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RESEARCH ARTICLE

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Differences in metabolic syndrome indicators by body mass index of women with endometriosis

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Abstract

Aim: The study aimed to identify the relationships between metabolic syndrome indicators and BMI in women with endometriosis.

Design: A retrospective observational study design was utilized to analyse secondary data from a longitudinal dataset.

Methods: A total of 281,810 women diagnosed with endometriosis and aged 15 through 49 were drawn from the National Health Insurance Service-National Health Screening Cohort data of the Republic of Korea from the year 2009 to 2016. Body mass index (BMI) and five indicators of metabolic syndrome were extracted. Descriptive statistics, Cochran–Mantel–Haenszel test, chi-square test and Cochran-Armitage test were used.

Results: Yearly changes in abnormal waist circumference, elevated fasting blood sugar and abnormally low levels of high-density lipoprotein cholesterol were statistically significant. The risk groups of these indicators all showed statistically significant differences according to BMI. The proportions of women with abnormal findings for all indicators significantly increased as BMI increased.

KEYWORDS
body mass index, endometriosis, metabolic syndrome, women

1 | INTRODUCTION

Endometriosis is a chronic, inflammatory disease characterized by the growth of endometrial tissue outside the uterus; its lesions may occur in the pelvic peritoneum, the ovary, and more rarely, the bladder, ureter or extrapelvic sites (Berek & Berek, 2019; Nisenblat et al., 2016). Since endometriosis is an oestrogen-dependent inflammatory disease, it shares a common pathophysiological background with other chronic health conditions. A particularly critical factor influencing oestrogen levels in women is adipose tissue, which is highly susceptible to disturbance by metabolic disruptors (Janesick & Blumberg, 2016). Imbalances in the inflammatory components of adipose tissue could induce metabolic syndrome-related complications (Torres et al., 2019).

Despite the increasing prevalence of obesity and metabolic syndrome in Korean women, little research has explored the relationships of comorbid health risks in women with endometriosis. Thus, it is necessary to examine the relationship of obesity in women with endometriosis with metabolic syndrome, especially utilizing representative national data, to generate evidence-based information for women's health education and nursing practice and to support the provision of integrated healthcare services.

2 | BACKGROUND

Endometriosis is estimated to affect up to 11% of women in reproductive age and 47% of women with infertility in the United States (Buck Louis et al., 2011; Meuleman et al., 2009), and approximately 10%–15% of women experience symptoms of endometriosis worldwide (Dai et al., 2018). In Korea, the number of women diagnosed with or treated for endometriosis increased from 53,474 in 2008 to 90,777 in 2014, corresponding to a 58.9% increase; in particular, women in their 30s and 40s accounted for 74% of the incidence of endometriosis (KOICD, 2019).

The typical symptoms of endometriosis are chronic pelvic pain, dysmenorrhoea and dyspareunia, which tend to vary with the menstrual cycle. Painful defecation, pelvic pain, and primary and secondary infertility also occur due to chronic inflammation of the lesions (Buck Louis et al., 2011; Culley et al., 2013; Hickey et al., 2014). Although surgical removal of endometriotic lesions is effective (Duffy et al., 2014), recurrence has been reported to be common, occurring in 21.5% of patients at 2 years and 40%–50% at 5 years after surgery (Guo, 2009; Tandoi et al., 2011). It is apparent that women with endometriosis experience both physical symptoms and psychological distress throughout their reproductive age.

Furthermore, endometriosis is an oestrogen-dependent inflammatory disease; thus, inflammatory factors could affect lipid metabolism, increasing the serum level of low-density lipoprotein (LDL) cholesterol, and reducing that of high-density lipoprotein (HDL) cholesterol (Giudice, 2010; Melo et al., 2010). An atherogenic lipid profile was revealed in women with endometriosis, who had higher total cholesterol, LDL, and triglyceride levels, as well as lower HDL levels, than women without endometriosis (Verit et al., 2008). Vascular changes due to hypertension increased inflammatory mechanisms, and chronic inflammatory conditions likewise elevated blood pressure (Guzik & Touyz, 2017). As explained by Petrie et al. (2018), chronic hyperglycaemia is associated with insulin resistance even before the diagnosis of diabetes, and central obesity has been found to increase the risk of vascular complications and inflammation (Madonna et al., 2017). Thus, endometriosis has a relationship with metabolic syndrome, which is defined in terms of multiple components: abdominal obesity, hypertriglyceridaemia, low HDL cholesterol levels, high blood pressure and high fasting glucose levels (Alberti et al., 2009; Lee et al., 2007). In Korean women over 19 years of age, the prevalence of obesity was reported to be 27.3%–28.4% from 2017 to 2019 (Korean Women's Development Institute 2021), and the overall age-adjusted prevalence of metabolic syndrome in the period of 2013–2015 was 16.1% (Huh et al., 2018). In the light of these epidemiological findings, these conditions are important health issues for nurses and public health professionals to address.

