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Association Between Age of Women when Diagnosed with Endometriosis and Infertility

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Walden University

College of Health Sciences

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Whitney L. Kennedy

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Walden University

2018

Abstract

Association Between Age of Women when Diagnosed with

Endometriosis and Infertility

by

Whitney L. Kennedy

BS, East Carolina University, 2012

MPH, Kaplan University, 2014

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Public Health

Walden University

May 2018

Abstract

Because endometriosis is considered to be the primary cause of infertility in women and the diagnosis is known to be delayed by many years, it is important to understand the association between endometriosis and infertility. The purpose of this cross-sectional, secondary data analysis study was to determine whether there was an association between the age of women when diagnosed with endometriosis and infertility. Using the general model of total patient delay (i.e., the Andersen model) as a theoretical foundation, data for this study was collected by assessing patient medical records of women with endometriosis at multiple OB-GYN clinics in Eastern North Carolina. Multiple logistic regression was conducted to determine potential association between variables. The results presented that diagnosis at an older age and presence of uterine fibroids are significant risk factors for infertility among women with endometriosis. From the results, it can be concluded that infertility may be preventable in women diagnosed with endometriosis and uterine fibroids in younger age. This study presents positive social change by preventing infertility amongst women who suffer from both endometriosis and uterine fibroids; potentially creating preventative programs aimed at better educating women on the risks of endometriosis and uterine fibroids (especially when presented together).

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Dedication

This study is dedicated to all women who have suffered from endometriosis—whether or not they have experienced unfortunate despair such as infertility. Furthermore, this study is dedicated to all physicians who are dedicated, or have been dedicated, to women’s health, providing women who have been diagnosed with endometriosis a chance to create life. Last, this study is dedicated to all researchers whose plan is to eradicate endometriosis.

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I also would like to thank my family and friends for encouraging me to stay focused during the duration of my dissertation, as well as throughout my entire doctoral studies. I thank them for always being understanding when working on my study required priority.

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Chapter 1: Introduction to the Study

Introduction

A diagnosis of endometriosis has been found to be delayed anywhere from 7-10 years and is often not recognized by physicians in practice, leading to misdiagnosis and/or suboptimal care (Johnston, Reid, & Hunter, 2015). Investigation concerning causes of female infertility is receiving less attention; although, there are optimal approaches to managing infertility that require a method associated with routine and timely measures (Bell, 2014). Earlier diagnosis of the disease (e.g., diagnosis at an earlier age) could serve as a preventative strategy towards infertility. If a statistically significant association between age of women when diagnosed with endometriosis and infertility is determined, beliefs that suppressive medical treatment does not benefit fertility (American Society for Reproductive Medicine, 2012) could be proven false, which could lead to fewer incidences of endometriosis-related infertility. Furthermore, determining a statistically significant association also could provide for more effective patient/doctor visits for women who suffer from common symptoms of endometriosis.

Although suppressive medical treatment of endometriosis does not benefit fertility, the age of a woman when diagnosed with endometriosis has not been taken into consideration (American Society for Reproductive Medicine, 2012). Determining diagnosis at an earlier age can serve as a preventative strategy against infertility. In this study, I contributed to the literature on women's health by determining whether age of women, when diagnosed with endometriosis, is associated with higher and lower incidences of infertility.

The findings of the study might lead to social change by adding new evidence to a topic within women's health that has been considered a controversial topic (Kovacs, 2015). The findings of the study are expected to provide information on existing information and theories about the disease that are false/misleading. The study is may provide information that may help individuals recognize and understand normal menstrual cycles versus abnormal menstrual cycles, as well as normal symptoms associated with menstrual cycles versus abnormal pain that can be linked to endometriosis. The study may also provide physicians with more information about prompt endometriosis diagnoses. Furthermore, the study may provide support for women who suffer from the disease. Women should be made aware that effective treatment is available if they seek it. Last, the study is expected to promote social change by further highlighting the effects of endometriosis that affect women and their families because the disease currently is not recognized as a medical disability (Jones, 2016).

Endometriosis may go undiagnosed for anywhere from 7-10 years, and endometriosis is associated with infertility (Johnston, Reid, & Hunter, 2015). Because there currently are no existing studies on the potential association between the age of women when diagnosed with the disease and infertility, the results of this study might aid in the development of better precautionary methods for avoiding infertility while living with endometriosis.

Background

Suppressive medical treatment of endometriosis does not increase fertility; yet, the age of women when diagnosed with the disease never has been taken into

consideration when assessing infertility rates amongst women diagnosed with the disease (American Society for Reproductive Medicine, 2012; Radhika, Chawla, Nanda, Yadav, & Radhakrishnan, 2016). Radhika et al. (2016) found that 73% of patients had moderate to severe endometriosis (age groups: <20, 21-30, >30 – with average age of participants being 29.6 years) with 31.46% of the participants classified as being infertile. Furthermore, correlations between stages and infertility per age have never been examined (Radhika et al., 2016). This study was needed in order to increase the understanding the association between endometriosis and infertility, especially in regards to how the age in which a woman is diagnosed with the disease might affect her ability to conceive.

Scholars have examined the process associated with diagnosing endometriosis, the sites inside a woman's body where endometriosis can occur, the impact endometriosis has on the lives of women and their families, the treatment for endometriosis, the potential link between endometriosis and infertility, and the potential impact uterine fibroids may have on women diagnosed with endometriosis. Although pregnancy rates for patients with endometriosis range from 24%-54%, estimated rates may be overestimated (Burghaus et al., 2016). Overlapping symptoms commonly associated with endometriosis should alert physicians to seek measures that aid in the formal diagnosis of the disease (Fauconnier et al., 2013). Furthermore, endometriosis poses detrimental impacts on women's lives due to negative effects on marital/sexual relationships, social life, and physical and psychological wellbeing (Moradi, Parker, Sneddon, Lopez, & Ellwood, 2014). Patients who suffer from endometriosis might also suffer from uterine

fibroids, potentially increasing their chances of infertility (Uimari, Jarvela, & Ryyanen, 2011).

The purpose of this study was to determine whether there was an association between the age of a woman upon diagnosis of the disease and infertility. Earlier diagnosis of the disease (e.g. diagnosis at an earlier age) could serve as a preventative strategy towards infertility. If a statistically significant association between age of women when diagnosed with endometriosis and infertility is determined, there could be fewer incidences of endometriosis-related infertility. Furthermore, determining a statistically significant association also could provide for more effective patient/doctor visits for women who suffer from common symptoms of endometriosis.

Problem Statement

Endometriosis is the primary cause of infertility in the United States, having a prevalence of 0.5%-5% in fertile women and 25%-40% in infertile women (Juneau Biosciences, 2016). The management of endometriosis-associated infertility, however, is unknown (Dunselman et al., 2014). There is a connection between infertility and endometriosis; however, the association between the two still remains uncertain (American Society for Reproductive Medicine, 2012). The longer that endometriosis goes undiagnosed, the more damage it can do; yet, there are few early diagnoses of the disease because many physicians are unaware of the common symptoms associated with the disease (Levett, 2016). Some patients have claimed that they visit their doctor with symptoms of lower abdominal and pelvic pain (common symptoms of endometriosis)

only to receive no support from physicians aside from receiving a prescription for opioids (i.e., painkillers; Johnston et al., 2015).

Diagnosis of endometriosis among women has been found to be delayed anywhere from 7-10 years and is poorly recognized by physicians in practice, leading to misdiagnosis and/or suboptimal care (Johnston et al., 2015). Investigation concerning causes of female infertility is receiving less attention; although, there are optimal approaches to managing infertility that require a method associated with routine and timely measures (Bell, 2014). Earlier diagnosis of the disease (e.g., diagnosis at an earlier age) could serve as a preventative strategy towards infertility. If a statistically significant association between age of women when diagnosed with endometriosis and infertility is determined, beliefs that suppressive medical treatment does not benefit fertility (American Society for Reproductive Medicine, 2012) could be proven false, which could lead to fewer incidences of endometriosis-related infertility. Furthermore, determining a statistically significant association also could provide for more effective patient/doctor visits for women who suffer from common symptoms of endometriosis.

Purpose of Study

The purpose of the study was to determine whether an association exists between the time in which a woman is diagnosed with endometriosis (i.e., age of woman when diagnosed) and infertility. To address this gap, I used a quantitative research method. I assessed a potential association between variables to address the lack of knowledge that exists in regards to the association between endometriosis and infertility and how the age in which a woman is diagnosed with the disease might affect her ability to conceive. The

independent variable for this study was age, which described the age in which a woman was formally diagnosed with endometriosis. The dependent variable for this study consisted of infertility, which described whether or not a woman was considered to be unable to conceive. The variables site/implantation and uterine fibroids also were used as potential confounders affecting the association between age upon diagnosis of endometriosis and infertility.

Research Questions and Hypotheses

RQ1: What is the association between infertility and age of women when diagnosed with endometriosis after controlling for history of uterine fibroids?

(H_01): There is no statistically significant association between infertility and age of women when diagnosed with endometriosis after controlling for history of uterine fibroids.

(H_11): There is a statistically significant association between infertility and age of women when diagnosed with endometriosis after controlling for history of uterine fibroids.

RQ2: What is the association between infertility and age of women when diagnosed with endometriosis after controlling for the specific sites of endometriosis?

(H_02): There is no statistically significant association between infertility and age of women when diagnosed with endometriosis after controlling for the specific sites of endometriosis.

(H_{12}): There is a statistically significant association between infertility and age of women when diagnosed with endometriosis after controlling for the specific sites of endometriosis.

Theoretical Foundation

The theoretical framework for this study consisted of the general model of total patient delay, also known as the Andersen model, which is used for a variety of disorders (Walter, Webster, Scott, & Emery, 2012). The Andersen model was developed by Andersen in 1968 (Andersen & Newman, 1973). Reducing diagnostic delays may result in improved prognosis for most disorders (Walter et al., 2012). The Andersen model is used to explain aspects regarding delay stages (e.g., appraisal, illness, behavioral, scheduling, treatment) and was used in this study as a means to test whether diagnosis of endometriosis might pose a higher incidence for risk (i.e., infertility) based on age. The model also aided in explaining why certain time intervals exist between onset of symptoms of endometriosis and formal diagnosis. According to the Anderson model, diagnostic delay results from conceptual beliefs about a person's symptoms; behavioral factors, such as strategies for self-appraisal; and techniques for coping with illness and emotional reaction (Walter et al., 2012). Such topics will be explained in further detail in Chapter 2.

Nature of Study

I used the quantitative approach in this study. Quantitative research was appropriate in determining whether there was a statistically significant association between age of women when diagnosed with endometriosis and infertility, as descriptive

quantitative researchers establish associations between variables (Creswell, 2013). Furthermore, because uterine fibroids and endometriosis may be associated with each other, the history of uterine fibroids may have an association with the age of women when diagnosed with endometriosis and infertility (Nezhat et al., 2016; Uimari et al., 2011). I used a cross-sectional design with the use of secondary data analysis of existing medical records. In regard to statistical methods, I used multiple logistic regression and crosstabulation to assess potential association between variables. Age acted as the independent variable, and infertility acted as the dependent variable.

Definitions

Age: The number of years from birth of the respondent to the date when she was formally diagnosed with endometriosis.

Endometriosis: The presence of endometrial glands or stroma in sites other than the uterine cavity (Jacobson et al., 2016).

Formal diagnosis: Endometriosis confirmed by laparoscopic procedure.

Infertility: Failure to achieve a successful pregnancy after 12 months or more of regular, unprotected sexual intercourse (Mascarenhas, Cheung, Mathers, & Stevens, 2012).

History of uterine fibroids: Having documentation by a physician concerning the presence of uterine fibroids on the uterus.

Laparoscopic procedure: Minimal invasive surgery where a slender viewing instrument (laparoscope) is inserted through a small incision near the naval for diagnosis and/or removing endometrial tissue through another small incision (Mayo Clinic, 2016).

Site and location of endometriosis: The part of the female anatomy where the endometriosis is implanted; it is important for explaining its potential side effects (Barcellos, Lasmar, & Lasmar, 2016).

Stage I or minimal endometriosis: Few isolated endometrial implants outside the uterus; there is minimal number of mild adhesions in one area, if any (Mashayekhi et al., 2017).

Stage II or mild endometriosis: Few isolated, slightly deeper endometrial implants outside the uterus; there is minimal number of mild adhesions in one area (Mashayekhi et al., 2017)

Assumptions

There were several assumptions that were assumed in this study. First, it was assumed that the diagnostic laparoscopic procedures performed on each of the women whose charts were assessed for this study were well performed and preceded by appropriate preoperative assessment. For example, it was assumed that each of the women's diagnostic laparoscopic procedures were followed by biopsies in order to obtain histological confirmation of the diagnosis. Second, it was assumed that all women whose charts were assessed for this study underwent laparoscopic procedure strictly for the reason to either confirm or deny the presence of endometriosis. Third, it was assumed that all women whose charts were assessed for this study did not seek any type of fertility treatment (e.g., fertility drugs, in vitro fertilization (IVF), intrauterine insemination (IUI), etc.) aside from the removal of endometriosis via laparoscopic procedure. The fourth and final assumption was that all women whose charts were assessed for this study wished to

conceive. Such assumptions were necessary in the context of the study given that poorly performed laparoscopic procedures not followed by biopsies can be less informative and of limited value (Dunselman et al., 2014). Furthermore, if women chose to undergo laparoscopic procedure for other reasons, such as having a history of pelvic infection, conclusions to be made from study results given the variables could be flawed. Last, if any of the women whose charts were assessed underwent any type of fertility treatment aside from the removal of endometriosis via laparoscopic procedure, bias could be introduced to the study results.

