Family history and its association to curve size and treatment in 1,463 patients with idiopathic scoliosis

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Received: 21 December 2012 / Revised: 14 May 2013 / Accepted: 7 June 2013 / Published online: 26 June 2013
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Abstract

Purpose To study family history in relation to curve severity, gender, age at diagnosis and treatment in idiopathic scoliosis.

Methods A self-assessment questionnaire on family history of scoliosis was administered to 1,463 untreated, brace or surgically treated idiopathic scoliosis patients.

Results Out of the 1,463 patients, 51 % had one or more relatives with scoliosis. There was no significant difference between females and males, nor between juvenile and adolescent study participants in this respect ($p = 0.939$ and 0.110 , respectively). There was a significant difference in maximum curve size between patients with one or more relatives with scoliosis (median 35° , interquartile range 25) and patients without any relative with scoliosis (median 32° , interquartile range 23) ($p = 0.022$). When stratifying patients according to treatment (observation, brace

treatment or surgery), we found that it was more common to have a relative with scoliosis among the treated patients ($p = 0.011$). The OR for being treated was 1.32 (95 % CI 1.06–1.64) when the patient had a relative with scoliosis, compared to not having.

Conclusions Larger curve sizes were found in patients with a family history of scoliosis than in the ones without. No relation between family history and gender or between family history and age at onset of idiopathic scoliosis was found. Although the presence of a family history of scoliosis may not be a strong prognostic risk factor, it indicates that these patients are at higher risk of developing a more severe curve.

Keywords Adolescent idiopathic scoliosis · Juvenile idiopathic scoliosis · Heredity · Prognosis · Curve severity

Introduction

Relatives to patients with idiopathic scoliosis have a higher prevalence of scoliosis than the population in general, suggesting hereditary factors in the aetiology of this disorder [1–3]. This is supported by twin studies showing that the heritability of scoliosis is 38 % and that the concordance for scoliosis is higher in monozygotic than in dizygotic twin pairs [4–7]. In the clinical setting, it is difficult to predict the prognosis of the scoliosis, implying possibly unnecessary follow-ups and brace treatments. Traditionally, the disorder is classified as juvenile or adolescent idiopathic scoliosis depending on the age at diagnosis. The degree of heredity in juvenile idiopathic scoliosis is less evaluated than in the adolescent type due to methodological difficulties based on a low prevalence. Furthermore, the degree of heredity in relation to the severity of the curve or the type of treatment has not been reported.

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In the largest study on heredity of idiopathic scoliosis to date, we aimed at investigating if the self-assessed family history of scoliosis is associated with the curve severity and the type of treatment of this disorder. In addition, we wanted to evaluate if the family history of scoliosis is different in juvenile compared to adolescent idiopathic scoliosis patients, as well as between girls and boys with idiopathic scoliosis.

Materials and methods

Patients

Patients diagnosed with juvenile (JIS) or adolescent idiopathic scoliosis (AIS) at four Swedish orthopaedic departments (Skåne University Hospital, Malmö, Karolinska University Hospital, Stockholm, Sahlgren University Hospital, Gothenburg and Sundsvall Härnösand County Hospital, Sundsvall) were invited to participate in the study: (1) Patients currently under treatment or observation during the time of investigation (year 2004–year 2010), (2) Patients formerly diagnosed with idiopathic scoliosis at the clinics, identified using in- and outpatient registers, (3) Patients from the Gothenburg Scoliosis Database, containing prospectively collected data on idiopathic scoliosis patients since the 1960's.

In total 3,762 patients were invited, 1,056 did not answer, 950 denied and 1,756 accepted participation. Out of these, 276 patients were excluded due to confirmed or suspected non-idiopathic scoliosis, missing radiographs or medical records and/or having a Cobb angle less than 10°. Furthermore, eight patients who got the diagnosis before 4 years of age and nine patients who were diagnosed above 20 years of age were excluded, leaving 1,463 patients for our current evaluation. Of the 1,463 patients, 315 (21 %) were currently under treatment or observation, 390 (27 %) were included from the in- and outpatient registers and 758 (52 %) were from the Gothenburg scoliosis database.

Written informed consent was obtained from all the participants. The ethical committee at Lund University and the ethical committee in Stockholm approved all parts of the study.