Nevertheless, only limited evidence has been reported for robust-related factors of endometriosis; specifically, earlier age at menarche and shorter menstrual cycle length are associated with a higher risk of endometriosis, whereas greater parity and higher body mass index (BMI) reduce its risk (Parasar et al., 2017; Parazzini et al., 2017). In addition to inconsistent findings about alcohol, smoking and physical activity as related factors, Shafrir et al. (2018) also indicated that factors such as fat intake and waist-to-hip ratio were still understudied in relation with endometriosis. Moreover, Mu et al. (2017), from the Nurses' Health Study II, the first prospective cohort study investigating this issue, showed that women with endometriosis had greater risks of developing hypercholesterolaemia and hypertension, and conversely, women with hypercholesterolaemia or hypertension had greater risks of having endometriosis, especially in the age group of under 40. As consistent findings were reported in a systematic review (Tan et al., 2019), it has become apparent that endometriosis should be investigated not as a single gynaecological disease, but rather in the context of comorbidities and chronic health problems.

Despite the increasing number of women with endometriosis and metabolic syndrome, little research in Korea has explored the relationships of those health risks in women with endometriosis. Since endometriosis shares a common pathophysiological background with other chronic health conditions, it is important to identify the relationships among these comorbid health indicators. Thus, the present study was conducted to address the following questions: (1) what were the distributions of age and BMI in women who were diagnosed with endometriosis? (2) how did the distribution of indicators of metabolic syndrome change over time in women with endometriosis? and (3) were there differences and changes in the indicators of metabolic syndrome according to BMI?

3 | METHODS

3.1 | Design

A retrospective observational study design was utilized to analyse secondary data from a longitudinal data set. Women were included if they had a health insurance claim with a Korean Standard Classification of Diseases, seventh edition code for endometriosis from the year 2009 to 2016 from the National Health Insurance Service-National Health Screening Cohort (NHIS-HEALS).

3.2 | Sample

The study used the NHIS-HEALS data from the Republic of Korea. The service provides general health examinations and medical tests for all adults who are at least 20 years of age without extra costs. The case group was composed of 281,810 women who had been diagnosed with endometriosis in the age group of 15 through 49 years (the reproductive age group defined by the World Health Organization) from 2009 to 2016 according to the Korean Standard Classification of Diseases, seventh edition (N80 [N80.0-N80.9]). The sampling process operated as follows: a clinic or a hospital sent a claim for medical expenses to the NHIS with the diagnosis of endometriosis, and then the NHIS shared the codes of the women in the national health screening cohort (Figure 1).

