Incidence of Perthes' disease in children born between 1973 and 1993

A Swedish nationwide cohort study of 2.1 million individuals

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Background and purpose — The incidence of Perthes' disease as reported in the literature varies widely between and within countries. The etiology of the disease is still unknown. Both environmental and genetic factors have been suggested to play a part in either causing the disease or increasing the susceptibility of an individual. We determined the incidence of Perthes' disease in Sweden and investigated possible relationships to parental socioeconomic status, ethnicity, marital status, mothers' age when giving birth, parity, number of siblings, and smoking habits.

Patients and methods — Six Swedish population-based registers were used, together covering all children born in Sweden from 1973 through 1993.

Results — The incidence of Perthes' disease in Sweden was 9.3 per 100,000 subjects. The ratio between boys and girls was 3.1:1. The educational level of the father and the mother of a child with Perthes' disease was lower than in the controls. The incidence was lower when the fathers were in the highest income bracket (above the 90th percentile). A higher proportion of parents of Nordic lineage had children with Perthes' disease than parental pairs with one or both who were not of such lineage.

Interpretation — This study confirms that there is an association between the incidence of Perthes' disease and the socioeconomic status of the parents.

Perthes' disease or Legg-Calvé-Perthes disease (LCPD) was first described in 1910. It is defined as an osteonecrosis of the femoral head usually diagnosed during childhood, and it is 3–4 times more common in boys than girls (Guille et al. 1998, Wiig et al. 2006). The reported incidence has varied in different studies from different parts of the world, and in different areas of a single country—for example, in urban areas as compared to rural areas (Purry 1982, Hall et al. 1983, Moberg and Rehnberg 1992, Wiig et al. 2006). In a review involving 21 studies from 16 countries, the incidence was found to range from 0.2 per 100,000 to 19.1 per 100,000 (Perry et al. 2012a). In the UK, a decline in incidence of the disease has been described, particularly in more deprived areas (Perry et al. 2012b).

The etiology of the disease has long been debated. Many factors may be involved, including gender, genetics, socioeconomic status, and environment. Pillai et al. (2005) showed a correlation between poor socioeconomic circumstances and the incidence of Perthes' disease. In a more recent study using data from the Scottish Morbidity Record for the period 2000–2010, the occurrence of Perthes' disease after stratification for socioeconomic deprivation showed similar rates in urban and rural areas of Scotland (Perry et al. 2012b).

Although there has been an abundance of studies on the incidence and etiology of Perthes' disease, there is still a lack of nationwide studies taking parental socioeconomic status and ethnicity into account.

We investigated the incidence of Perthes' disease in all children who were born in Sweden during the period 1973–1993 and possible relationships to parental socioeconomic status, ethnicity, marital status, mothers' age when giving birth, parity, number of siblings, and smoking habits.

Patients and methods

Registers

We collected data from several population-based registers using the personal identification number assigned to every person residing in Sweden. The registers included in the study were:

The Total Population Register (TPR) and the Education Register (ER). The TPR was established in 1968 and includes

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Table 1. List of variables and their categorization in the study

Variable	Categorization
Sex	Categorized into "boys" and "girls".
Cohort	Categorized into 4 levels according to year of birth, "1973–1977", "1978–1982", "1983–1987", and "1988–1993".
Educational level	Categorized into 3 levels: "elementary school, 9–10 years", "high school, 11–13 years", and "graduate/postgraduate, ≥ 14 years".
Parental country of origin	Dichotomized into "both parents from Nordic countries" and "one or both from non-Nordic countries".
Marital status	Categorized into 3 levels: "married", "unmarried", and "divorced/widowed".
Parental income	Income per year (SEK).
Smoking	Defined as the mother smoking on a daily basis. The amount of smoking was not known.
Perthes'	Children diagnosed with Perthes' disease according to the National Patient Register and who had been given one of the following diagnoses. ICD-8: 722,10-722, and 11 722,19; ICD-9: 732B; and ICD-10: M911, M912, and M913. All other individuals were considered to be the control/comparison group.

information on births, deaths, migrations and marital status. The ER contains information about the educational level of the population, which is collected continuously. These registers are held by Statistics Sweden.

