

Endometriosis in Monozygotic and Dizygotic Twins: A Review of Literature

Raimondo D^{1*}, Mastronardi M¹, Mabrouk M², Arena A¹ and Seracchioli R¹

¹Department of Obstetrics, Gynecology and Human Reproduction Physiopathology, Dipartimento di Scienze Mediche e Chirurgiche (DIMEC), S. Orsola Hospital, University of Bologna, Massarenti, Bologna, Italy

²Faculty of Medicine, Department of Obstetrics and Gynecology, University of Alexandria, Egypt

Abstract

Endometriosis is a common estrogen-dependent inflammatory disease and a major contributor to pelvic pain and subfertility in women of reproductive age. Its etiology and pathogenesis are not well known yet, but different studies had highlighted its multifactorial nature, influenced by both genetic and environmental components. This mini-review analyzes the prevalence of the disease and the concordance for the presence and stage of endometriosis in monozygotic (MZ) and dizygotic (DZ) twins. A higher concordance for the presence of the disease in MZ twins rather than DZ twins was observed, with a statistically significant difference (p -value < 0.05). Only one study had evaluated the concordance for endometriosis stage within MZ twins, observing a high rate of concordance. Genetic component seems to play a pivotal role in the development of endometriosis and its severity.

Keywords: Endometriosis; Twins

Introduction

Endometriosis is one of the most common benign gynecologic diseases and is characterized by the presence of ectopic endometrial tissue outside the uterus. It is an estrogen-dependent inflammatory disease and a major contributor to pelvic pain and subfertility in women of reproductive age [1]. Although its etiology and pathogenesis are largely unknown, evidence shows that it is a complex multifactorial disease, where both genetic and environmental components contributing to susceptibility [2]. Studies on heritability have demonstrated familial accumulation, increased concordance in monozygotic (MZ) twins, and a 3 to 15 times higher risk in first-degree relatives of women with endometriosis compared with those in the general population [2,3-8].

The aim of the present study was to achieve a comprehensive review of pertinent and recent literature published in order to analyze the prevalence of the disease and the concordance for the presence and stage of endometriosis in MZ and DZ twins.

Literature Review

The following key words were used to conduct a computerized search of PubMed/Medline: “endometriosis” AND “twins” OR “heritability” OR “familial endometriosis”. Relevant full-text articles written in English from January 1994 to November 2018 containing a table of references were retrieved. Articles with less than 5 cases were not considered for the study. All references were searched to identify other pertinent articles. Number of twin pairs, number of twin pairs affected by endometriosis, concordance and discordance for the presence of endometriosis, concordance for stage of the disease were evaluated in general and distinguishing between MZ and DZ twins. Comparison of concordance for the presence of the disease between MZ and DZ twin pair were performed using a Chi-squared test. Statistical significance was set to the conventional p -value \leq 0.05.

Results

After a comprehensive review of the literature, 5 studies met our inclusion criteria. Data obtained from the revision of the Literature are summarized in Tables 1 and 2.

Three studies selected twin pairs affected by endometriosis from

a National Twin Registry (2;5;19). Analyzing the data from these latter, the prevalence of endometriosis in twins was 8.6% (825 twin pairs affected by endometriosis out of 9543 twin pairs in total). More specifically, the prevalence was 8.6% in MZ (437 twin pairs affected by endometriosis out of 5072 in total) and 8.6% in DZ (388 twin pairs affected by endometriosis out of 4471 in total) (Table 1).

Authors	Number of twin pairs		Number of twin pairs with at least one sister E+		Prevalence of endometriosis (%)	
	MZ	DZ	MZ	DZ	MZ	DZ
Moen et al. [18]	8	0	8	0	NA	NA
Hadfield et al. [6]	16	1	16	1	NA	NA
Treolar et al. [2]	854	493	105	51	12.3%	10.3%
Zondervan et al. [19]	623	377	73	39	11.7%	10.3%
Saha et al. [5]	3595	3601	259	298	7.2%	8.3%
Total^a	9568		850		NA	
	5096	4472	461	389	NA	NA
Total^b	9543		825		8.6%	
	5072	4471	437	388	8.6%	8.6%

^aStudies used to evaluate the total prevalence of endometriosis.