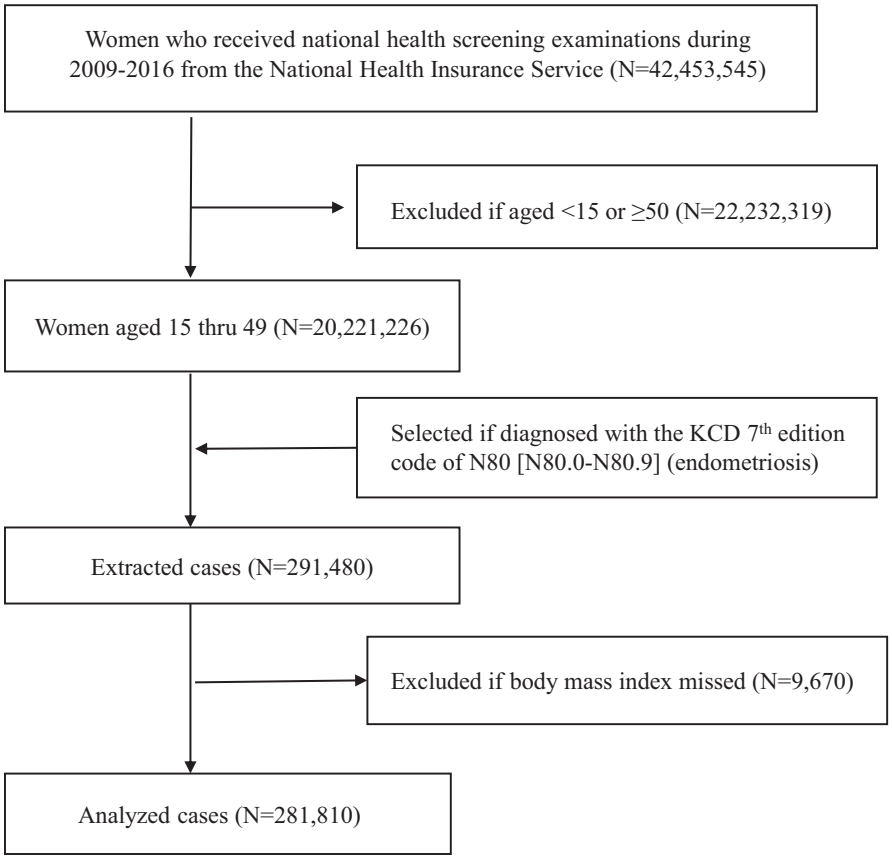

FIGURE 1 Flow Chart of the Sampling

3.3 | Measures

3.3.1 | Body Mass Index

BMI data were available from the cohort data set, and BMI was calculated based on height and weight measured at the time of the health screening. According to the criteria of the Korean Society for the Study of Obesity (2020), the data were classified into underweight (BMI < 18.5 kg/m^2), normal weight (18.5 kg/m^2 ≤ BMI<23.0 kg/m^2), overweight (23.0 kg/m^2 ≤ BMI < 25.0 kg/m^2) and obesity (BMI ≥ 25.0 kg/m^2).

3.3.2 | Indicators of Metabolic Syndrome

According to the criteria by Alberti et al. (2009), the following five indicators of metabolic syndrome were used in this study: waist circumference, blood pressure, fasting blood sugar, high-density lipoprotein cholesterol and triglyceride levels.

(1) Waist circumference (WC)

WC was measured during the health screening, with participants standing in a 25–30 cm stance, spreading their weight evenly on both feet, and breathing out comfortably, according to the general guidelines for measuring WC. The point between the bottom rib margin and the top of the pelvic bone (iliac crest) was measured with a tape measure to one decimal point. For women, a WC of less than 85 cm was classified as normal, while a WC over 85 cm was considered to indicate abdominal obesity (Korean Society for the Study of Obesity, 2020).

(2) Blood pressure (BP)

The BP value measured by an electronic manometer was classified as normal if the systolic BP was 120 mmHg or lower systolic BP and the diastolic BP was 80 mmHg or lower, whereas elevated BP was defined as a systolic BP of 121 mmHg or higher or a diastolic BP of 81 mmHg or higher.

(3) Fasting blood sugar (FBS)

FBS was classified as desirable if it was less than 100 mg/dl and elevated if it was 100 mg/dl or higher.

(4) High-density lipoprotein (HDL) cholesterol

An HDL cholesterol level of 50 mg/dl or higher was classified as desirable, while an HDL cholesterol level of less than 50 mg/dl was considered to be abnormally low.

(5) Triglyceride (TG)

A TG level <150 mg/dl was considered desirable, while a TG level of 150 mg/dl or higher was considered to be elevated.

3.4 | Ethical considerations

This study was approved by the institutional review board (CR318312) of the university with which the principal investigator was affiliated. The provided data were fully coded for anonymity, and access to and utilization of the data were only available within the analysis centre at appointed dates in advance upon request. A research assistant was

allowed to take out the results obtained on these dates after receiving permission from the committee of data provision.

3.5 | Analyses

The study utilized SAS version 9.3 (SAS Institute Inc., Cary, NC, USA) to answer the research questions, as follows. Descriptive statistics (frequency and percentage) were calculated for age, BMI, and indicators of metabolic syndrome in the women with endometriosis. Changes in each indicator of metabolic syndrome from 2009 through 2016 were analysed using the Cochran–Mantel–Haenszel test. The chi-square test was used to examine differences in the distribution of indicators of metabolic syndrome by women's BMI, and changes in the indicators in each of the BMI groups from 2009 through 2016 were analysed by the Cochran–Armitage test.