The Medical Birth Register (MBR) includes 97–99% of pregnancies that have resulted in births in Sweden since 1973, and contains information about the pregnancy and about the delivery and the neonatal health of the child. The register is based on the medical charts from maternal healthcare, obstetric care, and infant care.

The National Patient Register (NPR) contains information on all patients who have been discharged from hospital or treated in outpatient care. It contains information from the whole of Sweden since 1987.

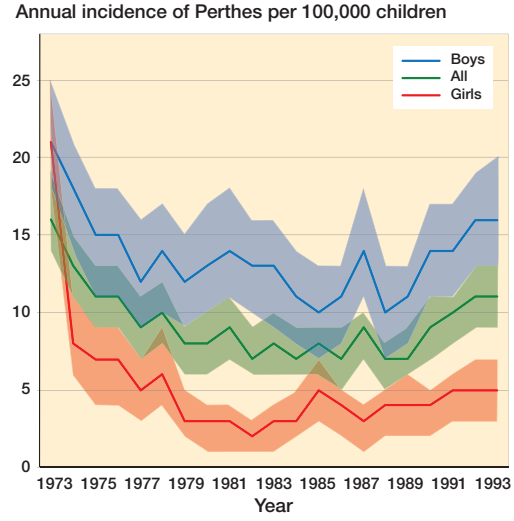
The Multi-Generation Register contains information on biological and adoptive parents, and was used to obtain information on the fathers.

The Cause of Death Register contains information on cause and date of death.

We divided the population into 2 major groups: parents born in Nordic countries and parents not born in Nordic countries. Swedish birth registers show the country of birth of all parents, so parents born in Sweden, Denmark, Finland, Norway, Iceland, Greenland, and the Faeroe Islands were assigned to the Nordic group. The number of parents assigned to this group was 1,903,452 and the number assigned to the other group was 214,766.

Study population

The study population was defined as all children born in Sweden between 1973 and 1993. To calculate the incidence, all individuals were included (2,131,111—of which 1,094,193 were boys and 1,036,918 were girls). In the further analyses, 2,120,192 individuals were included (1,088,464 boys and 1,031,728 girls), where both mothers and fathers could be identified since the use of maternal and paternal variables was included in the analyses.



The annual incidence of Perthes' disease in Sweden, 1973–1993.

Variables

Variables included in this study were categorized as in Table 1.

Statistics

Univariate relationships between the occurrence of Perthes' disease and parental socio-demographic factors and birth characteristics of the children were evaluated using Pearson's chi-square test. All statistical analyses were performed using SPSS version 22. Any p-value < 0.05 (two-sided) was considered statistically significant. As the estimated prevalence is a proportion (p) the corresponding 95% confidence interval (CI) will be $p \pm 1.96*\sqrt{(p(1-p)/n)}$. Thus, since the period prevalence during 1973–1993 was 0.001% and the total number of observations was 2,120,192, the CI would be:

$0.001 \pm 1.96*\sqrt{(0.001*0.999/2,120,192)} = \pm 0.00004$ (lower limit = 0.0006; upper limit = 0.00104).

Ethics

The study was approved by the Regional Ethics Committee in Linköping (entry no. 2010/403-31).

Results

Of the 2,131,111 children born between 1973 and 1993, 1,987 were diagnosed with Perthes' disease. The mean annual incidence was 9.3 per 100,000 children. The annual incidence showed no statistically significant changes over time (Figure).

