A STUDY OF VARIATIONS IN THE REPORTED HEMOPHILIA B PREVALENCE AROUND THE WORLD

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HEMOPHILIA
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FEDERACIÓN MUNDIAL DE HEMOFILIA
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ORIGINAL ARTICLE

A study of variations in the reported haemophilia B prevalence around the world

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Summary. The objectives of this article were to study the reported prevalence of haemophilia B (HB) on a country-by-country basis and to analyse whether the prevalence of HB varied by national economy. The *prevalence of HB* is the proportion of diagnosed, reported cases of HB in a population at a specific point of time. We collected data on the HB prevalence for 105 countries from the World Federation of Hemophilia annual global surveys. Our results showed that the HB prevalence varied considerably among countries, even among the wealthiest of countries. The HB prevalence (per 100 000 males) for the highest income countries was 2.69 ± 1.61 (mean ± SD), whereas the prevalence for the rest of the world was 1.20 ± 1.33 (mean ± SD). Ireland had the highest reported HB prevalence of 8.07 per 100 000 males. There was a strong trend of increasing HB prevalence (per 100 000 males) over time. Prevalence data reported from the WFH compared well with prevalence data from the literature. The WFH annual global surveys have some limitations, but they are the best available source of worldwide haemophilia data. Prevalence data are extremely valuable information for the planning efforts of national healthcare agencies in setting priorities and allocating resources for the treatment of HB.

Keywords: epidemiology, haemophilia B, prevalence

Introduction

It is critical for health care planning that reliable haemophilia B (HB) prevalence data be available. Many lower income countries neglect the on-going treatment and medical expense for haemophilia and focus their limited resources on acute conditions that have the biggest impact on public health, such as malnutrition, sanitation, infectious diseases, infant mortality, etc. With improved data collection needs can be highlighted and healthcare resources better managed and allocated.

Materials and methods

We collected HB prevalence data from the World Federation of Hemophilia (WFH) annual global surveys. The *HB prevalence* (per 100 000 males) in a population is the total number of cases at a given time divided by the total number of males. From 1998 to 2006, the WFH has reported on the number of people with HB for 105 countries [1–8]. We calculated the HB prevalence by dividing the number of people with HB by the male population in the appropriate year [9]. Participation in the WFH annual global survey is voluntary and requires collaboration among national organizations. Not all countries have provided data each year to the WFH. We also investigated the quality of the reported HB prevalence data from the WFH annual global surveys by comparing these data with the prevalence data from the literature for high income countries. We used the World Banks' economic classification as described in our previous article [10] to describe national economies.

Descriptive statistics were used to analyse the prevalence data. We used the mean, standard deviation (SD), and coefficient of variation (CV) to describe the distribution of prevalence data for each country or for each economic classification. We used analysis of variance (ANOVA) to compare the mean of the reported annual HB prevalence data from the WFH

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between economic classifications and with prevalence data for high income Organisation for Economic Co-operation and Development (OECD) countries reported in the literature. $P < 0.05$ is considered statistically significant.

Results

Table 1 presents the calculated HB prevalence from WFH data for years 1998–2006 [1–8]. For each country shown in Table 1, there were nine possible prevalence observations corresponding to the years 1998–2006, inclusive. The mean prevalence among high income OECD countries ranged from 0.47 per 100 000 males in Luxembourg to 8.07 per 100 000 males in Ireland,

among high income non-OECD countries from 0.30 in Saudi Arabia to 6.39 in Cyprus, among upper middle income countries from 0.58 in Mexico to 4.23 in Hungary, among lower middle income countries from 0.02 in Indonesia to 6.41 in Macedonia, and among low income countries from 0.01 in Nigeria to 0.70 in Zimbabwe. Three countries in Table 1 had unusually high prevalence when compared with the countries within their economic classification (Fig. 1), these being Ireland and Macedonia (three SDs) and Hungary (two SDs).

The reported HB prevalence varied considerably across economic classifications with prevalence increasing as economic capacity increased. The prevalence (per 100 000 males) for the high income OECD countries

Table 1. The reported haemophilia B prevalence (per 100 000 males) from 1998 to 2006 was determined from the number of people with haemophilia B in a country reported to the World Federation of Hemophilia [1–8] divided by its male population in the relevant year [9].