4 | RESULTS

4.1 | Distributions of age and BMI of the women with endometriosis

A total of 281,810 cases that met the inclusion criteria were drawn from the database. The mean age of the women was 40.6 years (standard deviation, 6.58 years), and three-quarters of the sample belonged to the age range of 40–49 years (n = 195,444, 69.35%).

More than half of the sample (56.18%) had a normal BMI. Women who were underweight comprised 7.78% of the sample, while women who were overweight (18.40%) and obese (17.64%) including higher grades of obesity accounted for more than one-third of the total sample (Table 1).

4.2 | Distributions and trends in changes of the risk groups of metabolic syndrome in women with endometriosis from 2009 through 2016

During this period, the proportion of the risk groups of metabolic syndrome changed as follows: abnormal WC from 9.24% to 12.56%, elevated BP from 17.15% to 18.27%, elevated FBS from 16.63% to 20.31%, abnormally low HDL cholesterol from 19.85% to 25.51% and elevated TG from 12.08% to 13.24%.

The yearly changes of the indicators were statistically significant for abnormal WC (Z = 19.16, p for trend<0.001) and elevated FBS (Z = 15.23, p for trend <0.001); moreover, abnormally low HDL cholesterol (Z = 20.09, p for trend <0.001) showed a significant decreasing trend (Figure 2).

4.3 | Differences in risk groups of the indicators of metabolic syndrome by BMI

The most common indicator of metabolic syndrome among women with endometriosis was abnormally low HDL cholesterol levels (21.55%), followed in order by elevated FBS (17.55%), elevated BP (16.46%), elevated TG levels (11.93%) and an abnormal WC (8.32%). The risk groups of the indicators all showed statistically significant differences by BMI groups, as follows: waist circumference (χ^2 = 67,175.24, p < .001), BP (χ^2=12,849.46, p<.001), FBS (χ^2 = 8,241.88, p < .001), HDL cholesterol (χ^2 = 10,692.28, p < .001) and TG levels (χ^2 = 14,219.77, p < .001). The proportions of women with abnormal findings for all indicators significantly increased as women's BMI increased from underweight to obesity (U = 8,142.27–54192.11, p for trend <.001) (Table 2).

5 | DISCUSSION

The motivation for this study lies in the growing interest in endometriosis as a women's health issue given the increasingly prevalent health concerns of metabolic syndrome and obesity. In a national data set encompassing 8 years from 2009 through 2016, data were analysed from 281,810 women with endometriosis. Thus, a significant aspect of this study is its use of government big data to ensure representativeness of the whole population with minimal sampling bias. Moreover, as endometriosis threatens women's quality of life through menstrual cycle-related pain, inflammation, and even infertility throughout their reproductive lives, the findings of metabolic factors for endometriosis provide useful insights into understanding

TABLE 1 Distribution of age, body mass index and indicators of metabolic syndrome in women with endometriosis (N = 281,810)

Characteristics	Classification	n (%)
Age (year) M = 40.6, SD = 6.58	15–19	104 (0.04)
	20–29	25,710 (9.12)
	30–39	60,552 (21.49)
	40–49	195,444 (69.35)
Body mass index (BMI) (kg/m^2)	Underweight (<18.5)	21,917 (7.78)
	Normal weight (18.5 ≤ BMI < 23.0)	158,330 (56.18)
	Overweight (23.0 ≤ BMI < 25.0)	51,866 (18.40)
	Obesity (25.0 ≤ BMI < 30.0)	49,162 (17.45)
	Severe obesity (≥30)	535 (0.19)