Scope and Delimitations

The delimitations of this study were age and being a patient at any OB-GYN/fertility clinic located in Eastern North Carolina. Given the geographical scope of the study, it is possible that the data were not representative of women living in other parts of North Carolina, and it also was possible that the data were not representative of other age groups outside from the ones assessed in this study (i.e., age 18-35). This study included data from medical charts of women of all races/ethnicities who were considered to be of reproductive age. Given that not just one particular race/ethnicity was considered, the study results do not favor one race/ethnicity over another. In order to meet the inclusion criteria, patients had to be in the age range of 18-35 years, as such age group is considered to be within good standards in regard to reproduction, with women's fertility decreasing substantially by their late 30s (Lezzoni et al., 2014). Furthermore, only patients diagnosed with Stage I (or minimal) or Stage II (or mild) were endometriosis used for this study. I did not include data on women who were over the age

of 35, as I wanted to avoid the factor of age as a possibility for infertility, alone. Also, I did not include data on women who possessed multiple locations of deep adhesions or implants (i.e., implants/adhesions involving multiple organs), as I wanted to accurately compare how site/location of endometrioma might affect the association between infertility and the age in which a woman is diagnosed with endometriosis separately.

The scope of this study was aided by the Andersen model, as this model has been used for a variety of disorders to explain aspects regarding delay stages of disease (e.g., appraisal, illness, behavioral, scheduling, and treatment; Walter et al., 2012). I used the Andersen model to determine whether diagnosis of endometriosis potentially poses a higher incidence for risk (i.e., infertility) based on age. The model also aided in furthering an explanation of why certain time intervals exist between onset of symptoms of endometriosis and formal diagnosis. The feminist standpoint theory (FST) also was considered for this study, but was found to be inappropriate given that many of its claims are argued by researchers and also given that its fundamental structure focuses on epistemologies of ignorance among male physicians towards female patients (Reid-Hresko & Goldman, 2016), which would not guide the research questions for this study.

I decided to study existing medical charts of women who were considered to be of good reproductive age (e.g. age 18-35 years) because women of such age groups are expected to be able to successfully conceive, especially without any given reproductive disease (Reid-Hresko & Goldman, 2016). I decided not to exclude the assessment of patients' medical charts based on certain races/ethnicities because I did not wish to consider any potential racial disparities in regard to endometriosis given that similar rates

of the disease are observed among women of different races (Gerlinger, Faustmann, Hassall, & Seitz, 2012).

Limitations

This study contained several limitations. The first limitation was the I only used a secondary analysis of existing data. The data were not originally collected in order to address the particular research question or to test the particular research hypotheses, which is a limitation to a study (Cheng & Phillips, 2014). Another limitation included the conducting of a secondary analysis of existing data, as I was not involved in the data collection process; therefore, I was unaware of any nuances in the data collection process that might be important to the interpretation of the key variables (Cheng & Phillips, 2014). A third limitation related to race/ethnicity. I did not assess race or ethnicity among women whose medical charts were assessed. The association between the age in which a woman is diagnosed with endometriosis and infertility might differ when the factor of race is considered; even though endometriosis rates are considered to be similar among races (Gerlinger et al., 2012). A fourth limitation related to the marital status of women. I did not take into consideration the marital status of the women whose medical charts were assessed. Such sociodemographic variable could influence fertility status given that married couples are considered to be more likely to try to conceive than unmarried couples (Laplante & Fostik, 2015).

Significance

Although suppressive medical treatment for endometriosis does not improve fertility, the age of a woman when diagnosed with endometriosis has not been taken into

consideration (American Society for Reproductive Medicine, 2012) prior to this study. Diagnosis at an earlier age can serve as a preventative strategy against infertility. Therefore, the purpose of this study was to determine if there was a statistically significant association between the age of a woman when diagnosed with the disease and infertility. The relationship between the two is not understood (Dunselman et al., 2014). Because there are no studies on the potential association between the age of women when diagnosed with the disease and infertility, the outcomes from the study might aid in the development of better precautionary methods for avoiding infertility while living with endometriosis.

The findings of the study are expected to provide information on theories about the disease that perhaps are false/misleading, as well as serve as an asset for supplying readers with knowledge regarding the topic; which ultimately should better help individuals recognize and understand “normal” menstrual cycles versus abnormal menstrual cycles, as well as “normal” symptoms associated with menstrual cycles versus serious abnormal pain that can be linked to endometriosis. Again, the study also is expected to serve as evidence for why confirming endometriosis diagnoses carefully and more promptly should be of higher concern to physicians. Furthermore, in regard to social change, the study hopefully will be able to provide a sense of support for women who suffer from the disease, inspiring them not to overlook health emergencies out of fear or frustration that there is no hope and/or relief exists. Women should be made aware that effective treatment is available if they seek it. All in all, the study is expected to promote social change by further supporting the devastating effects of endometriosis

that burden women and their families since the disease currently is not recognized as a medical disability (Jones, 2016).

Summary

Although endometriosis has been well-documented in medical texts for more than 4,000 years and was formally discovered microscopically by von Rokitansky in 1860 (Nezhat, Nezhat, & Nezhat, 2012), the disease still remains the subject of debate, especially over the last decade (Brosens & Benagiano, 2011). Furthermore, although laparoscopic procedure was introduced in the early 1960s, which can be used to distinguish between three different clinical presentations of endometriosis (i.e., peritoneal, deep adenomyotic, and cystic ovarian; Brosens & Benagiano, 2011), diagnosis of endometriosis is delayed anywhere from 7-10 years and is poorly recognized by physicians in practice, often leading to misdiagnosis and/or suboptimal care (Johnston et al., 2015).

In this chapter, the background of endometriosis was explained, along with its association to infertility. Introduction to the research literature regarding the topic was provided. The purpose of the study was established. In addition, the research questions and hypotheses, the nature of the study, important terms/definitions, assumptions, scope and delimitations, limitations, and significance of the study were discussed.

In Chapter 2, a detailed review of the literature is provided. In Chapter 2, I summarize a range of topics related to endometriosis: endometriosis as a disease, the impact of endometriosis on women's lives, the different sites/locations endometriosis can occur, treatment for endometriosis, the association between endometriosis and infertility,

and the presence of uterine fibroids among patients diagnosed with endometriosis. The theoretical framework is further discussed as well, along with implications for the use of a secondary data analysis in the form of patients' medical records.

Chapter 2: Literature Review

Introduction

Considered to be the primary cause of infertility in the United States, with a prevalence of 0.5%-5% in fertile women and 25%-40% in infertile women, endometriosis diagnosis is delayed among women anywhere from 7-10 years and is poorly recognized by physicians in practice (Juneau Biosciences, 2016; Johnston et al., 2015).

Endometriosis often is misdiagnosed and many women receive suboptimal care (Johnston et al., 2015). The optimal choice of management for endometriosis-associated infertility is unknown (Dunselman et al., 2014). Although infertility and endometriosis are connected, the association between endometriosis and infertility still remains uncertain (American Society for Reproductive Medicine, 2012). The longer endometriosis goes undiagnosed, the more damaging it can be to women's bodies; physicians often times misdiagnose common symptoms linked to endometriosis (Levett, 2016). For example, many patients claim to have a long history of doctor visits due to lower abdominal and pelvic pain only to receive no support from physicians aside from receiving a prescription for painkillers (Johnston et al., 2015).

Because the causes of female infertility is receiving less attention in the literature (Bell, 2014), the purpose of this study was to determine whether there was an association between the time in which a woman is diagnosed with endometriosis (i.e., age of woman when diagnosed) and infertility. The results of this study can may lead to improved understanding of the association between endometriosis and infertility, specifically in

regards to how the age in which a woman is diagnosed with the disease might affect her ability to conceive.

Because endometriosis is an estrogen-dependent condition characterized by endometrial glands and stroma located outside the uterine cavity (Bruggmann et al., 2016), sites where endometriosis can implant will be discussed. Furthermore, I will discuss how endometriosis can affect not only the woman suffering from the disease, but also those around her, such as a partner or spouse (Moradi et al., 2014). Although there is no cure for endometriosis (Endometriosis Association, 2016), treatment options available for women who suffer from the disease will be discussed. I will examine how endometriosis is considered to be the primary cause of infertility in the United States, and I will discuss the association between endometriosis and infertility. Last, I will explore how presence of uterine fibroids in women with endometriosis.

Literature Search Strategy

The literature was searched using the following databases: MEDLINE, CINAHL, EBSCO, PubMed, and Science Direct. Keywords used to search the literature included *endometriosis*, *endometriosis AND quality of life*, *endometriosis AND work productivity*, *endometriosis location*, *implantation of endometriosis*, *laparoscopy*, *laparoscopic procedure for endometriosis*, *endometriosis AND infertility*, *infertility*, *endometriosis AND reproductive function*, *reproductive function*, *endometriosis AND uterine fibroids*, *uterine fibroids*, *the general model of total patient delay*, and *the Andersen model*.

Theoretical Foundation

Various theoretical foundations have been used by researchers to study the delay in diagnosis of endometriosis. Chilet-Rosell (2014) used the FST to study why recognition of health problems specific to women (e.g., endometriosis and endometrial cancer) have been slow over the years. According to the FST, women's knowledge often is excluded from the construction of ideology, and traditional science ignores and marginalizes women's way of thinking (Borland, 2016). Chilet-Rosell suggested that there is gender bias in knowledge dissemination, often leading to the hindrance of the discovery of diseases that impact women. Similarly, various theoretical foundations have been used by researchers to study the link between endometriosis and infertility. Galhardo, Moura-Ramos, Cunha, and Pinto-Gouveia (2015) used the social cognitive theory and suggested that women who suffer from endometriosis and who are also considered to be infertile present a perception of failure and defeat and also feel that there is no solution to their infertility; women who do not suffer from endometriosis but also are considered to be infertile do not feel the same perception of failure and defeat, nor the feeling that there is no solution to their infertility.

Reducing diagnostic delays may result in improved prognosis for most disorders (Walter et al., 2012). The general model of total patient delay, also known as the Andersen model, can be used to explain delay in the stages of disease (e.g., appraisal, illness, behavioral, scheduling, and treatment; Walter et al., 2012). The initial Andersen model was used to predict and explain the use of health services, but was later revised to include systematic concepts of health care (e.g., current policy, resources, and

organization; Andersen & Newman, 1973). The second-generation model, however, extended into outcomes of interest beyond use to consumer satisfaction (Andersen & Newman, 1973). Eventually, the model began to include personal health practices as an antecedent to outcomes, which involved the acknowledgement of health services and satisfaction of health services among patients (Andersen & Newman, 1973). The latest iteration of the Andersen model turns to individuals as the unit of analysis, going beyond health care use and adopting health outcomes as the endpoint of interest (Andersen & Newman, 1973). Different from similar theories, the Anderson model includes a feedback loop to illustrate that health outcomes may affect aspects of health beliefs and need (Andersen & Newman, 1973).

The Andersen model was used in this study as a means to support whether diagnosis of endometriosis might pose a higher incidence for risk (i.e., infertility) based on age. The model also aided in explaining of why certain time intervals exist between onset of symptoms of endometriosis and formal diagnosis given that the model. According to the Anderson model, diagnostic delay results from conceptual beliefs about a person's symptoms; behavioral factors, such as strategies for self-appraisal; and techniques for coping with illness and emotional reaction (Walter et al., 2012). Evans, Ziebland, and McPherson (2007) used the Andersen model to account for diagnostic delays in a sample of British women with ovarian cancer. Evans et al. conducted semistructured interviews with 43 women (ages 33-80 years; mean age: 54 years), determining that most of the women (38 of 43 participants) reported prediagnostic symptoms and diagnostic delays. The recording of patient delays conformed to

Andersen's first four types of delays: appraisal, illness, behavioral, and scheduling. Furthermore, treatment delays, as drawn from Anderson's model, included noninvestigation of symptoms, treatment for noncancer causes, lack of follow-up, referral days, and system delays (Evans et al., 2007). By using the Andersen model as an analytic framework for the study, Evans et al. concluded why some British women experience delays in obtaining ovarian cancer diagnosis. Furthermore, Evans et al. used the analytical framework to explain how diagnostic delays for ovarian cancer could be minimized.

In a correlational, quantitative study, Ozturk, Fler, Hoekstra, Josetta, & Hoekstra-Weebers (2015) used Andersen's model of total patient delay to explain how delay in diagnosis of testicular cancer (TC) could pose higher incidence for risk for decreased survival. Ozturk et al. used a questionnaire to gain insight from 60 men (ages 17-45 years; median age: 26 years) who were diagnosed with TC at a university medical hospital in the Netherlands. Using the Andersen model, Ozturk et al. concluded that the median patient delay of 30 days (range 1-365 days) was due mostly to lower educated men and men embarrassed about their scrotal change ($r=-.25$, $r=.79$, respectively). Furthermore, Ozturk et al. used the model to support the conclusion that age, marital status, TC awareness, warning signals, and perceived limitations were not associated with patient delay. Ozturk et al. used the model to conclude that the most important risk variable in general practitioners was misdiagnosis and that TC awareness programs could decrease misdiagnoses and delays in diagnoses in order to improve disease survival.

Literature Review Related to Key Variables and/or Concepts

Endometriosis

Endometriosis is the presence of endometrial-like tissue outside the uterus, and it is a chronic disease associated with pelvic pain and subfertility (Nnoaham et al., 2011). Endometriosis is most commonly known to affect the ovaries, fallopian tubes, and the tissue lining the pelvis; although in rare cases, endometrial tissue has been found to spread beyond the pelvic organs (Mayo Clinic, 2016). In the case that endometriosis occurs, endometrial tissue that is displaced continues to act as it normally would by thickening and breaking down and bleeding with each menstrual cycle (Mayo Clinic, 2016). However, because the displaced tissue is prohibited from exiting the body, it becomes trapped and surrounds tissue, causing the tissue to become irritated, which causes the development of scar tissue and adhesions, further leading to the fusion of certain organs (Mayo Clinic, 2016).

Laparoscopy is a procedure used to diagnose endometriosis by inserting a lighted viewing instrument (i.e., laparoscope) through a small incision; this is the most common technique for removing mild to moderate endometriosis (WebMD, 2016). Laparoscopic procedure works by viewing the internal organs to look for signs of endometriosis and by removing visible endometriosis implants and scar tissue that causes pain or leads to infertility (WebMD, 2016). Because a definitive diagnosis is established only at laparoscopy, prevalence rates of endometriosis in the general population remains obscure (Nnoaham et al., 2011). Based on community prevalence of symptoms, however, it is estimated that endometriosis affects 10% of all women and 30%-50% of symptomatic

premenopausal women (i.e., ~176 million women affected worldwide; Nnoaham et al., 2011). Furthermore, the prevalence of endometriosis among fertile women is 0.5%-5%, and the prevalence of endometriosis among infertile women is 25%-40% (Juneau Biosciences, 2016).