Country	1998	1999	2000	2001	2002	2003	2004	2005	2006	Mean	SD	CV (%)	Econ
Albania	2.33	1.82	1.83	2.74	NA	1.87	2.24	1.27	1.90	2.00	0.44	22	4
Algeria	0.67	NA	NA	0.81	0.79	NA	1.00	NA	1.13	0.88	0.18	21	4
Argentina	0.93	1.15	0.91	0.93	NA	0.97	1.20	1.35	1.22	1.08	0.17	16	3
Armenia	NA	NA	0.41	0.49	NA	0.35	0.35	NA	NA	0.40	0.06	16	4
Australia	2.15	3.19	2.11	2.08	NA	NA	1.87	3.06	3.21	2.53	0.60	24	1
Austria	NA	1.34	1.34	NA	NA	1.32	1.31	NA	NA	1.33	0.02	1	1
Azerbaijan	NA	0.18	0.28	NA	NA	NA	0.50	NA	NA	0.32	0.16	51	4
Bangladesh	0.003	0.02	0.02	0.02	NA	0.03	0.04	0.05	0.06	0.03	0.02	64	5
Belarus	NA	NA	NA	1.54	NA	1.56	1.52	NA	2.12	1.68	0.29	17	4
Belgium	2.16	2.43	2.53	2.92	2.90	2.89	NA	NA	NA	2.64	0.32	12	1
Belize	NA	NA	2.42	2.36	NA	2.26	2.21	NA	NA	2.31	0.10	4	3
Bolivia	NA	NA	NA	0.09	0.09	0.09	NA	NA	NA	0.09	0.002	2	4
Bosnia-Herzegovina	NA	NA	0.54	0.53	NA	0.53	0.53	NA	0.52	0.53	0.01	1	4
Brazil	NA	1.14	1.03	1.01	NA	0.99	0.97	0.96	1.37	1.07	0.15	14	3
Bulgaria	1.34	1.58	1.51	1.52	NA	1.55	1.56	1.60	1.74	1.55	0.11	7	3
Canada	3.07	2.57	3.25	3.22	3.19	NA	3.48	3.54	3.55	3.23	0.32	10	1
Chile	1.36	1.54	1.69	1.67	1.65	1.63	NA	NA	NA	1.59	0.13	8	3
China	0.06	0.10	NA	NA	NA	NA	0.04	NA	NA	0.07	0.03	44	4
Colombia	0.49	0.56	0.68	0.71	NA	1.04	0.85	1.06	1.10	0.81	0.24	29	4
Costa Rica	1.15	1.38	NA	1.32	NA	1.32	1.30	1.27	NA	1.29	0.08	6	3
Croatia	NA	NA	NA	3.05	3.04	3.03	NA	3.47	3.65	3.25	0.29	9	3
Cuba	NA	NA	0.74	0.81	NA	1.03	1.12	1.12	1.08	0.98	0.17	17	4
Cyprus	3.69	4.96	4.91	4.86	NA	4.76	15.14	NA	NA	6.39	4.31	68	2
Czech Republic	2.08	2.03	2.15	NA	NA	NA	NA	NA	NA	2.09	0.06	3	1
Denmark	2.68	2.70	3.11	3.06	NA	3.04	3.78	3.47	NA	3.12	0.40	13	1
Dominican Republic	NA	NA	0.59	0.25	0.24	0.24	NA	NA	NA	0.33	0.17	53	4
Ecuador	NA	NA	NA	NA	NA	NA	NA	0.49	0.51	0.50	0.02	4	4
Egypt	NA	1.89	1.89	1.80	1.77	NA	1.81	2.07	2.16	1.91	0.15	8	4
El Salvador	0.48	NA	0.33	0.74	NA	0.75	0.77	NA	NA	0.62	0.20	33	4
Eritrea	NA	NA	NA	NA	NA	NA	0.05	NA	0.22	0.13	0.12	91	5
Estonia	NA	0.47	0.47	0.48	0.48	0.48	NA	NA	NA	0.48	0.004	1	2
Finland	NA	NA	NA	NA	NA	2.39	NA	2.53	2.48	2.47	0.07	3	1
France	2.34	2.44	2.60	NA	NA	NA	NA	2.04	2.42	2.37	0.21	9	1
Georgia	NA	0.57	0.58	0.72	NA	1.02	1.45	1.66	NA	1.00	0.46	46	4
Germany	NA	1.93	1.58	1.62	NA	1.75	1.85	1.84	1.84	1.77	0.13	7	1
Greece	1.86	1.87	2.12	2.15	NA	2.27	2.28	2.31	2.31	2.15	0.19	9	1
Guatemala	NA	NA	NA	NA	NA	NA	0.15	0.15	NA	0.15	0.003	2	4
Honduras	0.34	0.30	NA	NA	NA	0.12	0.42	0.44	0.43	0.34	0.12	36	4
Hungary	3.77	3.87	3.96	4.59	4.60	NA	4.54	4.56	3.90	4.23	0.38	9	3
Iceland	1.45	NA	NA	1.41	NA	1.38	1.36	1.35	NA	1.39	0.04	3	1
India	NA	NA	NA	0.09	NA	0.09	0.16	0.29	0.30	0.19	0.10	56	5
Indonesia	0.01	0.01	0.01	0.01	NA	0.02	0.02	0.02	0.03	0.02	0.01	45	4
Iran	1.84	1.89	1.76	1.75	NA	1.72	2.00	2.32	2.37	1.96	0.26	13	4
Iraq	NA	NA	NA	NA	NA	NA	0.86	1.18	1.21	1.09	0.19	18	4