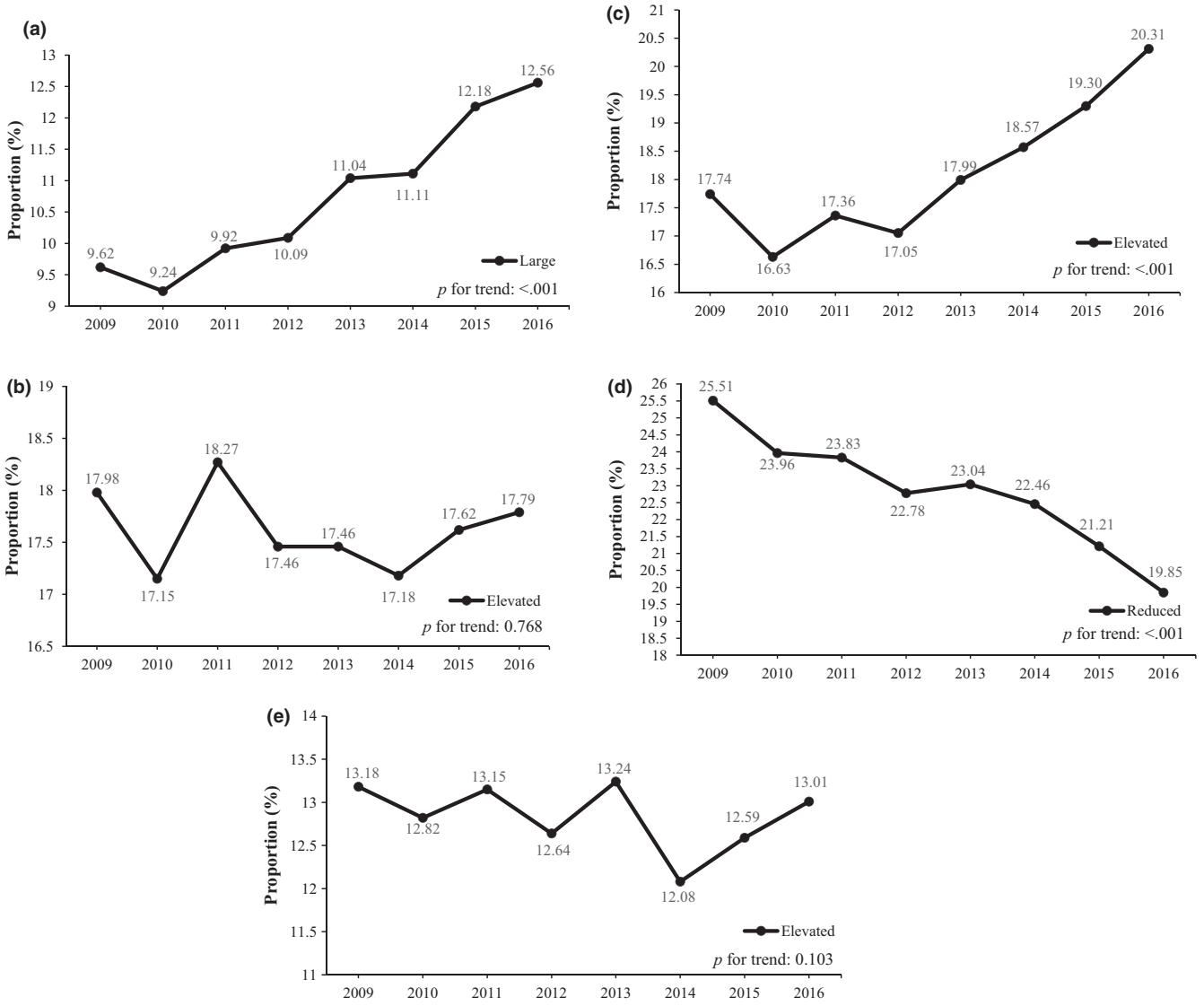

FIGURE 2 Changes in Abnormal Indicators of Metabolic Syndrome from 2009 to 2016 (*N*=281,810). (a) Trends in waist circumference over time. (b) Trends in blood pressure over time. (c) Trends in fasting blood sugar over time. (d) Trends in high-density lipoprotein cholesterol over time. (e) Trends in triglyceride levels over time

complex women's health conditions for integrated education and practice in the healthcare field.

It was noted that women in their 30s and 40s accounted for third-quarters of the incidence of endometriosis (KOICD, 2019), though in this study with women aged 15 through 49, 21.5% of women in 30s and 69.4% of women in 40s were composed of the sample. It showed clearly that endometriosis is one critical and prevalent reproductive health problem in women. In addition, previous studies have consistently shown inverse associations between BMI and the risk of endometriosis (Liu & Zhang, 2017; Parasar et al., 2017; Shahbazi & Shahrabi-Farahani, 2016), although the precise aetiology and mechanism have yet to be clarified. Likewise, this study confirmed the same general picture, finding that 7.78% of women with endometriosis were underweight, compared with 5.75% of the general population of women in Korea (KOSIS, 2021). A possible explanation for the relationship may be that decreases in the number of adipocyte stem cells and changes in gene expression related to oestrogen conversion and production may contribute to a low BMI in women with endometriosis (Cardoso et al., 2017). Importantly, lean body size was associated with endometriosis across the life course, with relationships found for body size at 8 years, at menarche, and at ages 20–25 years (Farland et al., 2017) and at age 18 (Shah et al., 2013). Since women frequently have the goal of weight loss and maintenance of a lean body image, they should avoid excessive diet and lifestyle changes to avoid contributing to the development of endometriosis. Thus, it seems to be critical to be aware of the relationship of BMI with the risk of endometriosis starting at younger ages to promote future reproductive health.