Endometriosis Implantation/Location

Because endometriosis is an estrogen-dependent condition characterized by endometrial glands and stroma outside the uterine cavity, implantations are found in the peritoneum, the ovaries, and the rectovaginal septum, which constitute three different disease entities (Burggmanet al., 2016). Via laparoscopic procedure, disease location and phenotype (i.e., superficial, deep infiltrating, endometriomata) can be determined (Menakaya, Lu, Infante, Lam, & Condous, 2014).

Menakaya et al. (2014) examined 104 women living with endometriosis. Menakaya et al. found that the most common phenotype of endometriosis among the women was superficial endometriosis, with sites of endometriosis located in the pelvic area, on and below the ovaries, and deep in the pelvis area behind the uterus. The most common diagnoses made among the sample of women via diagnostic laparoscopy for pelvic pain consisted of pelvic endometriosis and adhesions (Menakaya et al., 2014). The list of endometriosis implantations/locations among the women included the uterus, ovaries, fallopian tubes, pouch of Douglas (POD), uterovesical fold, uterosacral ligaments, rectovaginal space, left and right pelvic side walls (i.e., from pelvic brim to ureteric tunnel), and peritoneal surfaces throughout the pelvis and upper abdomen (Menakaya et al., 2014). Given all of the examined implantations/locations of

endometriosis among the women, only 24/100 (23%) had a history of infertility, with only 3/104 (2.9%) having undergone hysterectomy (Menakaya et al., 2014). There was no correlation between the site of pain and location of the disease (Menakaya et al., 2014).

Although the most common reason leading up to laparoscopic surgery—often ending in diagnosis of endometriosis—is pelvic pain, variation in the sites of endometriosis and how those sites may or may not affect chances of infertility are lacking (Maggiore et al., 2016). Pereira and Kilgman (2016) found that a 31-year-old woman presented to a clinic who had a 2-year history of infertility, when finally having undergone laparoscopic surgery, was determined to have endometriosis on her right fallopian tube. Whether the woman’s infertility was due to endometriosis or primary infertility was, however, undetermined (Pereira & Kilgman, 2016). Consideration regarding site/location in which endometriosis exists within a woman’s body might be helpful in regards to assessing the potential association between age of women when diagnosed with endometriosis and infertility, especially given that several variations in fallopian tube anatomy are notable during the evaluation of infertility because disease affecting the fallopian tubes account for nearly 25%-35% of all infertility cases (Pereira & Kilgman, 2016).

Impact of Endometriosis on Women’s Lives

The prevalence of endometriosis among women with pelvic pain is 20%-90%, although the etiology and pathogenesis is not known (Moradi et al., 2014). Often labeled as the missed disease, the average time between the onset of pain and diagnosis is nearly

8 years in the United Kingdom and nearly 12 years in the United States (Moradi et al., 2014). The quality of life for many patients with endometriosis is negatively affected, and some women experience the emotional impact of subfertility, anger about disease recurrence, and uncertainty about the future in regard to repeated operations and/or long-term medical therapy (Moradi et al., 2014). Moradi et al. (2014) identified impaired health related to quality of life and work productivity across countries and ethnicities, further concluding that women continue to experience a delay in diagnosis. From a sample of 35 women who were formally confirmed to have endometriosis via laparoscopy diagnosis and who were purposely recruited in order to avoid potential bias, Moradi et al. determined that most participants experienced pain, dyspareunia, heavy/irregular bleeding, and infertility, and all suffered from severe and progressive pain in areas such as the lower abdomen, bowel, bladder, lower back and legs during both menstrual and nonmenstrual phases. Other symptoms reported to negatively impact the women's lives included fatigue, tiredness, bloating, bladder urgency, bowel symptoms (e.g. diarrhea), bladder symptoms, and sleep disturbances due to intense pain (Moradi et al., 2014).

Among the three age groups included in Moradi et al.'s (2014) study (e.g., 16-24 years; 25-34 years; >35 years), Moradi et al. also showed that the most detrimental impact of endometriosis on the women's lives stemmed from negative effects on marital/sexual relationships, social life, and physical and psychological wellbeing. Most of the participants were either married or had a partner and had a history of living with endometriosis anywhere from 2 to 40 years (Moradi et al., 2014). The mean age in which

endometriosis-related symptoms were first experienced were reported by the participants to be 17.4 ± 6.8 years (range: 11-41), with diagnosis made at 25.6 ± 7.9 years (range: 15-42), and delay in diagnosis of endometriosis found to be 8.1 ± 6 years (range: 3 months - 24 years; Moradi et al., 2014). Furthermore, almost half of the participants (17 out of 35) reported that endometriosis interfered with their life and only 54.3% of participants (19 out of 35) reported moderate satisfaction with their treatment (Moradi et al., 2014).

According to the American Society for Reproductive Medicine (ASRM), stages of endometriosis are based on both the extent and location of endometriotic adhesions, with minimal endometriosis (Stage I) being indicative of minimal or superficial ovarian and peritoneal implants and severe endometriosis (Stage IV) consisting of deep, dense endometriotic implants (North Shore Medical Center, 2016). There is no correlation between stage and symptoms of endometriosis, which may result in misdiagnosis or delayed diagnosis of endometriosis (Gao, Yeh, Outley, Simon, Botteman, & Spalding, 2008). Because two-thirds of women with chronic pelvic pain (CPP) in the United States do not seek medical attention, Goa et al. (2008) evaluated the impact of endometriosis on the lives of the particular population. Goa et al. used the conceptual model developed by Wilson and Cleary, which states that biological and physiological variables may lead to physical and psychophysical symptoms that affect a person's functioning, general health perception, and overall health related quality of life (HRQL).

Goa et al. (2008) examined studies that measured the HRQL impact of endometriosis and its key symptoms; analyzed the impact of pharmacological and surgical treatments of endometriosis on HRQL; and reviewed the literature pertaining to

the presence and impact of endometriosis in adolescents, who are considered to be an overlooked patient population. Goa et al. found five dimensions of health status were addressed, which consisted of mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each of the five dimensions were divided into three levels: no problem, some problem, or extreme problem (Goa et al., 2008). Goa et al. determined that compared with a group of women not diagnosed with endometriosis, there were unfavorable results among the endometriosis group in regards to inference with daily activities, health distress, and pain during or after intercourse ($p < 0.05$ for all).

Furthermore, among those suffering from endometriosis, there were higher reports of anxiety-depression, sleeplessness, irritability, dyspareunia, painful defecation, dysuria, dysmenorrhea, and overall discomfort on the visual analogue scale (VAS; Goa et al., 2008). According to Goa et al., although it is known that endometriosis impacts fertility and sexuality, more researchers should focus on the impacts of endometriosis on the ability to work, the ability to play, and the ability to invest in personal relationships.

Diagnostic delay is believed to worsen the effects of endometriosis on the physical, emotional, and social wellbeing of patients and their ability to work (Giuliani et al., 2015). Pelvic pain, which represents the clinical problem of the disease (manifesting as dysmenorrhea, dyspareunia, chronic pelvic pain, and less frequently, dysuria and dyschezia) results in adverse effects on women's working abilities and psychosocial functioning (Giuliani et al., 2015). General quality of life (QoL) and sexual satisfaction are compromised in women with endometriosis (Giuliani et al., 2015). I stopped

reviewing here due to time constraints. Please go through the rest of your chapter and look for the patterns I pointed out to you. I will now look at Chapter 3.

An experimental study by Giuliani et al. (2015) aimed to evaluate QoL and sexual satisfaction in a group of Italian women affected by endometriosis while identifying specific sociodemographic variables that could impact the individual perception of the disease. A survey was conducted on 150 women with endometriosis who were recruited at a University hospital in Rome in the department of gynecology for service of endometriosis and pelvic pain (Giuliani et al., 2015). The control group included 150 women who were considered to be healthy (e.g. not diagnosed with endometriosis) and who were matched for age and relationship status. Age of participants ranged from 22-50 years (mean age=35.75; SD=6.90) (Giuliani et al., 2015). Sociodemographic questionnaires (i.e. the Italian version of the World Health Organization Quality of Life - Bref (WHOQOL-Bref), McCoy Female Sexuality Questionnaire (MFSQ), and the Visual Analogue Scale (VAS)) also were administered to participants. WHOQOL-Bref was used to assess the QoL perceived by participants in four different areas: physical, psychological, social relationships and environmental; and MFSQ was used to assess sexual and relationship satisfaction, analyzing two specific factors: sexuality and partnership (Giuliani et al., 2015). The level of pain related to dysmenorrhea, chronic pelvic pain, and dyspareunia were evaluated through VAS (e.g. 0=no pain, from 1-3=mild pain, from 4-7=moderate pain, from 8-10=severe pain) (Giuliani et al., 2015).

No statistical differences between the groups in relation to the sociodemographic variables (e.g. educational level, marital status, employment status, etc.) were found

except for the presence of children, with 86.7% of women in the experimental group not having children compared to only 58.7% of women in the control group not having children (Giuliani et al., 2015). Interestingly, though, data did show that the experimental group obtained a lower score than did the control group in the questionnaire total scores in terms of the sexual satisfaction domain ($P<0.01$) (MFSQ) and the physical, psychological and social relationships domains ($P=0.00$) (WHOQOL-Bref) (Giuliani et al., 2015).

Results from the experimental study suggest that clinical symptoms presented by endometriosis such as pain, tissue fibrosis, chronic inflammatory status, and the presence of neuroactive agents can severely affect sexual life (Giuliani et al., 2015). For example, women with endometriosis were found to be much less satisfied with their QoL in general, as well as in physical health, psychological and social relations domains when compared with women without endometriosis (Giuliani et al., 2015). Furthermore, women with endometriosis were found to have less sexual satisfaction than women without endometriosis (Giuliani et al., 2015). Given the higher percentage of women without children in the experimental group (86.7%) versus the percentage of women without children in the control group (58.7%), it is possible that many women without children in the experimental group faced problems of infertility – which actually was not explored in the aforementioned study. Given that there is a reason to believe that health-related quality of life is greater among parents than non-parents in regards to emotional support (Eiser & Varni, 2013), perhaps the quality of life of women with endometriosis in the study would have been greater if problems related to infertility were non-existent.

With that being said, assessing an impactful association between time in diagnosis of the disease and infertility in women might yield answers that provide a better quality of life for women who suffer from the disease by allowing them to conceive. In order determine such impactful association, though, formal diagnosis must first take place before appropriate options for treatment can be made available (Endometriosis Association, 2016).

Treatment

From patients' point-of-view, endometriosis is a nightmare of misfortune, myths, lack of diagnosis, and problematic "hit-and-miss" treatments, all of which are overlaid by the painful, chronic, stubborn disease (Moradi et al., 2014). Although there is no cure for endometriosis, there are a variety of treatment options that aim to relieve/reduce pain symptoms, shrink or slow down endometrial growths, preserve or restore fertility, and prevent and/or delay recurrence of the disease (Endometriosis Association, 2016). Such treatment options include: pain medication in the form of over-the-counter pain relievers, for instance aspirin and acetaminophen, as well as prostaglandin inhibitors like ibuprofen, naproxen sodium, indomethacin, tolfenamic acid, and in some cases the requirement of prescription drugs; pain relief such as ProSirona, which is a new product that targets endometriosis and is applied topically on the area of pain with the main ingredients being essential oils combined in a technologically advanced way; hormonal therapy aimed to stop ovulation for as long as possible, such as oral contraceptives, progesterone drugs, testosterone derivatives (e.g. danazol), and GnRH agonists (gonadotropin releasing hormone drug); surgery, which seeks to remove and destroy endometrial growths, relieve

pain, and increase the chances of pregnancy; and last, alternative treatments such as traditional Chinese medicine, nutritional approaches, homeopathy, allergy treatment, and immune therapy (Endometriosis Association, 2016).

When it comes to perceptions of endometriosis-related treatment, overall, the ideal outcome of surgical intervention in patients suffering from endometriosis-related infertility is for the anatomical relationship to be restored and for the function of the pelvic organs to be preserved (Gizzo et al., 2014). An observational cohort study by Gizzo et al. (2014) compared two large cohorts (Group A and Group B) of infertile women affected by endometriosis who underwent laparoscopic treatment strictly for the purpose of restoring/improving their fertility by either a skilled surgeon (Group A) or a surgeon strictly dedicated to endometriosis-related infertility (Group B). Comparisons among the two groups were made in regards to perioperative surgical outcomes, clinical/ongoing pregnancy and live birth rates, spontaneous pregnancy rate, and obstetrical outcome (Gizzo et al., 2014). Participants included in the study consisted of women aged 18-42 years, who had a preoperative suspicion of endometriosis confirmed by histology, who had a history of infertility, and who had a desire of pregnancy (Gizzo et al., 2014). Furthermore, participants were required to be of Caucasian ethnicity, have no history of previous concomitant malignant disease, no severely impaired ovarian reserve, and no systemic diseases which potentially could interfere with fertility (e.g. diabetes and disthyroidism) (Gizzo et al., 2014).

After it was determined that there was a significantly higher spontaneous fertility rate (particularly in the first year after surgery) and lower ectopic pregnancy rate in

Group B post surgery, Gizzo et al. (2014) concluded that in patients affected by endometriosis, the choice should be personalized in regards to deciding between expectant management versus intervention. For example, in the case that estimated probability of natural conception is low, surgery may need to be considered as a second-line treatment. However, in all other cases, surgery should be offered early (i.e. as a first-line approach) as it can improve the chance of spontaneous conception (Gizzo et al., 2014).