Medical records and radiology

Medical records, radiological data and images were retrieved for the patients currently under treatment ($n = 315$) and the patients who were recruited using in- and outpatient registers ($n = 390$). Radiological data were re-measured in 95 % of these patients. In 5 % of the patients, radiological data were accepted without re-measurement since the necessary information was found in the

medical records and radiological files and the measurements were made by experienced colleagues. In the patients from the Gothenburg database ($n = 758$), all data on radiology, diagnosis and treatment had already been gathered in a prospective manner. Medical records were scrutinized only in case of incomplete data ($n = 98$).

The following radiographical information was recorded: Data from the first available radiograph showing scoliosis and, if treated, the last radiograph prior to brace treatment and/or surgery. For all the patients, data from the last available radiograph before the age of 27 years were retrieved. The maximum curve size was defined as the Cobb angle [8] of the largest curve at the last follow-up before the age of 27 years, in untreated and brace treated patients. In patients who had undergone surgery, the Cobb angle of the largest curve prior to surgery was used to determine the maximum curve size.

Treatment

Patients were treated in line with existing protocols at the clinics during the specific time period. Treatment recommendations for patients in the 1960's and 1970's were brace treatment if they had a thoracic, thoracolumbar, or double primary curve between 24 and 50°, and lumbar curves of less than 60°. Larger curves were treated with surgery. For patients treated in the 1980's to 2000's, brace treatment was started in curves between 25 and 45° with remaining growth. Surgery was indicated in patients with curves larger than 45° and remaining growth. After cessation of growth, surgery was indicated if the curve was larger than 50°. In our study cohort 3 % were treated or observed during the 1960's or earlier, 34 % during the 1970's, 25 % during the 1980's, 10 % during the 1990's and 28 % after year 2000. Of the brace treated patients, 34 % wore a brace with a chin plate and 66 % a brace without chin plate. Among the surgically treated patients, 61 % received a Harrington implant, 25 % a pedicle-screw type of implant, 9 % an anterior implant and in 5 % other or combined techniques were used. In the analysis, all the patients who received brace treatment are accounted for as "brace treated" no matter type of brace, length of brace treatment and curve sizes prior to start of brace treatment. Patients who received brace treatment and subsequent surgery due to the failure of brace treatment are accounted for as "surgically treated". All the patients who underwent surgery are classified as "surgically treated", no matter the type of implant, age at surgery or curve sizes prior to surgery.

Juvenile or adolescent idiopathic scoliosis

The age at onset of scoliosis was set as the age of the patient when the scoliosis was acknowledged for the first

time by the patient (self-reported data). If the patient did not remember this, as was the case in 6 % of the patients, the age at onset was defined as the age of the patient at the first available radiograph with a Cobb angle exceeding 10°. Patients four to nine years old at the onset of scoliosis were classified as having JIS and patients 10 to 20 years old as having AIS.

Heredity

A self-assessment questionnaire on family history of scoliosis was administered to the study participants. They were asked if any of their biological parents, grandparents, siblings and children had scoliosis and how many biological siblings and children they had in total, no matter scoliosis or not. They were also asked to specify if they had any other biological relative with scoliosis. The information on heredity was entirely self-reported. We have not tried to verify the diagnosis or type of scoliosis in the relatives. In the analysis the relatives were classified as “any kind” (all biological relatives, no matter distance of relationship), “first-degree” relatives (biological parents, siblings and children) and “siblings” (biological siblings).

Statistics

Data is presented as mean with 95 % confidence intervals (95 % CI) or median and interquartile range. Group comparisons are made with the Chi-square test, odds ratios and the Mann–Whitney *U* test, in IBM SPSS statistics version 20.

Results

Descriptive data

In total, 1,463 patients were included in the study, 87 % women ($n = 1,273$) and 13 % men ($n = 190$); 14 % was classified as JIS ($n = 198$), and 86 % as AIS ($n = 1,265$), Table 1. The mean (SD) age of the patients at the time of the current investigation was 35 (14) years. Out of the JIS patients, 69 % were treated ($n = 137$, whereof brace $n = 69$ and surgery $n = 68$). Among the AIS patients, 65 % were treated ($n = 824$, whereof brace $n = 483$ and surgery $n = 341$). Information on mean age at onset and maximum curve sizes is displayed in Table 1. Age at onset of scoliosis in relation to gender is shown in Fig. 1.