Despite efforts made by the Korean government to reduce the prevalence of metabolic syndrome through health education and direct health services, there have been no meaningful outcomes; instead, the prevalence of metabolic syndrome increased from

TABLE 2 Differences and changes in indicators of metabolic syndrome by BMI ($N = 281,810$)

Indicators	Classification	*n* (%)*	Underweight (*n* = 21,917)	Normal weight (*n* = 158,330)	Overweight (*n* = 51,866)	Obesity (*n* = 49,697)	$X^2(p)$	*p* for trend
WC	Desirable	258,211 (91.68)	21,890 (99.93)	156,929 (99.15)	48,144 (92.86)	31,258 (62.99)	67,175.24	54,192.11
	Large	23,425 (8.32)	15 (0.07)	1,346 (0.85)	3,702 (7.14)	18,362 (37.01)	<0.001	<0.001
BP	Normal	235,406 (83.54)	20,485 (93.47)	139,645 (88.20)	41,248 (79.53)	34,028 (68.51)	12,849.46	12,577.11
	Elevated	46,369 (16.46)	1,430 (6.53)	18,679 (11.80)	10,616 (20.47)	15,644 (31.49)	<0.001	<0.001
FBS	Desirable	232,293 (82.45)	19,969 (91.18)	136,545 (86.26)	40,799 (78.67)	34,980 (70.40)	8,241.88	8,142.27
	Elevated	49,453 (17.55)	1,932 (8.82)	21,749 (13.74)	11,062 (21.33)	14,710 (29.60)	<0.001	<0.001
HDL	Desirable	221,026 (78.45)	19,765 (90.23)	131,508 (83.08)	37,859 (73.00)	31,894 (64.18)	10,692.28	10,634.90
	Reduced	60,732 (21.55)	2,141 (9.77)	26,791 (16.92)	14,002 (27.00)	17,798 (35.82)	<0.001	<0.001
TG	Desirable	248,143 (88.07)	21,176 (96.65)	146,414 (92.49)	43,637 (84.14)	36,916 (74.29)	14,219.77	13,843.11
	Elevated	33,622 (11.93)	733 (3.35)	11,888 (7.51)	8,226 (15.86)	12,775 (25.71)	<0.001	<0.001

Note: Missing cases excluded.

Abbreviations: BMI, body mass index; WC, Waist circumference; BP, Blood pressure; FBS, Fasting blood sugar, HDL, High-density lipoprotein cholesterol; TG, Triglyceride.

21.1% in 2007 to 22.4% in 2015 (Huh et al., 2018). In addition to the growing prevalence of endometriosis, the findings of this study have important implications about the relationship of endometriosis with the indicators of metabolic syndrome, which is a major chronic health condition in women with endometriosis. Meanwhile, among the indicators of metabolic syndrome, increasing trends in WC (9.6%–12.6%), FBS (16.6%–20.3%) and abnormally low HDL cholesterol (19.9%–25.5%) were apparent over the years from 2009 to 2016 in this study. Although the proportions of these indicators were low compared to women with metabolic syndrome, in whom elevated WC was found to be present in 23.6%, elevated FBS in 28.8%, and reduced HDL cholesterol in 30.3% (Korean Society of Cardiometabolic Syndrome Task Force Team, 2018), nurses should nonetheless take active steps to address these indicators because they are changeable through nursing interventions and education, including diet, exercise, and lifestyle modifications.