Due to difficulty in long-term management of endometriosis symptoms and unpredictability of treatment outcomes, treatment options such as herbal medicine stand necessary in endometriosis research (Stephens, Whitehouse, & Polley, 2013). With that being said, a study by Stephens, Whitehouse, & Polley (2013) reviewed commonly used herbs in the treatment of endometriosis, the effects of phytochemical constituents on endometrial cells, and the impact such treatment had on the epigenome. Stephens et al. (2013) defined treatment of endometriosis as reduction of pain and prevention of pain recurrence. Long history of documented evidence regarding herbal medicine for endometriosis-like symptoms has led to an increase in popularity of herbal medicine, specifically in the West, for treating endometriosis in attempt to overcome poor long-term success at resolving chronic pain or recurrence of the disease using conventional intervention (Stephens et al., 2013). Recent data on dienogest (a 19-nortestosterone derivative) for pain management in endometriosis presented by the Royal College of Obstetricians and Gynecologists (RCOG) actually reports, for example, that women with endometriosis prefer complementary medicine (e.g. herbal medicine) over nonsteroidal

anti-inflammatory drugs (NSAIDs) and analgesics (Stephens et al., 2013). Such increase in preference regarding herbal treatment was found to be attributed to known effects on the signaling pathways associated with pathogenesis of endometriosis, further demonstrating anti-proliferative, antioxidant, analgesic, and inflammatory effects on endometrial cells (Stephens et al., 2013).

Unfortunately, standard medication and surgical treatments of endometriosis show high recurrence of symptoms (Prather, MacLean II, Shi, Boadu, Paquet, & Hayashi, 2016). Due to such high rates of recurrence, it is suggested that current treatment options be improved (Prather et al., 2016). Long-term treatment of patients who experience chronic pelvic pain associated with endometriosis often involves repeated courses of therapy, whether surgical, medical or both (Prather et al., 2016). Laparoscopic surgery, for example, is found to provide relief of symptoms from the disease, only to have an estimated 50% recurrence rate after five years (Prather et al., 2016). Furthermore, GnRH agonist therapy is estimated to have a 50% or even higher rate of recurrence of symptoms over time (Prather et al., 2016). With that being said, it is suggested that therapeutic targets and efficient drugs that potentially could be improvements over current treatment options be identified (Prather et al., 2016).

In an experimental study by Prather et al. (2016), it was examined whether the non-steroidal drug niclosamide could be a useful drug for endometriosis in a preclinical setting. Niclosamide is defined as an efficacious, minimally toxic and FDA-approved anti-helminth drug that has been used in patients for decades (Prather et al., 2016).

Niclosamide is reported to aid in the disruption of multiple signaling pathways including

NFκB, STAT3, and WNT signaling in a variety of cancer models (Kim et al., 2013).

Given the history of the drug in cancer models, it was hypothesized that the drug could be an inhibitor of endometriosis progression by blocking signaling pathways (Prather et al., 2016). For the experimental study, endometriotic implants were surgically inserted into donor mice who were currently experiencing the diestrus stage of the reproductive cycle (Prather et al., 2016). After 3 days of recovery, recipient mice received niclosamide orally at a dose of 0 (n=8), 100 (n=5), or 200 (n=10) mg/kg b.w./per day for 3 weeks. More than 95% of mice ate their completed dosage of niclosamide within 30 minutes (which was mixed in gelatin with artificial flavors for taste). After the 3 weeks of treatment, the recipient mice were necropsied, and the endometriotic implants were distinguished under a Fluorescence Stereo Microscope and collected for further analysis (Prather et al., 2016). Further analysis included determining whether there was an effect of niclosamide treatment on reproductive functions, where mice then were randomly assigned for control (n=11) or niclosamide (n=7) group.

A significant difference in the pattern of growth of the endometriotic implants were discovered, with niclosamide treated mice at a dose of 100 mg/kg b.w./per day having showed a significant reduction of implant weight (0.023 ± 0.004 g) and growth (4.63 ± 1.00 fold from initial implant size) compared to controls (implant weight: 0.044 ± 0.007 g, and growth: 8.66 ± 1.10 fold) (Prather et al., 2016). Furthermore, niclosamide treated mice at a dose of 200 mg/kg b.w./day also presented a reduced implant weight (0.016 ± 0.003 g) and growth (1.90 ± 0.40 fold) compared to controls (Prather et al., 2016). Importantly, it was found that niclosamide had no effect on reproductive function,

as all mice exposed to niclosamide became pregnant and gave birth (Prather et al., 2016). Also, there were no alterations in regard to gestational length, number of pups, and weight of pups at birth upon the mice being exposed to niclosamide (Prather et al., 2016).

Such results from the experimental study indicate that treatment (i.e. niclosamide) can be effective for endometriosis, acting as an inhibitor of inflammatory signaling without disrupting normal reproductive functioning (Prather et al., 2016). As an important contribution to the present study, though, Prather et al. (2016) presented the importance regarding the stage in which the female mice were treated. For example, specifically given the fact that the recipient mice were strictly selected to receive treatment in the case that they were undergoing the diestrus stage, which is equivalent to the estrus stage in humans, classifying women as being at the most effective reproductive stage in their life (Kim et al., 2016), a 100% success rate in regards to reproduction from the mice post treatment provides support as to how effective treatment for endometriosis can be in regards to fertility if presented at an appropriate time.

Association Between Endometriosis and Infertility

Infertility typically is defined as the inability of couples to become pregnant after 12 months of regular unprotected sexual intercourse (Thoma et al., 2013). Endometriosis is considered to be the number one cause of infertility in the United States, having a prevalence of 0.5%-5% in fertile women and 25%-40% in infertile women (Juneau Biosciences, 2016). With that being said, in vitro fertilization (IVF) is represented as the most successful means of achieving conception in endometriosis patients struggling with infertility (Surrey, 2015). Interestingly, Surrey (2015) explored the impact of

endometriosis on IVF cycle outcomes as well as whether surgical or medical management of endometriosis could impact success rates. Conclusions formulated by the review study suggested that women with endometriosis have similar cycle outcomes to other patients going through IVF who do not suffer from endometriosis although several earlier studies such as Barnhart et al. (2002) and Barcelos et al. (2009) suggested poorer outcomes associated with IVF from women suffering from endometriosis in comparison to controls (Surrey, 2015). The conclusion of the study, which suggested that women with endometriosis have similar success rates to other patients going through IVF could be flawed, however, given the fact that the study did not control for other infertility variables that could have affected the outcome (Surrey, 2015). Importantly, discrepancy between Surrey (2015) and earlier studies was assumed to be attributed to the decreasing role of laparoscopy as a means to diagnose endometriosis in order to further explore potential infertility issues. For example, some patients in the study who potentially could have been suffering from endometriosis but who had never undergone laparoscopy were classified with the diagnosis of “unexplained infertility” (Surrey, 2015).

Although diagnosed in asymptomatic patients, endometriosis usually is diagnosed when patients present with pain and/or claims of infertility (Burghaus et al., 2016). With that being said, endometriosis actually is diagnosed during laparoscopy in a quarter of patients with infertility (Burghaus et al., 2016). Although various etiologies have been discussed and proposed, such as potential causes of infertility due to endometriosis being linked to anatomical changes of the adnexa, the association between endometriosis and infertility still remains unclear (Burghaus et al., 2016). Other etiologies, though, include

changes to the immunological milieu for implantation affecting sperm motility, as well as uterotubal transport disorders, and disorders of oocyte maturation (Burghaus et al., 2016). Although published pregnancy rates for patients with endometriosis range from 24%-54%, such estimated rates are thought to be an overestimation given that some patients may not have attempted spontaneous pregnancy prior to surgery for endometriosis (Burghaus et al., 2016).

Endometriosis is considered to be one of the most challenging clinical entities for gynecologists given the extreme difficulty linked to managing pain and infertility (McKenzie, 2015). With that being said, a study by McKenzie (2015) assessed a case study regarding the effects of endometriosis on infertility and suggests that “less is more” in regard to surgical management for endometriosis-associated infertility. The study assessed a case concerning a 34-year-old patient who presented a complaint to her physician in 2014 regarding infertility after attempting pregnancy for two years. However, the patient was only recently diagnosed with endometriosis via laparoscopy in December 2013 (McKenzie, 2015). Interestingly, before the diagnosis of endometriosis, prior fertility testing via ultrasound on the patient determined an occluded left Fallopian tube and an anti-Mullerian hormone (AMH) level of 1.6 ng per mL (McKenzie, 2015). Furthermore, via transvaginal ultrasound, bilateral endometriomas measuring approximately 5 and 10 cm were suspected (McKenzie, 2015). Fertility management (i.e. IVF) was immediately discussed versus the option of removing the endometriomas. Six months after the discovery of the suspected endometriomas, the patient decided to undergo IVF, which turned out to be unsuccessful (McKenzie, 2015). McKenzie (2015)

further concluded that although incidence of endometriosis can be asymptomatic in women trying to become pregnant/claiming to be suffering from infertility, laparoscopic diagnosis of endometriosis is important in regards to battling infertility. Given that laparoscopy for evaluation of endometriosis-associated infertility varies dramatically between 9%-50%, exactly how endometriosis impacts fertility remains uncertain (McKenzie, 2015). With that being said, perhaps assessing the association between the age in which a woman is diagnosed with endometriosis and infertility could help explain what currently is considered to be “unexplained infertility”.

Presence of Uterine Fibroids

Uterine fibroids are common, benign, smooth-muscle tumors that are known to cause major morbidity for women of reproductive age, often requiring them to undergo invasive treatment (Baird et al., 2015). Although uterine fibroids are considered, by many, to be both a personal and public health burden, there is a lack of studies that attempt to periodically screen women with ultrasound in order to detect incident disease and/or identify risk factors (Baird et al., 2015). Interestingly, uterine fibroids develop in the majority of reproductive-age women and are considered to be the leading cause of hysterectomy in the United States (Baird et al., 2015).

Heavily impacting women’s health and fertility, endometriosis and uterine fibroids are common indications for surgery (Ciarmela, Critchley, Christman, & Reis, 2013). A better understanding of the conditions – especially together – are essential for the development of successful medical therapies and are of interest to many clinicians and clinical researchers (Ciarmela et al., 2013). Although uterine fibroids and

endometriosis are known to contribute to a considerable amount of pain, potentially leading to subfertility or infertility in women, the relationship between the two is poorly understood (Nezhat et al., 2016). Nezhat et al. (2016) conducted a retrospective study in order to assess the rate of coexistence of endometriosis in women with symptomatic leiomyoma (i.e. uterine fibroids). The retrospective review collected medical records of 244 patients treated at a tertiary medical center, who were evaluated for symptoms of uterine fibroids. Out of the 244 patients, 208 of those underwent laparoscopic procedure, where 181 had concomitant diagnoses of uterine fibroids and endometriosis (Nezhat et al., 2016).

The most common form of uterine fibroids amongst the participants existed as solid pelvic tumors, which, alone, is known to affect 20%-25% of reproductive-aged women (Nezhat et al., 2016). Alarmingly, out of the 20%-25% of women who suffer from uterine fibroids in the form of solid pelvic tumors, 50% are usually symptomatic, where the symptoms are considered to depend on the number, size, and location of the tumor (Nezhat et al., 2016). The most common symptoms associated with uterine fibroids include abnormal uterine bleeding, pelvic pain, and extreme pressure, and risk factors include increased estrogen stimulation, family history of uterine fibroids, and race (Nezhat et al., 2016). Uterine fibroids seldom are the sole cause of infertility, but become a major concern when coexisting with endometriosis (Nezhat et al., 2016). Interestingly, Nezhat et al. (2016) suggested that dismissal of the diagnosis of endometriosis during surgical intervention for uterine fibroids can result in suboptimal treatment – especially in patients with chronic pelvic pain, infertility, or both. All in all, Nezhat et al. (2016) found

that because of the significant overlap of symptoms between uterine fibroids and endometriosis, it often is difficult to discern which pathology is responsible for patients' complaints. Nezhat et al. (2016) further concluded that because patients who have symptomatic uterine fibroids may be at a higher risk for endometriosis and vice versa, suspicion for both endometriosis and uterine fibroids should be of equal concern when patients undergo laparoscopic procedure.

Despite uncertainty regarding the relationship between uterine fibroids and endometriosis, through advances in pathogenetic knowledge of uterine fibroids, it has been suggested via studies such as Tocci et al. (2008) that sites in which pathological thickening or abnormality of sub-endometrial tissue occur also serve as the possible sites of origin of submucosal and intramural fibroids (Ciavattini et al., 2013). Furthermore, Ciavattini et al. (2013) mentioned that although in current time, it is not well established exactly how uterine fibroids might interfere with the endometrial environment and the sub-endometrial environment and vice versa, patients who suffer from both endometriosis and uterine fibroids definitely have an increased risk for infertility and/or miscarriage, strictly due to influences related to the association between the two conditions.

Summary and Conclusions

Endometriosis is considered to be the number one cause of infertility in the United States, with diagnoses of the disease found to be delayed anywhere from 7-10 years, and the disease being poorly recognized by physicians in practice (Juneau Biosciences, 2016; Johnston et al., 2015). This study is significant to the research topic

because it might increase the understanding of the issue concerning the lack of knowledge that exists in regards to the association between endometriosis and infertility; specifically in regards to how the age in which a woman is diagnosed with the disease might affect her ability to conceive.

The literature presented data on the prevalence of endometriosis, as well as the average years of delay that exists in regards to definitive diagnosis. The review further demonstrated the impact of endometriosis on women, such as pain, dyspareunia, heavy/irregular bleeding, and infertility, which significantly affects their daily lives (Moradi et al., 2014). The literature revealed patients' point-of-view regarding treatment for the disease and how available treatment options are problematic in that they often are found to be "hit-and-miss," even though most patients undergo treatment with the perception that the anatomical relationship regarding fertility can be restored and the function of the pelvic organs will be preserved (Moradi et al., 2014; Gizzo et al., 2014).

A number of studies have established a connection between endometriosis and infertility, but no researchers have considered the association between the age in which a woman is diagnosed with endometriosis and infertility. This study attempted to fill the gap in the literature by determining if there is a statistically significant association between the age in which a woman is diagnosed with endometriosis and being considered infertile. Chapter 3 will provide an overview of the research design and methodology. The discussion will include the target population; sampling and sampling procedures, including justification for effect size, alpha level, and power level; data collection

procedures, including access to secondary data; threats to validity; and ethical procedures.