Heredity

Among the patients, 51 % reported of having at least one relative (any kind) with scoliosis and 36 % reported of

Table 1 Descriptive data of the 1,463 idiopathic scoliosis patients included in the study, showing age at onset of scoliosis, age at investigation and curve severity

Study participants	<i>n</i>	Age at onset (years)	Maximum curve size (Cobb angle)
All	1,463	12.1 (2.6)	27 (12)
Gender			
Female	1,273	12.0 (2.5)	28 (12)
Male	190	12.7 (3.3)	28 (14)
Age at diagnosis			
Juvenile (onset 4–9 years)	198	7.3 (1.3)	26 (14)
Adolescent (onset 10–20 years)	1,265	12.9 (1.9)	28 (11)
Type of treatment and observation			
Untreated	502	12.4 (2.7)	24 (12)
Brace treated	552	12.0 (2.4)	31 (10)
Surgically treated	409	11.8 (2.8)	57 (15)

Data is presented as mean (standard deviation). The maximum curve size is defined as the Cobb angle of the largest curve at the last radiological follow-up before the age of 27 years, in the untreated and brace treated patients. In the surgically treated patients, the Cobb angle of the largest curve on the last radiograph prior to surgery was used to determine the maximum curve size. Age at onset of scoliosis was self-assessed

n number of patients

Fig. 1 Distribution of age at onset of scoliosis in relation to gender in the 1,463 idiopathic scoliosis patients included in the study

Table 2 The number (%) of idiopathic scoliosis patients with or without family history of scoliosis is shown in relation to gender, age at onset of scoliosis, curve severity, and treatment

Study participants	Family history of scoliosis	No family history of scoliosis	<i>p</i> value
All (<i>n</i> = 1,463)	743 (51 %)	720 (49 %)	
Gender			
Female	647 (51 %)	626 (49 %)	0.939
Male	96 (51 %)	94 (49 %)	
Age at onset			
Juvenile	111 (56 %)	87 (44 %)	0.110
Adolescent	632 (50 %)	633 (50 %)	
Curve severity			
Cobb less than 40°	441 (48 %)	471 (52 %)	0.017
Cobb 40° or more	302 (55 %)	249 (45 %)	
Type of treatment			
Untreated	232 (46 %)	270 (54 %)	0.026 ^a
Brace	293 (53 %)	259 (47 %)	0.033 ^b
Surgery	218 (53 %)	191 (47 %)	
Treatment or observation			
Untreated	232 (46 %)	270 (54 %)	0.011
Treated with brace or surgery	511 (53 %)	450 (47 %)	

Data on scoliosis in relatives have been obtained from the study participant with a self-assessment questionnaire. A family history of scoliosis is defined as having at least one biological relative with scoliosis. The *p* value refers to the Chi-square test

^a Comparison between brace-treated and untreated patients

^b Comparison between surgically treated and untreated patients

having at least one *first-degree* relative with scoliosis. Among the relatives reported to have scoliosis, 17 % were treated.

There was a significant difference in maximum curve size between patients with one or more relative (any kind) with scoliosis (median 35°, interquartile range 25) and patients without any relative with scoliosis (median 32°, interquartile range 23) (*p* = 0.022). When dividing the patients into two groups according to the maximum curve size (less than 40°, or 40° or more), we found that the odds ratio (95 % confidence interval) for having a Cobb angle of 40° or more was 1.30 (1.05–1.60) if the patient had a family history of scoliosis, compared to not having a family history, Table 2. We found no significant difference in maximum curve size between study participants with one or more *first-degree* relative with scoliosis and those without (data not shown).

We found no significant difference between males and females in proportion of study participants with one or more relative (any kind) with scoliosis (*p* = 0.939), Table 2. In addition, no differences were seen between

males and females in proportion of study participants with one or more *first-degree* relative with scoliosis, or one or more *sibling* with scoliosis (data not shown).