Table 1. Continued.

Country	1998	1999	2000	2001	2002	2003	2004	2005	2006	Mean	SD	CV (%)	Econ
Ireland	4.83	7.35	7.51	8.22	NA	8.30	9.13	10.12	9.12	8.07	1.59	20	1
Israel	NA	NA	NA	NA	NA	NA	1.85	2.14	NA	1.99	0.21	11	2
Italy	1.79	2.24	NA	NA	NA	NA	2.29	2.28	2.01	2.12	0.22	10	1
Jamaica	0.64	0.63	0.63	0.70	NA	0.61	0.61	NA	NA	0.64	0.03	5	4
Japan	1.13	1.17	NA	1.26	NA	1.35	NA	1.40	1.43	1.29	0.12	10	1
Jordan	NA	NA	1.41	NA	NA	NA	NA	NA	1.56	1.49	0.11	7	4
Kenya	0.22	0.29	0.28	0.26	0.25	NA	0.27	NA	0.24	0.26	0.02	9	5
Korea	0.78	0.84	0.88	0.93	0.93	NA	1.06	1.20	1.25	0.99	0.17	17	1
Latvia	1.17	1.54	1.37	1.57	NA	1.49	1.50	1.60	1.90	1.52	0.21	14	3
Lebanon	NA	NA	NA	0.43	0.42	NA	1.13	NA	NA	0.66	0.41	62	3
Lithuania	1.02	0.97	1.10	1.11	NA	1.24	NA	1.25	1.32	1.14	0.13	11	3
Luxembourg	0.48	0.47	0.47	NA	NA	NA	NA	NA	NA	0.47	0.01	1	1
Macedonia	NA	6.49	6.47	6.65	6.63	NA	5.82	NA	NA	6.41	0.34	5	4
Malaysia	0.90	0.92	0.94	0.94	NA	0.93	1.00	1.17	1.18	1.00	0.11	11	3
Malta	1.57	NA	NA	1.55	1.53	1.52	NA	NA	NA	1.54	0.02	1	2
Mexico	NA	0.41	NA	0.40	NA	0.45	0.57	0.77	0.87	0.58	0.20	35	3
Moldova	NA	NA	NA	NA	NA	0.74	NA	NA	NA	0.74	NA	NA	4
Mongolia	NA	NA	0.16	0.24	NA	0.32	0.39	NA	0.38	0.30	0.10	33	5
Morocco	0.40	NA	NA	NA	NA	NA	NA	NA	NA	0.40	NA	NA	4
Nepal	0.10	0.10	0.10	0.10	0.09	NA	0.20	0.22	0.13	0.05	42	5
Netherlands	2.70	3.19	3.17	3.16	NA	1.25	1.24	0.62	1.23	2.07	1.08	52	1
New Zealand	4.30	2.67	4.18	4.96	NA	4.58	2.31	2.58	4.12	3.71	1.03	28	1
Nicaragua	0.28	0.60	0.43	0.85	0.84	0.83	NA	NA	0.80	0.66	0.23	35	4
Nigeria	NA	NA	NA	NA	NA	NA	NA	0.01	NA	0.01	NA	NA	5
Norway	3.74	3.67	4.00	NA	NA	4.01	NA	4.17	4.14	3.95	0.21	5	1
Pakistan	NA	0.30	2.02	NA	NA	0.06	0.18	0.15	0.16	0.48	0.76	160	5
Palestine	NA	NA	2.31	NA	NA	NA	1.35	NA	1.37	1.68	0.55	33	4
Panama	0.77	0.68	1.07	1.05	NA	1.33	1.37	1.53	1.51	1.17	0.32	28	3
Paraguay	NA	0.75	NA	NA	NA	NA	NA	NA	NA	0.75	NA	NA	4
Peru	NA	0.98	0.16	NA	NA	0.33	0.38	0.53	0.48	0.31	65	4
Philippines	0.07	NA	0.18	0.22	NA	0.23	0.25	NA	0.28	0.20	0.07	36	4
Poland	1.53	1.60	1.65	1.70	NA	1.67	NA	1.83	1.92	1.70	0.13	8	3