Chapter 3: Research Method

Introduction

Diagnosis of endometriosis is delayed and poorly recognized by physicians in practice, often leading to misdiagnosis and/or suboptimal care (Johnston et al., 2015). In addition, investigation concerning causes of female infertility is receiving less attention. An optimal approach to managing infertility requires a method associated with routine and timely measures (Bell, 2014). However, scholars have not explored the association between the age of a woman when diagnosed with endometriosis and infertility. Earlier diagnosis of the disease (e.g., diagnosis at an earlier age) could serve as a preventative strategy towards infertility. If a statistically significant association between age of women when diagnosed with endometriosis and infertility is determined, there could be fewer incidences of endometriosis-related infertility. Furthermore, determining a statistically significant association also could provide for more effective patient/doctor visits for women who suffer from common symptoms of endometriosis.

In Chapter 3, I will explore the research design and rationale of the study, explain the system of methods used in order to carry out the study, introduce any factors that could serve as threats to the validity of the study, explain ethical procedures involved in the gathering of data, and include a brief introduction to Chapter 4.

Research Design and Rationale

Quantitative researchers focus on gathering numerical data to generalize results across groups of people or to explain a particular phenomenon (USC Libraries, 2016). Furthermore, quantitative methods are used to emphasize measurements and statistical,

mathematical, or numerical analyses of data through the collecting of polls, questionnaires, and surveys, or by manipulating preexisting statistical data using computational techniques (USC Libraries, 2016). The goal of a quantitative study is to determine the relationship between one thing (i.e., the independent variable) and another (i.e., the dependent variable) within a population (USC Libraries, 2016). In this quantitative study, I aimed to determine whether there was an association between the age in which a woman was diagnosed with endometriosis and infertility. The dependent variable in the study was infertility, and the independent variable in the study was age. Because I also aimed to determine how history of uterine fibroids and site/location of endometrioma influenced the association between age of women when diagnosed with endometriosis and infertility, uterine fibroids and site/location were used as covariates in the study.

The research design for this study was a cross-sectional design. The cross-sectional study design is considered to be one of the most common and well-known study designs (Olsen & St. George, 2004). In cross-sectional studies, either an entire population or a subset of a population is selected, and data from individuals within the population or subset population are collected to answer research questions (Olsen & St. George, 2004). A cross-sectional research design was appropriate for this study because data on a group of women diagnosed with endometriosis in Eastern North Carolina were assessed in order to answer the research questions.

Epidemiologists analyze preexisting data to find answers to questions (Olsen & St. George, 2004). A secondary data analysis of preexisting data retrieved from medical

records of patients at multiple OB-GYN clinics in Eastern North Carolina was used for this study. Incorporating secondary data from patients' medical records allowed me to search through a wider range of materials covering larger areas over longer periods of time in shorter duration than would have been possible using only primary data. By using statistical analysis, I could better understand the historical context behind patients' medical struggle with endometriosis. For example, via preexisting medical records, I was able to assess—through physician documentation—when patients first complained of onset of symptoms related to endometriosis, when patients underwent laparoscopic surgery to definitively diagnosis endometriosis, whether or not they were considered to be suffering from infertility, and the age in which all series of events took place.

These research designs are needed to advance knowledge in the social sciences discipline because they provide a basis for describing patterns of relation or association between variables (Frankfort-Nachmias & Nachmias, 2008). By using a cross-sectional research design, I was able to investigate the association between variables to further contribute to the knowledge concerning the association between endometriosis and infertility.

Methodology

Population

The target population for this study was women living in Eastern North Carolina, between the ages of 18 and 35 years, who were formally diagnosed with endometriosis via laparoscopic surgery. The pool of eligible women whose medical records were assessed for this study was made available by physicians. In the medical records, the

women stated that they underwent laparoscopic surgery (at some point in time, with the date of surgery noted) and were diagnosed with endometriosis following the procedure. Further, medical records from the pool of eligible women provided information regarding whether or not there currently was an issue with infertility.

The women who were eligible for this study were identified by number (ie., Patient 1, Patient 2, Patient 3, and so forth. Information concerning the date in which the patient underwent laparoscopic surgery, their current age, whether or not they had a history of uterine fibroids, where their sites of endometriosis occurred, and whether or not they experienced/had experienced issues with infertility were listed separately according to the patient.

Because that the target population was women between the ages of 18-35 years who had been diagnosed with endometriosis via laparoscopic procedure in Eastern North Carolina, the sample from the target population was retrieved by assessing the medical records of women who lived/visited a clinic in several of Eastern North Carolina's largest counties: Pitt County, Wayne County, Lenoir County, Bladen County, Jones County, and New Hanover County.

The target population was not restricted by race, as all racial/ethnic groups were considered. The sample size for this study consisted of 102 women who had been diagnosed with endometriosis. The sample size was calculated using G*Power version 3.0.10 under the parameters 80% statistical power, an alpha of .05, and an effect size of .5. A statistical power of .80 was chosen so that I could find a real treatment effect (or mean difference) 80% of the time. For example, if the study were repeated 100 times, the

null hypothesis would be rejected 80 times—if there is indeed an effect (Burkholder, n.d.). An alpha level of .05 was used so that there would only be a 5% chance for making a Type I error, incorrectly rejecting the null hypothesis (Burkholder, n.d.). Last, the effect size of .5 simply was preferred to achieve a medium effect size.

Sampling and Sampling Procedure

Preexisting medical records from a sample of approximately 102 women of multiple races/ethnicities, residing in Eastern North Carolina, suffering from endometriosis was used for this study. The factor of race/ethnicity was not be considered for this study because similar rates of endometriosis are observed among women of different races (Gerlinger et al., 2012). Only women between the ages of 18 and 35 years were used for this study as such age group is considered to be within good standards in regard to reproduction, with women's fertility decreasing substantially by their late 30s (Lezzoni et al., 2014). Women who are over the age of 35 were excluded to avoid the factor of age as a possibility for infertility. Preexisting medical records that were assessed were retrieved from OB-GYN clinics located in Eastern North Carolina.

Inclusion and exclusion criteria determined eligibility for the assessment of medical records of patients. Inclusion criteria were the following: women who were formally diagnosed with endometriosis (i.e., Stage I or Stage II) residing in Eastern North Carolina between the ages of 18-35, and women who provided full consent for their medical records to be assessed for research purposes. Diagnosis of endometriosis was assessed according to documentation in the medical records of each patient stating that the patient underwent laparoscopic surgery on a day within a certain year. Any other

diagnoses presented in the medical records—aside from diagnosis of uterine fibroids—were not be assessed. Exclusion criteria included the following: women who suspected endometriosis but had avoided formal diagnosis via laparoscopic procedure, women not between the ages of 18-35, women who did not provide full consent for their medical records to be assessed, and women diagnosed with Stage III (or moderate) or Stage IV (or severe). If there was no indication of laparoscopic surgery presented in a patient's medical record (i.e., no documented date of laparoscopic surgery), such patient was excluded from the study, and if a patient was found to possess multiple locations of deep adhesions or implants (i.e., implants/adhesions involving multiple organs), those patients were excluded as well.

As previously stated, the study consisted of preexisting medical records from a sample of 109 women. The sample size was calculated using G*Power version 3.0.10 under the parameters 80% statistical power, an alpha of .05, and an effect size of .5. Given those parameters, it was suggested that the study contain a sample size of 102. I was, however, able to achieve a slightly higher sample size. My reasoning for choosing a statistical power of .80 was so I could insure a real treatment effect 80% of the time, rejecting the null hypothesis 80 times in the case that the study was repeated 100 times, if there was indeed an effect (Burkholder, n.d.). For there to only be a 5% chance for making a Type I error, or incorrectly rejecting the null hypothesis, an alpha level of .05 was used. Last, the effect size of .5 simply was preferred to achieve a medium effect size.

Archival Data

The data collection process for this study required institutional review board (IRB) approval to assess secondary data in the form of patient medical records from OB-GYN clinics in Eastern North Carolina. IRB approval documents, along with the data use agreement form, were presented to physicians prior to the assessment of patient medical records. Physicians whom agreed to serve as my data provider signed the data use agreement form and asked me to sign a HIPAA confidentiality agreement form in the case that not all medical records were de-identified. Once the HIPAA confidentiality agreement forms were signed by physicians as well as myself, I was allowed temporary access to medical records of patients who suffered from and had been diagnosed with endometriosis. In the case that any patients were not diagnosed with endometriosis, their medical records remain nondisclosed to me.

Data Analysis Plan

The software that was used for the analysis of this study included IBM SPSS Statistics Version 24. SPSS was used to perform statistical regression analysis to assess the association between age of women when diagnosed with endometriosis (i.e., the independent variable) and infertility (i.e., the dependent variable). Furthermore, statistical regression analysis and stratified analysis was used to test for confounding by assessing the association between age of women when diagnosed with endometriosis and infertility when a second independent variable (e.g., history of uterine fibroids) was introduced. The research questions and hypotheses for this study included

RQ1: What is the association between infertility and age of women when diagnosed with endometriosis after controlling for history of uterine fibroids?

H_01 : There is no statistically significant association between infertility and age of women when diagnosed with endometriosis after controlling for history of uterine fibroids.

H_11 : There is a statistically significant association between infertility and age of women when diagnosed with endometriosis after controlling for history of uterine fibroids.

RQ2: What is the association between infertility and age of women when diagnosed with endometriosis after controlling for the specific sites of endometriosis?

H_02 : There is no statistically significant association between infertility and age of women when diagnosed with endometriosis after controlling for the specific sites of endometriosis.

H_12 : There is a statistically significant association between infertility and age of women when diagnosed with endometriosis after controlling for the specific sites of endometriosis.

The analysis included conducting multiple logistic regression to determine potential associations between variables. For example, age of women when diagnosed with endometriosis (i.e., age) served as the independent variable on a continuous scale, with ages ranging between 18 and 35 years. More specifically, ages of women were not be dichotomized into groups. Fertility status (i.e., infertility) served as the dependent variable on a binary scale where women were coded in the dataset as being fertile or

infertile (i.e., *fertile*=0; *infertile*=1). The variable history of uterine fibroids (i.e., uterine fibroids) was introduced as a potential confounding variable in the association between the variables age and infertility. To test whether history of uterine fibroids might act as a confounding variable—affecting the association between age of women when diagnosed with endometriosis and infertility—a stratified analysis was performed to examine the primary association at different levels of the potential confounding variable. For example, the association between age of women when diagnosed with endometriosis and infertility was tested separately among women with a history of uterine fibroids and among women without a history of uterine fibroids. In the initial analysis, before the effect of history of uterine fibroids was taken into consideration, uterine fibroids was be coded in the dataset as 0=*nonpresence of uterine fibroids* and 1=*presence of uterine fibroids*. Patients who suffer from endometriosis often suffer from uterine fibroids as well, and both are considered to potentially lead to subfertility or infertility in women (Uimari et al., 2011). For the second research question, age of women when diagnosed with endometriosis (i.e., age) served as the independent variable on a continuous scale, and fertility status (i.e., infertility) served as the dependent variable. Instead of including the variable uterine fibroids into the analysis, implantation/site location of endometriosis (i.e., site) was included, with the variable coded (1=*ovaries*, 2=*fallopian tubes*, 3=*uterus*, 4=*bladder*, 5=*rectum*, etc.).

The results were interpreted via scatterplots, which presented whether or not there was a statistically significant association between the age in which women are diagnosed with endometriosis and infertility. I also determined the usefulness of the logistic

regression model in terms of measuring the association between variables.

Crosstabulation, or a contingency table analysis, was performed. Table 1 represents the aforementioned data analysis plan:

Table 1

Data Analysis Plan

Research Questions	Variables	Statistical Analyses
RQ1: What is the association between age of women when diagnosed with endometriosis and infertility after controlling for history of uterine fibroids?	IV: Age when diagnosed with endometriosis. DV: Infertility Covariate: History of Uterine Fibroids	Test: Logistic Regression; ANOVA; Crosstabulation
RQ2: What is the association between age of women when diagnosed with endometriosis and infertility after controlling for specific sites of endometriosis?	IV: Age when diagnosed with endometriosis. DV: Infertility Covariate: Site/Location of endometriosis	Test: Logistic Regression; Crosstabulation

Access to Secondary Data

Access to secondary data in the form of electronic patient medical records was obtained by contacting multiple clinics in Eastern North Carolina by both phone and e-mail. After physicians at certain clinics agreed to allow me access to patient medical records, I personally met with each of the physicians at the clinics and presented them with a data use agreement form that was signed by myself, as well as the physicians who were responsible for granting me access to the medical records necessary for answering my research questions. All of the medical records used for the study were either de-identified so that patients' names, addresses, and other forms of contact information were not be available to me, or a HIPAA confidentiality form was signed to protect the identities of those whose charts were not de-identified.

Threats to Validity

External Validity

External validity explains the extent to which conclusions can be generalized to a wider population and/or across populations, treatments, settings/contexts, and time (Laureate Education, 2012). External validity is important in quantitative research due to because researchers strive to be able to report that their conclusions gathered from their research can be generalized, although the results are based solely on a sample (Laureate Education, 2012). With quantitative research designs, the level of external validity is affected by potential threats that may influence the ability to make generalizations (Laureate Education, 2012). The four main threats to external validity in quantitative research include selection biases; constructs, methods, and confounding; real world

versus experimental world; and history effects and maturation (Laureate Education, 2012). I stopped reviewing here. Please go through the rest of your chapter and look for the patterns I pointed out to you. I will now look at Chapter 4.

Given that this study included a secondary data analysis of existing medical records, selection bias could have been an issue given the fact that only medical records of women portraying specific factors, such as in age, race/ethnicity, marital status, and socioeconomic status were assessed (Laureate Education, 2012). Such threat to external validity, however, was addressed by assessing medical records of women of all races/ethnicities, marital statuses, socioeconomic statuses, and races/ethnicities.