Table 2. Socio-demographic information about parents

Perthes'	No		Yes		p-value
	n	%	n	%	
Educational level, father					
< 11	493,802	23	566	29	< 0.001
11–13	990,041	47	929	47	
≥ 14	580,572	27	445	22	
Missing	54,803	3	34	2	
Educational level, mother					
< 11	321,002	15	392	20	< 0.001
11–13	1,040,430	49	1,038	53	
≥ 14	721,578	34	528	27	
Missing	35,208	2	16	1	
Origin					
Both Nordic	1,903,452	90	1,846	94	< 0.001
One or both non-Nordic	214,766	10	128	6	
Marital status, mother					
Married	679,764	32	627	32	0.4
Unmarried	1,298,018	66	1,301	66	
Widowed/divorced	40,322	2	46	2	
Mother's age when she gave birth					
13–19	88,965	4	96	5	0.1
20–26	868,816	41	842	43	
27–33	890,507	42	785	40	
> 33	269,930	13	251	13	
Parity					
Primi	880,212	42	771	39	0.02
Multi	1,238,006	58	1,203	61	
Birth order					
1	877,094	41	765	39	0.3
2	777,687	37	757	38	
3	331,720	16	311	16	
4	93,632	4	89	4	
5	25,114	1.2	32	1.6	
6	7756	0.4	14	0.7	
7	2848	0.1	2	0.1	
8	1128	0.1	3	0.2	
9	661	0	1	0.1	
10	297	0	0	0	
11	140	0	0	0	
12	73	0	0	0	
13	34	0	0	0	
14	14	0	0	0	
15	12	0	0	0	
16	4	0	0	0	
17	3	0	0	0	
18	1	0	0	0	
Number of siblings					
1	941,347	23	513	26	0.06
2	941,983	44	869	44	
3	496,672	23	440	22	
4	139,867	7	119	6	
5	34,008	2	24	1	
6	9735	0.5	6	0.3	
7	2937	0.1	3	0.2	
8 or more	1669	0.1	0	0.0	
Annual income, mother					
≤ 10th percentile	209,921	10	174	9	0.2
>10th and < 90th	1,623,177	78	1,545	79.0	
≥ 90th percentile	248,093	12	237	12	
Annual income, father					
≤ 10th percentile	207,953	10	192	10	0.03
> 10th and < 90th	1,657,300	80	1596	82	
≥ 90th percentile	206,044	10	159	8	
Annual income, family					
≤ 10th percentile	207,683	10	182	9	0.08
> 10th and < 90th	1,643,196	79	1,584	81	
≥ 90th percentile	218,143	11	180	9	
Smoking [a]					
No	43,610	71	34	49	< 0.001
Yes	17,550	29	35	51	

[a] Only available for the years 1990–1993.

Table 3. Educational level of the parents in relation to the incidence (per 100,000) of Perthes' disease

Years of education	Men	Women
< 11	11.5	12.2
11–13	9.4	10.0
≥ 14	7.7	7.3

Table 4. Annual income of the parents in relation to the incidence (per 100,000) of Perthes' disease

Income	Men	Women
≤ 10th percentile	9.2	8.3
> 10th and < 90th percentile	9.6	9.5
≥ 90th percentile	7.7	9.5

The ratio between boys and girls was 3.1:1. The median age at diagnosis was 8 years for boys (mean 9.2 (SD 6.2)) and 9 years for girls (mean 10.7 (SD 6.9)).

The educational level of the father and the mother of a child with Perthes' disease was lower than in the controls (Tables 2 and 3). Concerning annual income, the only statistically significant difference was seen in fathers, where the incidence was lower in the top income bracket (Tables 2 and 4).

Perthes' disease was more common in children with both parents of Nordic origin. Mothers of children with Perthes' disease were often multiparous. The marital status, the mothers' age when she gave birth (mean age 28 (SD 5) in those with a child diagnosed with Perthes' as opposed to 27 (SD 5) in the controls), birth order, and the number of siblings showed no statistically significant differences. Smoking by the mother was associated with Perthes' disease (Table 2).