Portugal	1.76	1.77	1.70	1.75	NA	1.87	2.02	1.97	2.01	1.86	0.13	7	1
Qatar	NA	NA	NA	NA	NA	NA	NA	NA	4.53	4.53	NA	NA	2
Romania	NA	1.46	1.49	1.51	NA	1.49	NA	1.53	1.62	1.52	0.06	4	3
Russia	0.33	0.56	2.20	2.21	NA	2.22	2.26	0.92	1.02	1.46	0.83	57	3
Saudi Arabia	NA	NA	NA	NA	NA	0.30	0.30	NA	NA	0.30	0.004	0	2
Senegal	NA	NA	NA	NA	NA	NA	NA	0.08	0.08	NA	NA	5
Serbia[1]	1.87	1.92	1.26	1.26	NA	1.28	1.29	1.33	1.22	1.43	0.29	20	3
Sierra Leone	0.09	NA	NA	NA	NA	NA	NA	NA	NA	0.09	NA	NA	5
Singapore	NA	NA	1.09	0.97	0.95	NA	NA	1.15	1.27	1.09	0.13	12	2
Slovak Republic	2.67	2.67	2.48	2.48	NA	2.49	2.45	NA	2.68	2.56	0.11	4	3
Slovenia	NA	NA	NA	NA	NA	1.64	1.64	NA	NA	1.64	0.001	0	2
South Africa	NA	1.01	1.00	1.03	NA	1.01	1.09	1.10	1.11	1.05	0.05	5	3
Spain	1.74	1.53	1.51	1.88	NA	1.82	1.25	1.25	1.27	1.53	0.26	17	1
Sri Lanka	NA	NA	NA	NA	NA	NA	0.13	NA	NA	0.13	NA	NA	4
Sudan	NA	NA	NA	NA	NA	NA	0.32	NA	0.14	0.23	0.12	54	5
Sweden	3.68	3.68	3.63	3.71	NA	3.76	3.72	NA	NA	3.70	0.05	1	1
Switzerland	2.75	2.40	2.82	2.75	NA	2.73	2.83	2.79	2.92	2.75	0.15	6	1
Thailand	0.12	0.09	0.11	0.09	NA	0.11	0.17	0.22	0.46	0.17	0.12	73	4
Togo	0.04	NA	NA	NA	NA	NA	NA	NA	NA	0.04	NA	NA	5
Tunisia	NA	NA	0.46	0.76	NA	0.74	NA	NA	0.99	0.74	0.22	30	4
Turkey	0.09	0.17	0.18	0.49	NA	0.64	0.93	1.13	1.31	0.62	0.47	76	3
Ukraine	0.01	0.03	NA	NA	NA	NA	NA	NA	NA	0.02	0.01	48	4
United Kingdom	3.98	4.23	3.83	3.88	NA	3.78	NA	5.02	4.36	4.16	0.44	10	1
United States	2.26	2.23	2.40	2.42	NA	2.37	2.38	2.42	2.47	2.37	0.08	3	1
Uruguay	0.63	0.75	0.75	0.81	NA	0.81	0.56	NA	NA	0.72	0.10	14	3
Uzbekistan	NA	NA	NA	0.34	NA	NA	0.25	0.83	0.86	0.57	0.32	57	5
Venezuela	1.82	2.08	2.13	2.23	NA	2.40	2.64	2.67	2.79	2.35	0.34	14	3
Vietnam	NA	NA	0.18	NA	NA	NA	0.09	0.43	0.42	0.28	0.17	61	5
Zimbabwe	0.41	NA	NA	0.79	0.79	NA	0.77	NA	0.76	0.70	0.17	24	5

[1]In 1992, Yugoslavia was a federation of Serbia and Montenegro. In 2003, it was renamed the State Union of Serbia and Montenegro, and officially abolished the name Yugoslavia. In 2006, Serbia and Montenegro declared independence.