Likewise, no significant difference was seen when comparing the proportion of JIS and AIS study participants with one or more relatives with scoliosis (any kind), Table 2, as well as the proportion of JIS and AIS study participants with one or more *first-degree* relatives with scoliosis, or one or more *siblings* with scoliosis (data not shown). In addition, since the classification of idiopathic scoliosis into JIS or AIS is arbitrary, we divided the study participants into four different age groups based on the age of diagnosis (4–8, 9–12, 13–16 and 17–20 years). No difference was found in the proportion of study participants with one or more relatives (any kind) between the age groups (data not shown).

When comparing treated and untreated patients there was a significant difference in the proportion of patients with one or more relatives (any kind) with scoliosis Table 2. The odds ratio for being treated was 1.32 (95 % confidence interval 1.06–1.64) if the patient had a family history of scoliosis compared to a patient without a family history. We found no significant difference in proportion of patients with one or more *first-degree* relative with scoliosis between the treatment groups (*p* = 0.547).

Prevalence of scoliosis in relatives

The 1,463 study participants had 5,462 first-degree relatives over the age of 15 years, and 692 (13 %) of these had scoliosis according to the self-assessment questionnaire. There was no significant difference in the proportion of *first-degree* relatives with scoliosis when comparing female and male study participants, Table 3. The 1,463 study participants had 714 sons and daughters above the age of 15 years. Among the sons, 34 out of 362 (9 %) had scoliosis and among the daughters, 74 out of 352 (21 %), with no significant difference between male and female study participants, Table 3. There was no significant difference in the proportion of first-degree relatives with scoliosis when comparing JIS and AIS study participants (*p* = 0.398; data not shown).

Discussion

This study, to the best of our knowledge the largest study on heredity of idiopathic scoliosis to date, has shown that the heredity of scoliosis seems to be related to the severity of this disorder.

Heredity

In this study, 51 % of the participants had one or more relative (any kind) with scoliosis and 36 % had at least one

Table 3 The number (%) of first-degree relatives (biological parents, siblings and children) with scoliosis to the 1,463 study participants with idiopathic scoliosis

	Female patients	Male patients	<i>p</i> value
First-degree relatives without scoliosis*	4,201 (87 %)	569 (86 %)	0.357
First-degree relatives with scoliosis	601 (13 %)	91 (14 %)	
Brothers without scoliosis*	674 (91 %)	102 (89 %)	0.579
Brothers with scoliosis	66 (9 %)	12 (11 %)	
Sisters without scoliosis*	746 (85 %)	114 (85 %)	0.928
Sisters with scoliosis	134 (15 %)	20 (15 %)	
Sons without scoliosis*	313 (91 %)	15 (88 %)	0.731
Sons with scoliosis	32 (9 %)	2 (12 %)	
Daughters without scoliosis*	257 (80 %)	21 (72 %)	0.365
Daughters with scoliosis	66 (20 %)	8 (28 %)	

Data on scoliosis in the first-degree relatives have been obtained from the study participants by a self-assessment questionnaire. Only first-degree relatives older than 15 years of age are presented, since younger ones may not yet have developed scoliosis. The *p* value refers to the comparison of the number of first-degree relatives with scoliosis between male and female study participants (Chi-square test)

* The number of relatives without scoliosis include relatives in which the study participant did not know if the relative had scoliosis or not

first-degree relative with scoliosis. The heredity of idiopathic scoliosis varies in the literature. Wynne-Davies et al. [1] reported that 27.2 % of the study participants were having at least one first-degree relative with scoliosis. In a cohort of 82 surgically treated patients, Ward et al. [3] found a relative with scoliosis within four generations in 69 of the pedigrees (82 %). The relatively high proportion of patients with one or more relative with scoliosis (any kind) and the high prevalence of scoliosis among *first-degree* relatives in our study compared to some of the earlier studies may partly be a result of a selection bias. It is not unreasonable to think that patients with heredity for scoliosis are more prone to participate in a study on genetics and heredity. However, our study population is older and both siblings and children have had the possibility to develop scoliosis, thereby increasing the amount of affected relatives.