Assessing the medical records of women belonging to a wide variety of ages, ranging from the teens to mid-thirties, also addressed such threat to external validity.

Furthermore, since extraneous variables also can limit the generalizability of results by studying only certain characteristics within a sample/population (i.e. endometriosis), such threat the validity was addressed by taking history of uterine fibroids into consideration when studying the association between the independent and dependent variables as well (Laureate Education, 2012). By addressing such threats, the sample is more generalizable to larger populations of women suffering from endometriosis, possibly facing infertility.

Internal Validity

Internal validity explains the extent to which our conclusions made from our dissertation research accurately reflect what we are studying (Laureate Education, 2012). With that being said, as researchers, we want to be able to state our conclusions with as much certainty as possible. In quantitative studies, internal validity can be affected by the

type of quantitative research design adopted (i.e. descriptive, experimental, etc.) and potential threats (Laureate Education, 2012). Threats to internal validity might include: instrumentation, selection bias, history effects, testing effects, statistical regression, and compensation (Laureate Education, 2012). Again, given that this study uses a secondary analysis of existing medical records, and no actual patients were needed for the study, internal validity was high.

Construct Validity

Construct validity refers to the extent to which a measurement procedure measures given constructs in a study (Laureate Education, 2012). In other words, construct validity is viewed as the process that researchers go through in order to assess the validity of a measurement procedure (e.g. questionnaire) when used to measure a given construct (e.g. depression, trust, commitment, etc.) (Laureate Education, 2012). For construct validity to exist, a clear link between the construct of interest and the measures and/or interventions used to operationalize it should be clear; and furthermore, a clear distinction between constructs should exist (Laureate Education, 2012). With that being said, there are a number of threats to construct validity, which include: inexact definitions of constructs, mono-operation bias, reducing levels of measurements of constructs, mono-method bias, treatment-sensitive factorial structure, and construct confounding (Laureate Education, 2012).

In order to avoid such threats, broad constructs of interest were narrowed down and adequate definitions of constructs were provided. Furthermore, given that this study consisted of one independent variable (i.e. age) and one dependent variable (i.e.

infertility), taking into consideration the co-variables and potential confounding variables “uterine fibroids” and “sites/locations,” threats to construct validity in regards to construct confounding were addressed by thoroughly explaining how the constructs uterine fibroids and endometriosis relate to one another, as well as explaining the boundaries between the two, and how differences in site/location of endometriosis provide for different outcomes (Laureate Education, 2012).

Ethical Procedures

In order to ensure that the study was conducted ethically, the protection of patients whose medical records were assessed was taken highly into consideration. This study was conducted in compliance with ethical standards provided by Walden University. Informed consent and the assessment of medical records received Walden IRB approval prior to the initiation of the study. For example, IRB was contacted via e-mail, and all study procedures (e.g. requirement of obtaining de-identified patient medical records) were presented to IRB prior to data collection. As suggested by IRB, a Data Use Agreement form was signed by myself as well as physicians as an agreement to gain temporary access to patient medical records for use in research in accord with laws and regulations of the governing bodies associated with the Data Provider (i.e. physicians), Data Participant (i.e. myself), and Data Participant’s educational program (i.e. Walden University). The signed Data Use Agreement document was submitted along with my IRB application, which was formally approved before any data was assessed. Patient medical records remained inside the clinics at all times during the assessment process. Furthermore, I was not allowed to leave the clinics with any medical records at any time

as to ensure confidentiality and avoid dissemination. As the student researcher, I was the only individual allowed access to the medical records aside from the physicians of the clinics. Importantly, the names, addresses, and telephone numbers of patients whose medical records were assessed were not disclosed in the study. The IRB approval number for this study is: 07-11-17-0561657.

Summary

In this chapter, I discussed the research design, methodology, data collection and analysis plan, threats to validity and ethical considerations associated with the study. A detailed explanation of how this study was conducted in order to obtain and gather the data necessary to determine whether or not an association exists between the age in which a woman is diagnosed with endometriosis and infertility was provided. The purpose of this study, which was to fill the gap concerning whether an association exists between the time in which a woman is diagnosed with endometriosis (i.e. age of woman when diagnosed) and infertility was thoroughly explained. In Chapter 4, I will present the results of the analysis of the data collected in the study.

Chapter 4: Results

Introduction

The purpose of this study was to determine whether an association between the age of women when diagnosed with endometriosis and infertility existed. Both uterine fibroids and endometriosis are known to lead to subfertility or infertility in women; yet, the relationship between the two is poorly understood. In this study, I also aimed to determine whether an association between the age of women when diagnosed with endometriosis and infertility existed when history of uterine fibroids also was present. Further, given that site/location of endometrioma might affect the association between infertility and the age in which a woman is diagnosed with endometriosis, I also aimed to determine the affect different sites/locations have when assessing the relationship between infertility and the age in which a woman is diagnosed with endometriosis. The research questions this study aimed to answer included the following:

RQ1: What is the association between infertility and age of women when diagnosed with endometriosis after controlling for history of uterine fibroids?

H_0 1: There is no statistically significant association between infertility and age of women when diagnosed with endometriosis after controlling for history of uterine fibroids.

H_1 1: There is a statistically significant association between infertility and age of women when diagnosed with endometriosis after controlling for history of uterine fibroids.

RQ2: What is the association between infertility and age of women when diagnosed with endometriosis after controlling for the specific sites of endometriosis?

H_{02} : There is no statistically significant association between infertility and age of women when diagnosed with endometriosis after controlling for the specific sites of endometriosis.

H_{12} : There is a statistically significant association between infertility and age of women when diagnosed with endometriosis after controlling for the specific sites of endometriosis.

In Chapter 4, I will present the findings of this study, as well as the data collection process. The sample size for this study was calculated using G*Power version 3.0.10 under the parameters 80% statistical power, an alpha of .05, and an effect size of .5. A statistical power of .80 was chosen so that I could expect to find a real treatment effect (or mean difference) 80% of the time. An alpha level of .05 was used so that there would only be a 5% chance for making a Type I error, incorrectly rejecting the null hypothesis (Burkholder, n.d.). Last, the effect size of .5 simply was preferred to achieve a medium effect size. An accurate sample size for the study consisted of 102 women diagnosed with endometriosis. After collecting necessary data, however, I was fortunate to receive data on a total of 109 who satisfied my inclusion criteria.

Data Collection

The data for this study were collected over a period of 3 weeks, with the time frame ranging from December 4, 2017 to December 22, 2017. Although I was able to retrieve the data in a short period of time, the process for meeting all requirements by the

clinics/hospitals before the actual retrieval of data was permitted was lengthy. For example, to retrieve data from the clinics/hospitals, I was required to receive several vaccinations and present proof of updated vaccination records, and I also was required to present both a state and federal level background check to each of the clinics/hospitals. Although I received my state background check within a few weeks, retrieval of my federal background check took a total of 4 months to receive, having applied for one in July 2017 and not receiving feedback from the FBI until the end of October 2017. Without both the state and federal background checks presented to the hospitals/clinics, physicians were unable to sign my data use agreement forms, which were required to complete my IRB application.

Once IRB permitted me to proceed with the collection of my data, all physicians were immediately contacted, and all physicians worked around their schedules to accommodate my needs. After I visited with all clinics/hospitals approved in my IRB application, a total of 109 participants were assessed for this study. All of the participants were women between the ages of 18 and 35 who were diagnosed with endometriosis via laparoscopic procedure. Any medical charts gathered for my assessment that included women outside of the inclusion criteria were excluded from the study. For example, several participants, I found, were not within the age criteria, and some participants presented to physicians with suspicion of endometriosis, but never underwent laparoscopic procedure to confirm a diagnosis. The final analysis of this study was conducted on 109 patients, with a power analysis conducted to calculate achieved power,

using an appropriate alpha level ($\alpha = .05$), sample size ($n = 109$), and effect size ($\eta^2 = .5$). The achieved power was calculated to be 0.80.

All data retrieved for this study consisted of preexisting medical records from a sample of 109 women of multiple races/ethnicities, residing in Eastern North Carolina, who suffered from endometriosis. The factor of race/ethnicity was not considered in this study because similar rates of endometriosis are observed among women of different races (Gerlinger et al., 2012). Only women between the ages of 18 and 35 years were used for this because such an age group is considered to be within good standards in regard to reproduction, with women's fertility decreasing substantially by their late 30s (Lezzoni et al., 2014). Women over the age of 35 were excluded from the study to avoid the factor of age serving as a possibility for infertility. I did not include data on women who possessed multiple locations of deep adhesions or implants (i.e., implants/adhesions involving multiple organs), as I wanted to compare how site/location of endometrioma might affect the association between infertility and the age in which a woman was diagnosed with endometriosis, separately. All medical records assessed were retrieved from OB/GYN clinics/hospitals located in Eastern North Carolina.

Because this study included a secondary data analysis of existing medical records, selection bias could have been an issue if only medical records of women portraying factors (i.e., in age, race/ethnicity, marital status, and socioeconomic status) were assessed (Laureate Education, 2012). Such threat to external validity, however, was addressed by assessing medical records of women of all races/ethnicities, marital statuses, socioeconomic statuses, and races/ethnicities. Assessing the medical records of women

belonging to a wide variety of ages, ranging from the teens to mid-30s, also addressed such threats to external validity. Furthermore, because extraneous variables also can limit the generalizability of results by studying only certain characteristics within a sample/population (i.e., endometriosis), such threats the validity were addressed by taking history of uterine fibroids into consideration when studying the association between the independent and dependent variables (Laureate Education, 2012). By addressing such threats, the sample was more generalizable to larger populations of women suffering from endometriosis, possibly facing infertility.

Results

Descriptive Statistics

Participant characteristics. As part of the inclusion criteria, all participants were required to be between the ages of 18 and 35 years and had had been diagnosed with endometriosis, with diagnoses having been documented in the medical records of each patient. All patients with the presence of uterine fibroids—along with their diagnosis of endometriosis—were gathered from documentation in the medical records. Descriptive statistics for the continuous variable age are presented in Table 2.

Table 2

Descriptive Statistics

	<i>N</i>	Minimum	Maximum	Mean	Median	Std. Deviation
Age	109	18	35	28.59	29	5.403

Frequencies and percentages for age. Out of 109 participants aged 18 to 35 years, the most common age at time of diagnosis was 35 years, with 17 women (15.6%)

being aged 35 when diagnosed with endometriosis. The second most common age at time of diagnosis was 33 years, with 14 women (12.8%) being aged 33 when diagnosed with endometriosis. In turn, the least common age at time of diagnosis was 23 years, with only one patient (0.9%) being 23 when diagnosed with endometriosis. The frequency for age is presented in Table 3.

Table 3

Frequency for Age

Age	Frequency	Percent (%)
18	4	3.7
19	7	6.4
20	3	2.8
21	2	1.8
22	7	6.4
23	1	0.9
25	4	3.7
26	6	5.5
27	7	6.4
28	8	7.3
29	7	6.4
30	6	5.5
31	5	4.6
32	3	2.8
33	14	12.8
34	8	7.3
35	17	15.6

Frequencies and percentages for fertility status. Out of 109 participants, only 30 participants (27.5%) were considered to be suffering from infertility, while 79 participants (72.5%) expressed no concerns of infertility, despite endometriosis diagnosis. The frequency for fertility status is presented in Table 4.

Table 4

Frequency for Fertility Status

Fertility Status	Frequency	Percent (%)
Fertile	79	72.5
Infertile	30	27.5
Total	109	100.0

Frequencies and percentages of site/implantation. Out of 109 participants, the most frequent location for endometriosis occurred equally amongst the ovaries and the fallopian tubes, with 34 participants (31.2%) found to have endometrioma on their ovaries and 34 participants (31.2%) found to have endometrioma on their fallopian tubes. The least frequent location amongst the study sample was the rectum, with only two (1.8%) participants found to have endometrioma located on their rectum. By assessing the frequencies for the site/locations of endometrioma amongst the study sample, I determined that two of the five site/locations (i.e., bladder and rectum) had low cell counts when a crosstabulation is performed. The frequencies for site/location of endometrioma is presented in Table 5.

Table 5

Frequencies for Site/Location of Endometrioma

Site/Location	Frequency	Percent (%)
Ovaries	34	31.2
Fallopian Tubes	34	31.2
Uterus	28	25.7
Bladder	11	10.1
Rectum	2	1.8

Total	109	100.0
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Frequencies and percentages of uterine fibroids. Out of 109 participants diagnosed with endometriosis, only 14 women (12.8%) had reported uterine fibroids. The majority of endometriosis patients in the sample, consisting of the remaining 95 women (87.2%), had not reported uterine fibroids. The frequency for uterine fibroids is presented in Table 6.

Table 6

Frequency for Uterine Fibroids

Uterine Fibroids	Frequency	Percent (%)
No	95	87.2
Yes	14	12.8
Total	109	100.0

Analysis of variance of the data. One-way ANOVA was performed for age and fertility status. The number of fertile woman in the sample was 79, with the mean age being 27.51 years, which presented a lower bound of 26.22 years and an upper bound of 28.79 years. The number of infertile women in the sample was 30, with the mean age being 31.43 years, which presented a lower bound of 30.32 years and an upper bound of 32.55 years. Further, the minimum age for those women considered fertile was 18 years, while the maximum age was 35 years. The minimum age for those women considered infertile, however, was 26 years; although, the maximum age also was 35 years.

According to the ANOVA statistics, on average, the fertile women were of younger age

when diagnosed with endometriosis than the infertile women. The p -value was found to be statistically significant with $p=.001$. The means are presented in Table 7.