SD, standard deviation; CV, coefficient of variation; NA, not available, no data provided; Econ, Economic Classification according to the World Bank: 1, high income OECD (Organisation for Economic Co-operation and Development); 2, high income non-OECD; 3, upper middle income; 4, lower middle income; 5, low income.
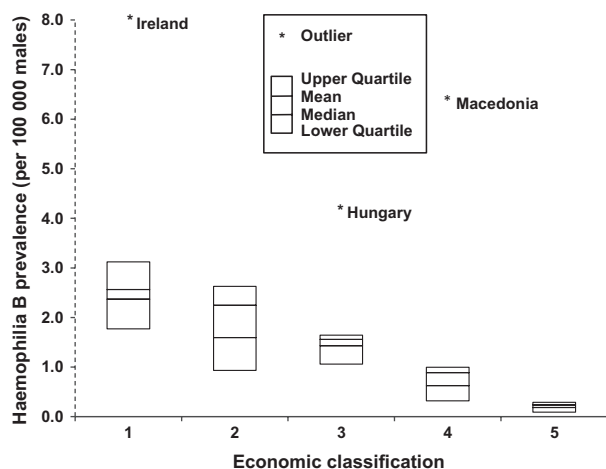
Fig. 1. Distribution plot with economic classification on the abscissa and haemophilia B prevalence (per 100 000 males) values on the ordinate. The prevalence values represent the mean prevalence for each of the 105 countries reporting prevalence data to the World Federation of Hemophilia (Table 1). The economic classification according to the World Bank is as follows: 1, high income OECD (Organisation for Economic Co-operation and Development); 2, high income non-OECD; 3, upper middle income; 4, lower middle income; 5, low income. *An outlier falls outside two standard deviations from the mean.

was 2.69 ± 1.61 (mean ± SD), whereas the prevalence for high income non-OECD countries was 2.40 ± 3.00 (mean ± SD), upper middle income countries was 1.56 ± 0.90 (mean ± SD), lower middle income countries was 0.99 ± 1.20 (mean ± SD) and low income countries was 0.27 ± 0.32 (mean ± SD). The mean HB prevalence was significantly different between all economic classifications except the comparison between high income OECD countries and high income non-OECD countries (P = 0.455). On a country-by-country basis, the mean prevalence was moderately correlated (R = 0.56, P < 0.001) with GNI per capita.

We compared the annual reported prevalence data from the WFH (Table 1) with the prevalence data from the literature. There were 11 comparisons. The reported prevalence (per 100 000 males) data from the WFH was 3.75 ± 0.71 (mean ± SD) and 3.55 ± 0.79 (mean ± SD) for the reported prevalence data from the literature and the means were not significantly different (P = 0.525). The average absolute error was 13% and the relative errors ranged from −28% to 44%.

Discussion

Ideally, national prevalence data would be collectively exhaustive and mutually exclusive [10]. Unfortunately, there can be under-reporting when countries count only patients from specialized-care facilities and there can be over-reporting when the countries fail to remove patients who have died or emigrated or double-count patients who are treated at more than one care facility. Our research shows no significant difference between the reported HB prevalence data of high income OECD countries from the WFH and literature. The WFH annual global surveys have some limitations, but they are the best available source of worldwide data.

Our findings in HB are generally the same as those in our study on haemophilia A [10]. The reported HB prevalence is significantly different across national economies, even among the wealthiest countries. The HB prevalence in the high income OECD countries is significantly greater than the other economic classifications. On a country-by-country basis, the reported HB prevalence in the WFH annual surveys increases over time for 72% of the countries. The increasing prevalence over time could reflect increased survival, improved diagnosis, improved access of haemophilia care, immigration of patients to countries with better care and improved data collection and reporting. The high prevalence for Ireland is likely contributed to by a founder effect, but those for Hungary and Macedonia require additional investigation.

With treatment advances and improved data collection and reporting procedures, there will likely continue to be an overall increase in the number of reported cases. Such epidemiological information will be important for health care planning and the resource allocation. Given the variability of the reported HB prevalence, further research is needed to investigate what the 'true' prevalence is and whether the incidence is the same for all populations.

Disclosures

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