Heredity in relation to severity of the disorder, gender and age at onset

The heredity of scoliosis was related to the curve severity and treatment. We found no significant differences in the heredity of scoliosis between females or males nor between juvenile and adolescent idiopathic scoliosis patients. The

maximum curve size was larger in patients with heredity compared to the ones without, although the difference was small. However, the patients in our cohort have been treated when needed and this could be one reason for underestimation of the true difference in curve size between patients with and without heredity. Cobb angle values may be affected by the measurement error, reported to be up to 5°–6° [9] but we do not believe that there is a systematic error that could inflict bias in relation to the possible association with heredity. A relation between heredity and curve size has been reported by Miller and coworkers [10].

Prevalence of scoliosis in relatives

When looking at the proportion of first-degree relatives having scoliosis, Wynne-Davies et al. reported a prevalence of scoliosis in first-degree relatives of 6.9 % (10/144), Rizeborough et al. 16 % (87/552) and Ward 24 % (372/1,513) [1–3]. We found a prevalence of scoliosis of 13 % (692/5,462) in first-degree relatives. When comparing these figures, one has to bear in mind that the other studies are all made on young study participants with varying selection criteria. The mean age at investigation in the present study is higher than in the previous studies, and the children of the study participants are included in the analysis, which may explain some of the difference.

Since the risk for males to obtain idiopathic scoliosis is less than for females, it has been suggested that the genetic threshold for males to exhibit scoliosis is higher. In this study, the risk of obtaining scoliosis was less in the sons (9 %) than in the daughters (21 %) of the study participants. In addition, the recurrent risk was less for male siblings (9 %) than female siblings (15 %) supporting the data of Tang et al. [11], who reported a sibling recurrent risk of 12 % in males and 23 % in females in a cohort of 415 female study participants. When we looked at the sibling recurrent risk in our *male* study participants only, the prevalence of scoliosis in brothers was 10 % (12/114) and in sisters 15 % (20/134), with no significant difference compared to siblings to the female study participants. Ward et al. [3] showed a large difference in sibling recurrent risk between brothers, 27 % (3/11), and sisters, 64 % (4.5/7), to *male* idiopathic scoliosis patients. However, this large difference should be interpreted cautiously due to the small number of study participants.

Limitations

One disadvantage with this study is that the diagnosis of scoliosis in relatives is not confirmed with radiographs or medical records. One of the aims with this study, however, was to investigate if a simple question on heredity in the

clinical setting would give any information on the prognosis of the patient. In the clinical setting, we usually do not have access to medical records or radiographical information of relatives and cannot verify the information on a family history given by the patient. Due to the large sample of patients, any confounding by other types of scoliosis is negligible. We have chosen to use the self-reported age of diagnosis. Although this might introduce uncertainty, we believe this age to be more consistent than the age of the first medical record or radiographic examination due to both doctors and patients “delay”.

The generalizability of our results may be questioned due to the number of patients that did not want to participate in the study. The size of the cohort is very large though, including the most numerous group of male idiopathic scoliosis patients ($n = 190$) as well as JIS patients ($n = 198$) reported so far. One could speculate that the presence of a relative with scoliosis has predisposed patients to treatment with brace and/or surgery, explaining the difference in heredity. The difference in curve size indicates that this is not the case.

Conclusion

In this study of 1,463 patients with idiopathic scoliosis, we found larger curve sizes in patients with a family history of scoliosis than in the ones without. We found no relation between heredity and gender or between heredity and age at onset of idiopathic scoliosis. Although the presence of a family history of scoliosis may not be a strong prognostic risk factor, it indicates that these patients are at higher risk of developing a more severe curve. A closer monitoring of these patients may be indicated.

Acknowledgments We thank all the patients that participated in the study. We would like to acknowledge the research personnel in Malmö, Stockholm, Gothenburg and Sundsvall who were involved in the recruitment of the patients. In addition to the authors, the following orthopaedic surgeons contributed to the collection of patients: Henrik Düppe, Ralph Hasserijs, Anders Möller and Tage Sahlstrand at the Skåne University Hospital, Malmö; and Hans

Möller, Tomas Reigo and Kourosh Jalalpour at the Karolinska University Hospital, Stockholm, Sweden. Financial support was provided by funds from the regional agreement on medical training and clinical research (ALF) between Stockholm County Council and Karolinska Institutet, and research funds from Västernorrland County Council.

Conflict of interest The authors have no conflicts of interest.

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