

## Hysterectomy with Ovarian Preservation in Premenopausal Women: Predisposition to Early Ovarian Failure

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### Abstract

*Introduction: Hysterectomy is the most common surgical procedure among the women aged 30 to 47 worldwide. The aim of this study is to estimate the risk of early ovarian failure in premenopausal age group women undergoing hysterectomy with ovarian preservation. Methods: A prospective study was conducted among the women aged 30 to 47 years undergoing hysterectomy with or without bilateral oophorectomy (n=546) during 2010. Blood samples and questionnaire data were obtained annually for up to 5 years after hysterectomy. Ovarian failure defined as follicle-stimulating hormone (FSH) levels 40 IU/L or higher, was calculated. Results: Ovarian failure occurred in among 106 women from total 543 women with hysterectomy without bilateral oophorectomy. Women undergoing hysterectomy were at nearly a twofold increased risk for ovarian failure as compared to women with intact uteri. Conclusions: Increased risk of earlier ovarian failure is a possible consequence of premenopausal hysterectomy. The cause of earlier ovarian failure is unresolved whether it is the surgery itself or the underlying condition leading to hysterectomy, physicians and patients should take into account this possible sequela when considering options for treatment of benign conditions of the uterus.*

**Keywords:** *Premenopausal Hysterectomy; Ovarian Failure; Bilateral Oophorectomy.*

### Introduction

Hysterectomy is the most common surgical procedure among women

world wide. Data from the Behavioral Risk Factor Surveillance System shows that up to 40% of women will have a hysterectomy during their lifetimes [1]. In addition, hysterectomy rates vary within countries according to both patient's related factors such as race, socioeconomic and education status, private health insurance and attitudes toward surgery, as well as the training and practice of the surgeon. Although uterine artery embolization, endometrial ablation or progestin-releasing intrauterine devices are increasingly used for treating common indications for hysterectomy such as fibroids and dysfunctional uterine bleeding, hysterectomy rates still remain high, [1]. At the time of hysterectomy the ovaries can either be removed or retained. Oophorectomy does not add significantly to the duration or immediate complications of hysterectomy, but may have significant implications for both short and long-term health, like surgical menopause may be associated with long-term cardiovascular, psycho-sexual and cognitive dysfunction [2,3] makes it timely to evaluate the role of oophorectomy at the time of hysterectomy for benign disease. Further, it remains unclear whether HT taken following surgical menopause modifies subsequent cardiovascular or cognitive function. The American College of Obstetricians and Gynaecologists (ACOG) has recently changed its recommendation regarding retention or removal of normal ovaries at the time of hysterectomy from suggesting that aged 45 years should be the 'cut off' for oophorectomy to advice that 'strong consideration should be made for retaining normal ovaries in premenopausal women who are not at increased genetic risk of ovarian cancer' (<http://www.acog.org/>).

An unresolved concern with hysterectomy with ovarian preservation is whether it increases risk for early menopause [4]. The majority of women having premenopausal hysterectomies retain at least one ovary [4]

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because of evidence that the physical and psychological benefits derived from keeping the ovaries outweigh the possibility of ovarian pathology, including cancer [5, 6]. Although it is clear that most women do not lose ovarian function in the short-term after hysterectomy without bilateral oophorectomy, there has long been suspicion that these women are at increased risk for early ovarian failure [7]. Earlier menopause in turn has serious health implications including increased risk for osteoporosis, cardiovascular disease and all-cause mortality.

In this report we estimate the risk of earlier ovarian failure (defined as a serum follicle stimulating hormone (FSH) greater than equal to 40 IU/L) after pre-menopausal hysterectomy using data from a prospective study of ovarian function after hysterectomy conducted in rural institutional hospital in south India.

## Methods

A total of 546 patients who had undergone hysterectomy in the department of obstetrics and gynaecology, Adichunchunagiri Institution of Medical sciences, Bellur, during 2010. Blood samples and questionnaire data were obtained annually for up to 5 years after hysterectomy with ovarian preservation (n-106), and also asked about vegetative and psychological problems after the operation. All were under 45 years old and had at least one ovary left intact. Ethical approval was obtained from Ethics Committee for each year of the study. Potentially eligible women for the hysterectomy group were identified from the gynaecological surgical records. Written informed consent was obtained. Women were eligible for inclusion in the hysterectomy group if they were aged <46 years at the time of surgery, did not have a gynaecological malignancy. Data were collected on demography and gynaecological history. Surgical details, including the primary reason for surgery (patient defined), type of hysterectomy, post-operative complications. An FSH level > 40 IU/L was used to define the menopause [37]. Women after hysterectomy FSH levels were measured yearly after surgery for a total of five years. If any FSH measurement was > 40 IU/L, the participant was deemed to be menopausal and was not included in any further follow up of FSH levels. All women were followed up to five years, or until FSH measurement of >40 IU/L was reported and statistical analyses were performed and calculated risk of ovarian failure among premenopausal

women who underwent hysterectomy with ovarian preservation was calculated.