Discussion

In this nationwide study of all children born in Sweden between 1973 and 1993, the incidence of Perthes' disease, 9.3 per 100,000 subjects, was in the same range as found in 2 other Nordic studies (8.6 and 9.2 per 100,000 subjects) (Moberg and Rehnberg 1992, Wiig et al. 2006). There is good reason to believe that almost all patients with this disease who live in countries like Sweden, with a well-functioning healthcare system that collects extensive data, will eventually be detected due to symptoms such as pain and limping (Moberg and Rehnberg 1992). Thus, we believe that our results represent the true incidence for our country—and perhaps what can be expected in a mainly Caucasian population.

Our study confirms that there is a socioeconomic association between lower level of education and the incidence of Perthes' disease. However, the incidence showed no major dif-

ferences when related to income. The level of education and income may signal the presence of confounding factors such as smoking and other health-related forms of behavior, which are more prevalent in people with a lower level of education. Although we have only limited material concerning smoking, there was a clear association between smoking by the mother and the incidence of Perthes' disease.

Since we have no genetic data, nothing can be said about the relative importance of genetic factors in determining the incidence of Perthes'. There is a possibility that Perthes' disease may be associated with other traits, for example, learning disabilities, ADHD, or some other factor that is in some way related to level of education and/or level of income (Hailer and Nilsson 2014).

To our knowledge, this is the first study on the incidence of Perthes' disease in a nationwide cohort. The major strengths of using data from national registries are the completeness and large size of the data collected and the fact that population-based information is free from recall bias. The Swedish Medical Birth Register covers almost 100% of all births in Sweden. However, registry data can also involve misclassification problems caused by incorrect registration of diagnostic codes, and this limitation may have affected the validity of the data we used. If so, the incorrect registration was random and not systematic.

Nevertheless, not all sources of errors can be eliminated. It is possible that the estimated prevalence of Perthes' disease has been underestimated due to under-reporting—or even overestimated due to over-reporting. In this setting, we have collected data on all men and women born between 1973 and 1993 (no exclusion criteria were used for the prevalence estimation). Since we have data on all of these individuals to the end of 2012 and since Perthes' disease is a diagnosis that is usually set during childhood, we have minimized the risk of underestimation. Thus, the question is whether the Swedish registers themselves are reliable. In the validations that have been performed, the registers have been deemed of good quality, with a high coverage rate and precision (some variations regarding precision exist, but they are not alarming).

As already noted, our study could not address the relative importance of genetic factors as opposed to environmental factors, since we have no genetic data. An interesting finding in the study was that the incidence of Perthes' disease in children of Nordic parents was greater than in the children whose parents (one or both) were not Nordic. Given the wide range of ethnicities in the non-Nordic group, any suggestion of a fundamental genetic difference would be premature. A study of 3 different "population groups" in a region of South Africa found very disparate incidence between a group designated "white" and one designated "black", with an average incidence of 10.8 in white individuals and 0.45 in black individuals per 100,000 subjects (Purry 1982). Since the historical record of healthcare for these 2 groups may well show great difference, the apparently different incidences of the disease must be viewed with caution. In a universal healthcare system such as the Swedish system, most children with significant symptoms of a serious disease will be diagnosed. In Sweden, all child healthcare is free of charge until the age of 18. Regular check-ups are offered according to national standardized guidelines. In any country where one or more population subgroups have much more limited access to medical care than the group with best access, one can be certain that many children are not diagnosed, so the true incidence may be difficult to determine. This makes it difficult to compare incidence levels and even more difficult to even begin to discuss causality between socioeconomic and genetic factors and incidence of Perthes' disease. For a better understanding, there should be more high-quality epidemiological studies from different parts of the world.

TJ, AJ, and GS conceptualized and designed the study, drafted the initial manuscript, and approved the final manuscript as submitted. ML drafted the initial manuscript and approved the final manuscript as submitted. MB performed the statistical analyses, critically reviewed the manuscript, and approved the final manuscript as submitted.

No competing interests declared.

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