Table 7

ANOVA Descriptives

Age	N	Mean	St. deviation	St. Error	95% C.I for Mean		Minimum	Maximum
					Lower Bound	Upper bound		
Fertile	79	27.51	5.735	.645	26.22	28.79	18	35
Infertile	30	31.53	2.979	.544	30.32	32.55	26	35
Total	109	28.59	5.408	.518	27.56	29.61	18	35

Note. (P=.001)

A contingency table analysis for uterine fibroids and fertility status was performed. Regarding the entire study population ($n=109$), it was determined that the majority of the fertile population (78.9%) did not have a presence of uterine fibroids, and only 28.6% of the fertile population did have a presence of uterine fibroids. Further, it was determined that the majority of the infertile population (71.4%) did have a presence of uterine fibroids, with only 21.1% of the infertile population not having a presence of uterine fibroids. From the crosstab results, amongst the study sample, women diagnosed with endometriosis who also have fibroids were more likely to be infertile. The p -value was calculated to be .000, which was statistically significant. Therefore, there was a statistically significant association between uterine fibroids and fertility status. The crosstabulation for uterine fibroids and fertility status is presented in Table 8.

Table 8

Fibroids and Fertility Status Crosstabulation

Fibroids	Frequencies	Fertile	Infertile	Total
No	95	78.9%	21.1%	100.0%
Yes	14	28.6%	71.4%	100.0%
Total	109	72.5%	27.5%	100.0%

Note. ($P=.000$)

Last, a contingency table analysis for site/location of implantation of endometrioma and fertility status was performed. Regarding the participants who were considered to be facing issues with infertility ($n=30$), the majority (44.1%) experienced endometrioma on their ovaries, followed by 41.2% of the infertile having experienced endometrioma on their fallopian tubes, and only 3.6% of the infertile having experienced endometrioma on their uterus. None (of the infertile participants [0.0%]) were found to be suffering from endometrioma on their bladder or rectum. From the crosstab, there was a small cell count for location of endometrioma on the bladder and on the rectum (e.g., expected count <5). The p -value for the Fisher's Exact Test was calculated to be .000, which was statistically significant. Therefore, there was a statistically significant association between site/location of implantation of endometrioma and fertility status. The crosstabulation for uterine fibroids and fertility status is presented in Table 9.

Table 9

Implantation and Fertility Status Crosstabulation Fisher's Exact

Site/Implantation Location	Frequencies	Fertile	Infertile	Total
Ovaries	34	55.9%	44.1%	100.0%
Fallopian Tubes	34	58.8%	41.2%	100.0%
Uterus	28	96.4%	3.6%	100.0%
Bladder	11	100.0%	0.0%	100.0%
Rectum	2	100.0%	0.0%	100.0%
Total	109	72.5%	27.5%	100.0%

Note. ($P=.000$)

Research Question 1

What is the association between age of women when diagnosed with endometriosis and infertility after controlling for history of uterine fibroids?

Hypothesis 1

Null hypothesis: There is no statistically significant association between age of women when diagnosed with endometriosis and infertility after controlling for history of uterine fibroids.

Alternative hypothesis: There is a statistically significant association between age of women when diagnosed with endometriosis and infertility after controlling for history of uterine fibroids.

Infertility and age when diagnosed with endometriosis. A logistic regression was performed to determine the effects of the independent variable (i.e. age when diagnosed with endometriosis) on the likelihood that participants suffer with infertility without

considering the effects of the covariates (i.e. history of uterine fibroids, site/location of endometrioma).

The model summary determined a -2 Log likelihood of 115.182^a, with a Cox and Snell R square of .113 and a Nagelkerke R square of .164. These statistics provide incentive that 11.3%-16.4% of the variability in the dependent variable (i.e. infertility) is accounted for by the independent variable (i.e. age when diagnosed with endometriosis). The model summary table is presented in Table 10.

Table 10

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	115.182 ^a	.113	.164

A Hosmer and Lemeshow test was performed, which presented a chi-square of 9.658 and a p-value of .209. Given that the p-value is greater than .05, we learn that the model is significant in regard to the data. The Hosmer and Lemeshow test is presented in Table 11. Furthermore, given concern for which participants are considered to be infertile and whether or not the predictor variables are predicting infertility, the differences between observed and expected fertile versus infertile participants were calculated. Observing the differences between the observed and expected fertile versus infertile patients, again, provides evidence that there is no indication of poor fit in regard to the model; with the model, for example, predicting ~9 (8.782) out of 11 participants' fertility status. The contingency table for the Hosmer and Lemeshow test is presented in Table 12

Table 11

Hosmer and Lemeshow Test

Step	Chi-square	Df	Sig.
1	9.658	7	.209

Table 12

Contingency Table for Hosmer and Lemeshow Test

	Fertile		Infertile		Total
	Observed	Expected	Observed	Expected	
1	11	10.392	0	.608	11
2	12	10.979	0	1.021	12
3	9	9.291	2	1.709	11
4	12	11.863	3	3.137	15
5	6	9.514	7	3.486	13
6	4	5.310	4	2.690	8
7	10	8.400	4	5.600	14
8	4	4.470	4	3.530	8
9	11	8.782	6	8.218	17

The overall predictive capacity of the model when only looking at the association between the independent variable (i.e. age) and the dependent variable (i.e. infertility) was determined to be 72.5%, which indicates that although the model is not strong, it is significant. The classification table is presented in Table 13.

Table 13

Classification Table

Observed	Fertile	Infertile	Percentage Correct
Fertility	Fertile	79	100.0

Overall Percentage	Infertile	30	0	.0 72.5
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Again, the B value for age was found to be .170, which can be interpreted to mean that greater values of age at time of diagnosis (e.g. increases in age) are associated with greater probability of being infertile. In other words, a 1-unit (e.g. 1-year) increase in age is associated with a .170 increase in the logit variable – or the probability of being infertile. Given that the p-value for age is .001, the variable is still considered to be a statistically significant predictor of infertility. Last, with an odds ratio of 1.185, it can further be concluded that a 1-unit (e.g. 1-year) increase in age is associated with a 1.185 times greater odds of experiencing infertility. Importantly, the analysis was interpreted with the variable “age” being measured on a continuous scale – with ages ranging from 18-35 years. In other words, the variable “age” was not categorized in to specific age groups. With that being said, it is appropriate to report that compared to a woman diagnosed with endometriosis at age 18 years, a woman diagnosed with endometriosis at age 35 years has a higher odds of experiencing infertility. Variables in the equation are presented in Table 14.

Table 14

Variables in the Equation

	B	S.E.	Wald	Df	Sig.	Exp(B)	95% for Lower	C.I. Exp(B) Upper
Age	.170	.053	10.153	1	.001	1.185	1.067	1.315

Constant	-6.001	1.649	13.249	1	.000	.002
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Presence of uterine fibroids. A logistic regression was performed, taking the covariate “uterine fibroids” into consideration in order to determine the effects of the independent variable (i.e. age when diagnosed with endometriosis) on the likelihood that participants suffer with infertility. With the variable “uterine fibroids” present, the odds ratio for age experienced a slight decrease, but remained statistically significant (p-value=.011), and the odds ratio for fibroids was 6.300, which also was found to be statistically significant (p-value=.006). With an Exp(B) of 6.300, we learn that patients with uterine fibroids have a 6.3 times greater odds of having infertility after controlling for age. In other words, presence of uterine fibroids was found to be a stronger independent predictor than age. Importantly, the results showed that the odds of infertility are higher for the women in the study sample who were diagnosed at an older age even after adjusting for fibroids. Variables in the equation are presented in Table 15.

Table 15

Variables in the Equation

	B	S.E.	Wald	Df	Sig.	Exp(B)	95% for Lower	C.I. Exp(B) Upper
Age	.141	.055	6.530	1	.011	1.151	1.033	1.282
Fibroids	1.841	.666	7.641	1	.006	6.300	1.708	23.232
Constant	-5.426	1.684	10.384	1	.001	.004		

A Hosmer and Lemeshow test was performed after the variable “uterine fibroids” was introduced, which presented a chi-square of 14.317 and a p-value of .074. Given that

the p-value is greater than .05, again, we learn that the model adequately describes the data. The Hosmer and Lemeshow test is presented in Table 16. Given concern for which participants are considered to be infertile and whether or not the predictor variables are predicting infertility when presence of uterine fibroids is introduced, the differences between observed and expected fertile versus infertile participants were calculated. Again, the contingency table for the Hosmer and Lemeshow test provides evidence that there is no indication of poor fit in regard to the model; with the model, for example, predicting 4 out of 4 participants' fertility status as being fertile and predicting 10 out of 10 participants' fertility status as being infertile. The contingency table for the Hosmer and Lemeshow test is presented in Table 17.

Table 16

Hosmer and Lemeshow Test

Step	Chi-square	Df	Sig.
1	14.317	8	.074

Table 17

Contingency Table for Hosmer and Lemeshow Test

	Fertile		Infertile		Total
	Observed	Expected	Observed	Expected	
1	11	10.371	0	.629	11
2	12	11.020	0	.980	12
3	8	7.785	1	1.215	9
4	12	12.379	3	2.621	15
5	6	9.381	6	2.619	12
6	4	5.124	3	1.876	7

7	9	6.868	1	3.132	10
8	3	4.591	4	2.409	7
9	10	7.481	2	4.519	12
10	4	4.000	10	10.000	14

Research Question 2

What is the association between age of women when diagnosed with endometriosis and infertility after controlling for specific sites of endometriosis?

Hypothesis 1

Null hypothesis: There is no statistically significant association between age of women when diagnosed with endometriosis and infertility after controlling for specific sites of endometriosis.

Alternative hypothesis: There is a statistically significant association between age of women when diagnosed with endometriosis and infertility after controlling for specific sites of endometriosis.

Site/location of endometrioma. A logistic regression was performed, taking the covariate “site/implantation” into consideration in order to determine the effects of the independent variable (i.e. age when diagnosed with endometriosis) on the likelihood that participants suffer with infertility. Specifically, dummy variables were made for each site/location (i.e. implantation(1)=ovaries; implantation(2)=fallopian tubes; implantation(3)=uterus; and implantation(4)=bladder) except for the dummy variable “rectum”, which was used as a reference category. Output from the logistic regression, however, showed that the model was poorly fit. The logistic regression for fertility status and site/location of implantation is presented in Table 18. Further, the chi-square test

also provided indication of poor fit, with three cells (30%) having an expected count of less than 5. The chi-square test is provided in Table 19. Therefore, testing research question 2 was not possible. However, referencing back to Table 9, the contingency table analysis for implantation and fertility, the only information we can gather in regards to RQ2 is that out of the participants who were considered to be facing issues with infertility (n=30), the majority (44.1%) experienced endometrioma on their uterus, which was proceeded by 41.2% of the infertile participants having experienced endometrioma on their fallopian tubes, and then only 3.6% of the infertile participants having experienced endometrioma on their uterus. Interestingly, none of the infertile participants (0.0%) were found to be suffering from endometrioma specifically on their bladder or rectum. Importantly, the p-value was calculated to be .000, which is statistically significant. From that, the only conclusion that can be made from those results – in regard to the second research question – are that there is a statistically significant association between site/location of implantation of endometrioma and fertility status amongst the study sample.

Table 18

Logistic Regression for Variables in the Equation

	B	S.E.	Wald	Df	Sig.	Exp(B)	95% for Lower	C.I. Exp(B) Upper
Age	.206	.072	8.247	1	.004	1.228	1.068	1.414
Implantation			9.969	4	.041			
Implantation(1)	21.214	26465.582	.000	1	.999	1633916054	.000	
Implantation(2)	20.860	26465.582	.000	1	.999	1146835331	.000	
Implantation(3)	16.819	26465.582	.000	1	.999	20150132.92	.000	
Implantation(4)	.272	28703.660	.000	1	1.000	1.313	.000	

Fibroids	2.630	1.120	5.516	1	.019	13.847	13.847	124.567
Constant	-	26465.582	.000	1	.999	.000	.000	
	27.650							

Table 19

Chi-Square Statistics

	Value	Df	Asymptotic Significance (2-sided)
Pearson Chi-Square	20.860	4	.000
Likelihood Ratio	26.909	4	.000
Linear-by-Linear Association	16.710	2	.000
N of Valid Cases	109	27.5%	100.0%

a. 3 cells (30.0%) have expected count less than 5. The minimum expected count is .55.

Summary

The purpose of the study was to determine whether an association exists between the time in which a woman is diagnosed with endometriosis (i.e. age of woman when diagnosed) and infertility after controlling for covariates of site/location of implantation of endometrioma (i.e. implantation) and presence of uterine fibroids (i.e. fibroids). In regard to RQ1, it was determined that a statistically significant association exists between age of women when diagnosed with endometriosis and infertility after controlling for history of uterine fibroids; thus, the null hypothesis for research question one was rejected. However, in regard to RQ2, due to low cell counts for the nominal variable “site/location” of endometrioma, the desired logistic regression analysis was not valid; hence, making it impossible to answer research question two. Only from the contingency

table analysis (Table 8) regarding RQ2 could it be concluded that there is a statistically significant association between site/location of implantation of endometrioma and fertility status amongst the study sample, with higher percentages of endometrioma found on the ovaries and fallopian tubes amongst those women considered to be infertile; lower percentages of endometrioma found on the uterus amongst those women considered to be infertile; and no reports of endometrioma located on the bladder or rectum amongst those women considered to be infertile ($p=.000$).

The findings of this study will be discussed further in Chapter 5, comparing the results and the statistical findings to existing literature. Chapter 5 also will provide a detailed discussion concerning the limitations of the study, implementing incentive for future research on the current study topic.

Chapter 5: Discussion, Conclusions, and Recommendations

Introduction

The purpose of this quantitative, cross-sectional study was to determine whether association existed between the age of women when diagnosed with endometriosis and infertility after controlling for the covariates site/location of implantation of endometrioma and presence of uterine fibroids among women in Eastern North Carolina. Diagnosis of endometriosis has been found to be delayed anywhere from 7-10 years and is considered to be poorly recognized by physicians in practice, often leading to misdiagnosis and/or suboptimal care (Johnston et al., 2015). Earlier diagnoses of the disease (e.g., diagnosis at an earlier age) could serve as a preventative strategy towards infertility.

Before this study, the age of women when diagnosed with endometriosis and the effects age at time of diagnosis might have on likelihood of infertility had not been studied (American Society for Reproductive Medicine, 2012). The findings of the study are expected to provide more information about the disease. Further, the study may supply readers with knowledge regarding the topic, which is expected to better help individuals recognize and understand normal menstrual cycles versus abnormal menstrual cycles, as well as normal symptoms associated with menstrual cycles versus serious abnormal pain that can be linked to endometriosis.

