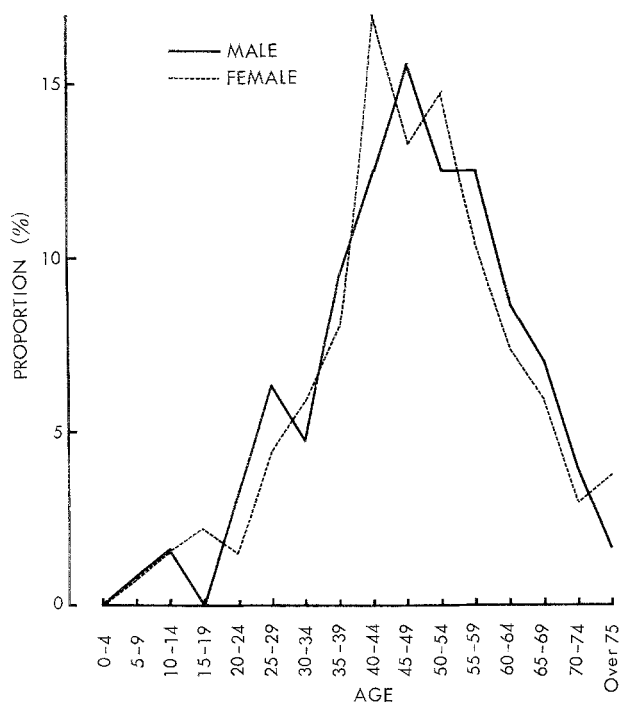   Figure 1 shows the secular changes in the mean age at death from HD in each

Fig. 2.   Distribution of age at death in Huntington disease by sex, during 1969–1985.

sex during the period from 1969 to 1985.   The mean age at death in HD was 47.8 years for both sexes in 1969–1971 and the corresponding age in 1984–1985 was 48.5 years for males and 50.9 years for females.   Then mean age at death in HD was nearly constant during the period for both sexes, and overall mean age±S.D. at death was 48.1±1.6 years for males and 48.2±2.1 years for females.

Figure 2 shows the distribution of age at death in HD, which values were obtained from Table 2.   Age at death in HD ranged from 5–9 years to over 75 years. Among the 263 cases six percentage of HD patients died under 25 years old and 54.4% under 50 years.

DISCUSSION

According to Kurtzke (1979), it was possible to obtain all deaths listed as HD anywhere on the certificates in Sweden (1969 to 1974) and Denmark (1961–1975). In these countries, the HD death rates were separately obtained for "underlying cause of death," which constitutes of 68% of all deaths listed as HD, and remaining 32% for "contributory cause of death" or an "associated condition."   However, these values are not obtained in Japan.   Routinely reported death data on the certificate record are based solely on deaths coded as underlying (primary) cause.

Therefore the HD death rate (0.15 per million) in the present study was under-estimate.

The HD death rate in Japan was approximately one-tenth the values from the Western Hemisphere (Kurtzke, 1979) and United States whites (Kurtzke *et al.*, 1977). Similar tendency was also observed in the prevalence rates of HD (McKusick, 1988; Kishimoto *et al.*, 1957). As to geographical variation, the prevalence rate in HD was three times higher in Aichi (Kishimoto *et al.*, 1957) than in Ibaraki prefecture (Kanazawa, 1983), whereas the corresponding HD death rates per million in the present study were 0.20 and 0, respectively. It is suggested that the geographical variations in the HD death rate may represent these in the prevalence rate in Japan. Hogg *et al.* (1979) computed regional HD death rates for the entire United States during the period from 1968 to 1974, where regional variation in rates of death due to HD was not marked. In the present study the HD death rate varied from zero in 13 prefectures to 1.03 per million in Tokushima prefecture (Table 5). Hogg *et al.* (1979) mentioned that regional mortality rates may reflect morbidity patterns and be useful in planning health care facilities and research centers.

According to Kurtzke *et al.* (1977), the age-group specific HD death rate was highest at 60 to 70 years in all studied populations, except among the Japanese, with earlier peak at 50 years. In the present study the age-group specific HD death rate was highest at 55 to 59 years for males and at 50 to 54 years for females.

According to Kishimoto *et al.* (1957), the estimate of relative fitness in HD was 0.65 in Japan. Fitness has two main components: viability and fertility. The latter component consists of the rates of marriage and of leaving offspring. In the present study, the proportion of the single group in HD deaths for the size of the population at 15 years and over was 24% for both sexes during the period from 1979 to 1985 (Table 3), whereas the values in all deaths were 7% (177,146/2,675,672) for males and 5% (120,210/2,275,347) for females. Then the rate of marriage was 76% among HD deaths and 94% among all deaths. Accordingly the rate of marriage was reduced 19% (1–0.76/0.94) in HD patients.

According to Walker *et al.* (1981), the mean age$\pm$S.D. at onset and at death in HD was 41.2 ± 12.7 and 56.5 ± 12.2 years in South Wales, respectively. In the present study, overall mean age at death in HD was 48 years for both sexes. Therefore the Japanese HD patients may have a short life span compared with those in South Wales. Mean age at death in HD can be used as a parameter of genetic counselling.

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