Abnormal findings for these indicators of metabolic syndrome mostly showed higher proportions in women with overweight and obesity; above all, it was noteworthy that 37% of women in the abnormal WC group were obese. BMI and WC are generally used as anthropometric measures, although WC is considered to be a better indicator of the amount and distribution of adipose and muscle tissue than BMI (Backonja et al., 2017). Moreover, women with a waist-to-hip ratio lower than 0.60 had almost a threefold higher risk of endometriosis than women with a waist-to-hip ratio of 0.70–0.79 (Shah et al., 2013). As peripheral fat accumulation has been associated with a higher ratio of oestrogens to androgens (de Ridder et al., 1990), it is suggested that future nursing research should incorporate suitable markers of women's body composition and adiposity to achieve a better understanding of metabolic syndrome and endometriosis.

Regarding the mechanisms underlying cardiovascular disease (Petrie et al., 2018), obesity and dyslipidaemia are known risk factors of hypertension and diabetes, which frequently coexist, and in turn, these conditions exacerbate atherosclerosis and vascular inflammation (Parazzini et al., 2017). In this study, elevated BP, FBS, TG and abnormally low HDL cholesterol were more commonly found in the obesity group. Reflecting their vulnerability to atherosclerotic changes, women with endometriosis had increased arterial stiffness (Kilic et al., 2021) and higher relative risks of developing hypertension and hypercholesterolaemia than women without endometriosis (Mu et al., 2017; Tan et al., 2019). Women with prior endometriosis were found to experience gestational hypertension–preeclampsia 2.27 times more frequently than women without endometriosis (Pan et al. 2017). Considering these mutual and complex influences, nurses should have a holistic perspective on women's body composition and risk for metabolic syndrome, especially for women with endometriosis.

Generally, high BMI and high WC are known to be associated with diabetes (Han et al., 2019), although 64% of people with normal BMI were found to have a high per cent body fat and a 1.55 times higher

risk of abnormal blood glucose (Jo & Mainous 2018). In addition to the fact that body fat was strongly associated with type 2 diabetes (Han et al., 2019), Melo et al. (2010) showed that women with endometriosis demonstrated an unfavourable lipid profile including TC, HDL cholesterol, LDL cholesterol and TG than healthy women, while no significant differences were found in BMI, WC and BP levels. Similarly, in this study, elevated FBS (17.55%) and abnormally low HDL cholesterol (21.55%) occurred in a considerable proportion of women with a normal or lower weight. Nevertheless, little research has investigated the underlying and comorbid risks of endometriosis with metabolic diseases, particularly in women with high BMI. Future nursing research therefore needs to incorporate a wide variety of health indicators to expand our understanding of women's gynaecological disorders and to provide high-quality care for their health.

6 | LIMITATIONS

This study did not incorporate a comparison; therefore, the findings might need further replication in research including a comparison group of same-aged women without endometriosis to clearly explain the differences in the indicators of metabolic syndrome according to BMI between these groups.

7 | CONCLUSION

Endometriosis is a critical gynaecological disorder that negatively influences women's reproductive health outcomes and quality of life. Considering its development and progression to a chronic inflammatory disease, it is necessary to incorporate information on possible comorbid metabolic characteristics and body composition, including adiposity, to understand women's health risks. Thus, this study makes a meaningful contribution by demonstrating the relationships among BMI and five indicators of metabolic syndrome in women with endometriosis for the first time, through an analysis of 8 years of Korean national data. Overall, increasing trends of abnormal WC, FBS and HDL cholesterol levels were apparent over the years, whereas this was not the case for BP and TG. Moreover, significant relationships were noted between the proportions of indicators of metabolic syndrome and women's BMI status.

Both future research and clinical practice should utilize a greater variety of health measures and lifestyle factors to understand the health status of women with endometriosis in broader ways and to apply guidelines for the early prevention of comorbid health conditions. A future study with an endometriosis case–control design would be useful to identify risk factors of metabolic syndrome; based on those risk factors, a cohort study could then be implemented to examine the prevalence of endometriosis in women with metabolic syndrome.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to report.

AUTHOR CONTRIBUTIONS

Conceptualization or/and methodology were done by Park SM and Chung CW. Data curation, funding acquisition and analysis were performed by Park SM. Writing original draft or/and Review and editing were done by Park SM and Chung CW.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study were from the National Health Insurance Service-National Health Screening Cohort of the Republic of Korea. So the data are not publicly available due to privacy and ethical restrictions.

ETHICAL APPROVAL

This study was approved by the institutional review board (CR318312) of the Wonju Severance Christian Hospital.

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