I took a quantitative approach, which was appropriate for measuring an association between variables (Creswell, 2013). The cross-sectional design consisted of a secondary data analysis of existing medical records of patients formally diagnosed with

endometriosis. Logistic regression analysis was performed with age acting as the independent variable, fertility acting as the dependent variable, and fibroids and location of endometrioma acting as covariates. A contingency table analysis also was performed to determine which age group(s) and which site(s)/location(s) were most commonly associated with infertility.

In the findings of the study, I found a statistically significant association between infertility and age in which a woman is diagnosed with endometriosis exists. Further, there was no indication of evidence of poor fit regarding the model used to determine the association between variables. The covariates, uterine fibroids, and site/location of implantation of endometrioma were both found to influence the association between infertility and the age in which a woman is diagnosed with endometriosis.

Interpretation of the Findings

The overall scope of the study was to determine the association between infertility and the age in which a woman is diagnosed with endometriosis. The population of this study consisted of 109 women aged 18 to 35 years. The most common age at time of diagnosis within the study population was found to be the oldest age in the study sample (i.e., 35 years), with 17 women (15.6%) being aged 35 years when diagnosed with endometriosis. The second most common age at time of diagnosis within the study population was 33 years, with 14 women (12.8%) being aged 33 years when diagnosed with endometriosis, which also is one of the oldest ages at time of diagnosis within the study population. The least common age at time of diagnosis was 23 years, with only one patient (0.9%) being aged 23 years when diagnosed with endometriosis. In contrast to the

most common age at time of diagnosis (i.e., 35 years), which also was the oldest age considered in the study population, age 23 years at time of diagnosis was one of the youngest ages at time of diagnosis within the study population. Further, the youngest age at time of diagnosis in the study population (i.e., 18 years), accounted for only four of the 109 participants in the study population (3.7%). These frequency statistics for ages at time of diagnosis for the study population can be considered consistent with claims that endometriosis diagnoses are delayed (i.e., diagnosed at a later age opposed to a younger age). Many patients claim to have a long history of doctor visits due to lower abdominal and pelvic pain, receiving no support from physicians in regard to the pain aside from being written a prescription for painkillers (Johnston et al., 2015). The frequency statistics for ages at time of diagnosis for the study population reflected such claims given that older ages (i.e., 33-35 years) at time of diagnosis were more common than younger ages (i.e., 18-23 years) at time of diagnosis.

Uterine fibroids and endometriosis may be associated with each other (Nezhat et al., 2016; Uimari et al., 2011). Although uterine fibroids seldom are the sole cause of infertility in women, they become a concern when coexisting with endometriosis, especially because of significant overlap of symptoms between endometriosis and uterine fibroids when it is difficult to discern which pathology is responsible for patients' complaints (Nezhat et al., 2016). Further, patients who suffer from both endometriosis and uterine fibroids have an increased risk for infertility, which is thought to be due to influences related to the association between the two conditions (Ciavattini et al., 2013). The first research question addressed in this study included the following: What is the

association between infertility and age of women when diagnosed with endometriosis after controlling for history of uterine fibroids?

Although I found that most of the population considered to be suffering with infertility did not have a history of uterine fibroids (66.7%), in a logistic regression analysis, I determined that patients within the study population had a 6.3 times greater odds of having infertility based on age when diagnosed with endometriosis when a history of uterine fibroids was present, than when based off age of diagnosis alone. Further, the value associated with the effects of uterine fibroids on the association between age at time of diagnosis and infertility was found to be statistically significant (p -value=.006).

The most common phenotypes of endometriosis among women is superficial endometriosis, with sites of endometrioma located in the pelvic area, most commonly presented on and below the ovaries (Menakaya et al., 2014). Variation in the sites of endometrioma and how those sites may or may not affect chances of infertility are lacking (Maggiore et al., 2016). The second research question addressed in this study included the following: What is the association between infertility and age of women when diagnosed with endometriosis after controlling for the specific sites of endometriosis?

The frequency analysis for site/location of implantation of endometrioma was found to be consistent with the literature in that the majority of the 109 participants (31.2%) in the study population had an area of concern located on the ovaries. However, the exact same percentage of participants (31.2%) in the study population had an area of

concern located on the fallopian tubes. Disease affecting the fallopian tubes accounts for nearly 25%-35% of all infertility cases (Pereira & Kilgman, 2016). In the contingency table analysis for site/location of implantation of endometrioma and infertility, I found that out of the 30 participants who were considered to be infertile, the majority, or 15 out of 30 (50%), had endometrioma located on the ovaries, where 14 out of 30 (46.7%) participants who were considered to be infertile had endometrioma located on the fallopian tubes. I stopped reviewing here. Please go through the rest of your chapter and look for the patterns I pointed out to you. I will now look at your references.

Beyond the scope of the literature, however, the association between infertility and the age in which a woman is diagnosed with endometriosis when considering the covariate “site/location” of implantation of endometrioma could not be determined from this study given the inability to answer research question two due to low cell count for the nominal variable “site/location”. However, from the contingency table analysis, it could be concluded that there is a statistically significant association between site/location of implantation and fertility status ($p=.000$).

Limitations of the Study

This study contained several limitations. The first limitation includes the fact that this study uses a secondary analysis of existing data. One major limitation regarding the conducting of a secondary analysis of existing data includes the fact that the data was not originally collected to address the particular research question or to test the particular research hypotheses (Cheng & Phillips, 2014). Another major limitation regarding the conducting of a secondary analysis of existing data for this study includes the fact that I,

as the researcher, was not involved in the initial data collection process; therefore, being unaware of any nuances in the data collection process that might be important to the interpretation of the key variables (Cheng & Phillips, 2014). A third limitation relates to the fact that race/ethnicity among women whose medical charts were assessed was not taken into consideration. Perhaps the association between the age in which a woman is diagnosed with endometriosis and infertility, even after taking the covariates site/location of implantation of endometrioma and presence of uterine fibroids into consideration, might differ when the factor of race is considered, even though endometriosis rates are considered to be very similar among races (Gerlinger et al., 2012). A fourth limitation relates to the fact that marital status of women whose medical charts were assessed also was not taken into consideration. Perhaps such sociodemographic variable could influence fertility status among the study population given that married couples are more likely to try to conceive than unmarried couples (Laplante, & Fostik, 2015). For example, given that some of the younger participants in the study population (i.e. 18-21 years) might not be married and/or trying to conceive, the status from their medical charts stating that they are considered to not be infertile (or not struggling with infertility issues) might not be accurate given that they might not be at a stage in their lives where they are trying to have a baby or are even sexually active. The most important limitation to consider for this study is the fact that there simply were not enough cases in the study sample. Had there been more cases, it is likely that there would have been a higher cell count for the specific site/locations of endometrioma that currently are lacking. Due to low cell count for the variable site/location of implantation of endometrioma, research

question two simply could not be answered. As previously mentioned, perhaps more controls such as race and marital status – to name a few – could have contributed to the relevance of this study.

Recommendations

I have a few recommendations for further study. The first recommendation for further study involves repeating this study with a broader cross-section among study participants. For example, a larger sample size might strengthen the generalization of the study results in regard to how accurately they reflect and represent a broader population. The second recommendation for further study involves introducing more covariates to be considered when assessing the association between infertility and the age in which a woman is diagnosed with endometriosis. Introduction of more covariates could, for example, further control for any potential confounding effects on the association between variables. In other words, I would recommend taking race/ethnicity into consideration, as race/ethnicity might have effects on infertility, alone. Further, taking marital/relationship status into consideration might affect whether an individual is sexually active or not; hence, trying to conceive versus not trying to conceive. Such covariate could better represent the fertility status of participants, especially given that single participants might not be evaluated to be suffering from infertility, but given their marital/relationship status, may actually be unaware of infertility due to not being sexually active and/or not trying to conceive. For example, there were study participants in my sample population who were diagnosed with endometriosis but not documented to be suffering from infertility. With that said, it is possible that the data used for this study is flawed given

that fertility status for some of the participants diagnosed with endometriosis and not considered to be suffering from infertility might solely be due to the fact that some of those participants are single and/or not sexually active. All in all, future research should include a significantly higher count of both cases and variables.

Implications

Social Change

The findings of the study might lead to social change by adding new evidence to a topic within women's health that has been considered a controversial topic for far too long (Kovacs, 2015). The findings of the study are expected to provide accurate information for the use of disproving currently existing information and theories about the disease that perhaps are false/misleading. The study is expected to serve as an asset for supplying readers with knowledge regarding the topic, which ultimately is expected to better help individuals recognize and understand "normal" menstrual cycles versus abnormal menstrual cycles, as well as "normal" symptoms associated with menstrual cycles versus serious abnormal pain that can be linked to endometriosis. The study also is expected to serve as evidence for why physicians should be more concerned for endometriosis being diagnosed carefully and more promptly. Furthermore, in regard to social change, the study hopefully will be able to provide a sense of support for women who suffer from the disease, inspiring them not to overlook health emergencies out of fear or frustration that physicians might dismiss them. Women should be made aware that effective treatment is available if they seek it. The study also is expected to promote social change by further supporting the devastating effects of endometriosis that burden

women and their families since the disease currently is not recognized as a medical disability (Jones, 2016). In regard to the study results, specifically, social change is expected to be implemented by preventing infertility amongst woman who suffer from both endometriosis and uterine fibroids, who are at risk for infertility due to the cluster of endometriosis and uterine fibroids, together. In other words, preventative programs aimed at better educating women on the risks of endometriosis and uterine fibroids should be better implemented.

Theoretical Framework

Again, the theoretical framework for this study consisted of the General Model of Total Patient Delay, also known as “the Andersen Model,” which is widely used for a variety of disorders (Walter, Webster, Scott, & Emery, 2012). The theory suggests that reducing diagnostic delays may result in improved prognosis for most disorders (Walter et al., 2012). With that said, the Andersen Model explains important aspects regarding delay stages (e.g. appraisal, illness, behavioral, scheduling, treatment) and was used in the current study as a foundation for whether diagnosis of endometriosis poses a higher incidence for risk (i.e. infertility) based on age – especially upon considering the co-variates uterine fibroids and site/location of implantation of endometrioma. The theoretical model also aided in the explanation of why certain time intervals exist between onset of symptoms of endometriosis and formal diagnosis given that the model suggests that diagnostic delay results from conceptual beliefs about one’s symptoms; behavioral factors such as strategies for self-appraisal; and techniques for coping with illness and emotional reaction (Walter et al., 2012).

Recommendations for Practice

The findings from this study highlight the importance of earlier diagnosis of endometriosis opposed to later diagnosis of endometriosis in order to potentially prevent issues with infertility. For example, the data has shown that a statistically significant association exists between infertility and the age in which a woman is diagnosed with endometriosis, with infertility being more frequent among those aged 35 years at time of endometriosis diagnosis opposed to those aged 23 years at time of endometriosis diagnosis. Further, the findings of the study address the implications associated with the presence of uterine fibroids when paired with diagnosis of endometriosis, as well as conclusions that can be made in regard to the specific site/location of implantation of endometriosis when considering the odds of infertility.

Conclusion

Although endometriosis has been well-documented in medical texts for more than 4,000 years and was formally discovered microscopically by Karl von Rokitansky in 1860 (Nezhat, Nezhat, & Nezhat, 2012), the disease remains the subject of debate – especially over the last decade (Brosens & Benagiano, 2011). Furthermore, although laparoscopic procedure was introduced in the early 1960s, which stands successful in distinguishing three different clinical presentations of endometriosis (i.e. peritoneal, deep adenomyotic, and cystic ovarian) (Brosens & Benagiano, 2011), diagnosis of endometriosis still is found to be delayed anywhere from 7-10 years and is poorly recognized by physicians in practice, often leading to misdiagnosis and/or suboptimal care (Johnston et al., 2015).

Although there is reason to believe that an optimal approach to managing infertility requires a method associated with routine and timely measures, investigation concerning causes of female infertility is increasingly receiving less attention (Bell, 2014). With that said, this study aimed to determine whether earlier diagnosis of endometriosis (e.g. diagnosis at an earlier age) could be considered as a preventative strategy towards infertility. Although currently existing literature suggests that suppressive medical treatment of endometriosis does not benefit fertility, the potential importance concerning the age of women when diagnosed with the disease never has been taken into consideration (American Society for Reproductive Medicine, 2012; Radhika et al., 2016) before this study.

This study examined the association between infertility and the age in which a woman is diagnosed with endometriosis when the covariates, uterine fibroids and site/location of implantation of endometrioma, are taken into consideration. The findings from this quantitative study add support to the idea that delayed diagnosis (or diagnosis at a later age opposed to a younger age) is associated with higher frequency of infertility; further supporting claims that earlier diagnoses could be considered as preventative strategies against infertility. Since addressing the gap in the literature, this study has provided important information related to delayed diagnosis of endometriosis and how such delays in diagnoses are associated with higher incidence of infertility, with a statistically significant association existing between infertility and the age in which a woman is diagnosed with endometriosis after controlling for the presence of uterine fibroids among the study population. Findings from this study demonstrate and support

the importance of managing infertility by eradicating the delay that exists in regard to endometriosis diagnoses.

In conclusion, applying attention to this research study is critical to the elimination regarding the contribution endometriosis has on the fate of young women potentially being faced with infertility issues. Given the findings of this study, it is evident that endometriosis can be eliminated as the number one cause of infertility in women if the delay in diagnosis of the disease, which currently exists, is eradicated. For example, if women being diagnosed at age 35 years could be lowered, with more diagnoses taking place between the ages of 18-25 years, infertility among women aged 18-35 years, specifically, could be reduced significantly; especially given that the results of this study show a 62% greater odds of facing infertility based on age when diagnosed with endometriosis, with 20% of infertile participants in the study population being diagnosed at age 35 years and 0% of infertile participants being diagnosed between the ages of 18 and 25 years. Given that endometriosis can not be self-diagnosed, it is critical that physicians in practice aim to better recognize the disease.

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