E+: Patient affected by endometriosis

MZ: Monozygotic twin pairs

DZ: Dizygotic twin pairs

NA: Not applicable

^aTotal considering all the studies

^bTotal considering only the studies with*

Table 1: Prevalence of endometriosis in twin pairs.

***Corresponding author:** Dr. Diego Raimondo, Department of Obstetrics, Gynecology and Human Reproduction Physiopathology, DIMEC, S. Orsola Hospital, University of Bologna Massarenti, 13 - 40138 Bologna, Italy, Tel: + 39 051 2144389; Fax: +39 051 2144392; E-mail: die.raimondo@gmail.com

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Authors	Concordance for Endometriosis (E+E+); n (%)		Discordance for Endometriosis (E+E-); n (%)	
	MZ	DZ	MZ	DZ
Moen et al. [18]	6 (75%)	0	2 (25%)	0
Hadfield et al. [6]	14 (87.5%)	1 (100%)	2 (12.5%)	0 (0%)
Treolar et al. [2]	18 (17.1%)	3 (5.9%)	87 (82.9%)	49 (94.1%)
Zondervan et al. [19]	13 (17.8%)	2 (5.1%)	60 (82.2%)	37 (94.9%)
Saha et al. [5]	30 (11.6%)	15 (5%)	229 (88.4%)	283 (95%)
Total	102 (12%)		749 (88%)	
	81 (17.6%)	21 (5.4%)	380 (82.4%)	369 (94.6%)

MZ: Monozygotic twin pairs
DZ: Dizygotic twin pairs
E+: Patient affected by endometriosis
E-: Patient without endometriosis

Table 2: Concordance and discordance for endometriosis in twin pairs.

The concordance for the presence of endometriosis between MZ and DZ twins was analyzed considering all the 5 studies. In MZ twins the concordance was 17.6% (81 twin pairs of 461), while in DZ twins it was 5.4% (21 twin pairs on 389), with a statistically significant difference (p -value < 0.05) (Table 2). Regarding concordance for endometriosis stage, only Hadfield et al. had investigated a possible concordance within MZ twins, observing a high rate of concordance. Out of 14 MZ twins with concordance for the presence of disease, 9 (64.3%) were concordant for stage III-IV [6].

Discussion

The true prevalence of endometriosis in the general population is unknown, mainly because diagnosis is often overlooked by primary care doctors leading to an average delay of 10 years [9-12]. In literature, the estimated prevalence of endometriosis in women of reproductive age is between 2% and 10%, reaching 50% among infertile patients [2,5,13]. In accordance with these data, the prevalence among twins was 8.6%.

A higher concordance for disease in MZ twins rather than DZ twins was observed, with a statistically significant difference. In agreement with this finding, Somigliana et al. had documented an association between endometriosis and pigmentary traits [14]. They had observed a two-fold increase in the risk of disease in women with green/blue eyes and in those who had frequently/always skin burn reaction to first sun exposure. Considering pigmentary traits as heritable traits in humans, these findings suggest a shared genetic background between women with endometriosis [14,15]. We observed a different percentage of endometriosis concordance through the different studies. This discrepancy could be explained considering the selection bias (type of population included in the study: case series or patients from a National Twin Registry) and the several diagnostic methods adopted to detect endometriosis (questionnaires, medical records analysis, histological confirmation). Furthermore, many women affected by endometriosis are asymptomatic and in many symptomatic ones the disease is not diagnosed.

Only one study evaluated the concordance for endometriosis stage within MZ twins, observing a high rate of concordance. Therefore, genetic component seems to play a pivotal role in the development of endometriosis and its severity. Although the environmental effect (i.e., urban setting, diet) is suspected to be responsible for development of

the disease and pattern of endometriosis, scientific evidence evaluating the impact and types of environmental factors on the occurrence of endometriosis is up to date poor and of low-quality [5,16-19].

Conclusion

More studies are needed to elucidate the role of genetic and environmental components on the pathogenesis of endometriosis among monozygotic twin not sharing the same environment.

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