Because of the possibility that dysfunctional uterine bleeding may herald the menopause, women who

**Table 1:** Age-Majority of women (42%) were between 41- 45 yr

Age (years)	Number	Per cent
< 30		-
31- 35	27	25%
36-40	34	32%
41-45	45	42%

**Table 2:** Parity-Majority (81%) of them were multiparous women

Parity	Number	Percent
Nulliparous	20	19%
Multiparous	86	81%

**Table 3:** The most common symptoms the women presented with Hot flush (29%)

Symptoms	Number	Percent
Hot flushes	31	29%
Vaginal irritation	30	28%
Pelvic pain	25	23%
Depression/Mood swing	20	18%

**Table 4:** The primary reason for hysterectomy was Fibroid uterus (34%)

Primary reason for hysterectomy	Number	Percent
Heavy menstrual bleeding	22	21%
Pelvic pain including endometriosis	15	14%
Infection/Adhesion	10	9%
Fibroid	36	34%
Prolapse	17	16%
Dysmenorrhoea (Adenomyosis)	06	6%

**Table 5:** Majority of women had undergone Abdominal hysterectomy with bilateral ovaries preserved (41%)

Abdominal hysterectomy with unilateral opherectomy	30	28%
Abdominal hysterectomy without bilateral opherectomy	43	41%
Laparoscopic hysterectomy with unilateral opherectomy	15	14%
Laparoscopic hysterectomy without bilateral opherectomy	18	17%

**Table 6:** Histological finding, majority (48%) was Fibroid

Histological Findings	Number	Percent
Uterine fibroids	51	48%
Adenomyosis	20	19%
Endometrial Hyperplasia	15	14%
Endometrial polyps	17	16%
No pathology	03	3%

**Table 7:** Majority of women were defined menopause by serum FSH value > 40 after 4- 5 years of hysterectomy with ovarian preservation

Duration after surgery(years)	Serum FSH>40	Percent
1	06	6%
2	10	9%
3	13	12%
4	15	14%
5	20	19%

**Table 8:** About (60%) of women, the serum FSH level was > 40 among total 106 women in whom ovaries was preserved back during surgery

FSH < 40	42	39%
FSH > 40	64	60%

had hysterectomies were stratified into those with pathology (fibroids, adenomyosis, endometrial hyperplasia or polyps) and those without.

## Results

Total 546 hysterectomy was performed in 1 year duration and among them about 106 women were studied in whom ovaries were preserved during hysterectomy. Majority of women (42%) were between 42- 45yr. Majority (81%) of them were multiparous women. The most common symptoms the women presented with Hot flush (29%). The primary reason for hysterectomy was Fibroid uterus (34%). Majority of women had undergone abdominal hysterectomy with bilateral ovaries preserved (41%). Histological finding, majority (48%) was Fibroid. Majority of women were defined menopause by serum FSH value > 40 after 4-5 years of hysterectomy with ovarian preservation. About (60%) of women, the serum FSH level was > 40 among total 106 women in whom ovaries was preserved back during surgery.

## Discussion

This prospective study showed the risk of ovarian function after hysterectomy in which serial hormone measurements were performed. Farquhar and colleagues also reported an increased risk for ovarian failure among women within 3.7 years of hysterectomy that was more pronounced for women having unilateral oophorectomy [8]. The strength of our study include its large sample size, prospective design, serial measurements of hormone levels and the mid to late premenopausal years (35 to 44 years). The limitation of our analysis is the use of FSH as a marker of ovarian failure. Although FSH is the biomarker most commonly used to categorize menopausal status, it is well-recognized that there is no cut-point that absolutely distinguishes premenopausal from postmenopausal women [9]. A value of 40 IU/L, which is commonly used in the menopause literature, is a very specific but less sensitive indicator of ovarian failure. Few premenopausal women will have an FSH value >40

IU/L, but some post-menopausal women will have lower FSH values. Using a cut-point of 20 or 30 IU/L would likely have increased sensitivity, but more premenopausal women would have been classified incorrectly as having ovarian failure. The cause of ovarian failure after hysterectomy with ovaries preserved is unknown but there are explanations like, one of the most prominent hypotheses is that the surgery to remove the uterus compromises the blood flow to the ovaries, which could result in reduced production of hormones leading to earlier ovarian failure [10]. The evidence for this mechanism is mixed, with most but not all studies finding a reduction in ovarian blood flow after hysterectomy. Another hypothesis is that the uterus has an inhibitory influence of pituitary FSH secretions and consequently has an effect on follicular atresia [10]. It is posited that removal of the uterus allows FSH levels to rise and accelerates follicular depletion, leading to earlier menopause. An alternative explanation for the earlier menopause observed among women undergoing hysterectomy is that it is not the surgery itself but the condition that led to the surgery that ovarian failure associated with common indications for hysterectomy such as dysfunctional uterine bleeding, fibroids or endometriosis [11]. It is possible that certain cases of dysfunctional uterine bleeding that lead to hysterectomy are a more extreme manifestation of the menstrual changes that many women experience in the months or years preceding natural menopause.

While it is unresolved whether it is the surgery itself or the underlying condition leading to hysterectomy that is the cause of earlier ovarian failure, it is important that physicians consider this possible sequela when discussing with patients options for treatment of benign conditions of the uterus. In addition, because not all women will experience overt symptoms of menopause, women who have undergone premenopausal hysterectomy may warrant closer monitoring of bone density or cardiovascular risk factors because of their possible risk of early ovarian failure.

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