



## COMPARISON OF SERUM ESTRADIOL LEVEL BETWEEN SURGICAL AND NATURAL MENOPAUSE

**Mehnaz Rashida Hossain<sup>1\*</sup>, Nigar Sultana<sup>2</sup>, Jenifa Haque Zuthy<sup>3</sup>, Rawshon Jahan Bithi<sup>4</sup>**

<sup>1</sup>Registrar, Dhaka Community Medical College & Hospital, <sup>2</sup>Medical Officer, OSD, DG Health, Mohakhali, Dhaka, <sup>3</sup>Assistant Registrar, NICRH, Mohakhali, Dhaka, <sup>4</sup>Assistant Surgeon, Sheikh Hasina Medical College Hospital, Tangail.

**\*Corresponding Author: Mehnaz Rashida Hossain**

Registrar, Dhaka Community Medical College & Hospital, Tangail.

Article Received on 01/01/2023

Article Revised on 21/01/2023

Article Accepted on 10/02/2023

### ABSTRACT

Surgical menopausal women suffer from sudden hormonal imbalance due to decrease in ovarian function even after simple hysterectomy without any oophorectomy. Many postmenopausal symptoms were observed in women with surgical menopause. The aim of this study was to compare the serum estradiol level between surgical and natural menopause. This cross-sectional comparative study was conducted in outpatient Department of Obstetrics and Gynaecology, Institute of Child and Mother Health (ICMH), Matuail, Dhaka from March 2019 to June 2020. A total of 60 subjects were selected based on exclusion and inclusion criteria, where group A consisted of 30 surgical menopausal women and group B consisted of 30 natural menopausal women. Data was collected in pre-fixed questionnaire form by the researcher herself. Mean serum estradiol was found  $10.6 \pm 3.0$  pg/ml in group A and  $20.3 \pm 8.0$  pg/ml in group B. The difference was statistically significant ( $p=0.001$ ) between two groups. Normal serum estradiol level in menopause is 10-25 pg/ml with an average of 15 pg/ml. In group A, 19 (63.3%) and 11 (36.7%) study subjects had serum estradiol level of  $\leq 10.0$  pg/ml and 10.1-20 pg/ml, and in group B, 1 (3.3%), 19 (63.3%), 6 (20%) and 4 (13.3%) had serum estradiol level of  $\leq 10.0$  pg/ml, 10.1-20 pg/ml, 20.1-30 pg/ml and  $>30$  pg/ml respectively. After analyzing the results, it can be concluded serum estradiol level was significantly decreased in surgical menopause than natural menopause.

**KEYWORDS:** Surgical menopause, natural menopause, serum estradiol.

### INTRODUCTION

Natural menopause is defined as complete cessation of menstruation due to depletion of follicular activities of the ovaries and gradual decrease in production of hormones. It takes at least 12 consecutive months of amenorrhea to confirm, and usually occurs at age of 45 to 55 years. If it occurs before the age of 40, it can be considered as premature menopause.<sup>[1]</sup> Surgical menopause is not physiological and can be defined as cessation of menstruation due to surgical removal of the uterus (hysterectomy), leaving one or both ovaries or the removal of both ovaries.<sup>[2]</sup> When both the ovaries are removed during hysterectomy, ovarian hormones (estradiol and progesterone) level decrease abruptly. About one-third of hysterectomized women may lose their ovarian function following one to two years, even after preservation of both ovaries during operation.<sup>[3]</sup> The mechanism by which the ovarian hormone levels decrease is not clear. But it is thought that decrease level of ovarian hormones is due to interruption in ovarian blood flow. The ovary is supplied by the ovarian artery and uterine artery. The uterine artery makes an anastomosis with the ovarian artery. During

hysterectomy this anastomosis is disrupted, which results decreased blood supply to the ovary and subsequent reduction in ovarian function. In surgical menopausal women, due to decrease in ovarian hormones many physiological and metabolic conditions are altered. As a result, they suffer from severe vasomotor symptoms, hypertension, dyslipidemia, cardiovascular disease, osteoporosis, and many others systemic complication.<sup>[4]</sup>

Different studies have been revealed that decreased level of serum estradiol level may be associated with development of various complications in surgical menopausal women like that of natural menopause. So, surgical menopausal women are at higher risk of vasomotor symptoms, anxiety, hypertension, osteoporosis, and cardiovascular diseases.

### METHODS

This cross sectional comparative study was conducted in the department of Obstetrics and Gynecology, Institute of Child and Mother Health (ICMH), Matuail, Dhaka from March 2019 to June 2020. Total 60 menopausal women who attended in the Outpatient Department were

enrolled in this study after getting ethical approval from the institutional review board (IRB), ICMH. The study subjects were divided into two groups. Group A (Consisted of 30 surgical menopausal women) and group B (consisted of 30 natural menopausal women). Patients age between 44 to 52 years with surgical removal of Uterus in past 1-3 years, and women with permanent cessation of menstruation in past 1-3 years women were included in this study. Women with history of hypertension, diabetes mellitus, hypothyroidism, hyperthyroidism, renal disease, history of taking any hormone replacement therapy, steroids, any history of ovarian malignancy treated with chemotherapy or radiotherapy for any types of disease were excluded from the study. Informed written consents were obtained from all participants. Subjects were selected purposively according to availability of patients. Detailed personal history, family history and medical history was taken. Cases were assigned into two groups based on the nature of menopause surgical and natural. 5ml of fasting blood

sample was collected from each patient of both groups by venipuncture and was kept in a clot activated red capped tube. Then centrifuged for at least 15 minutes and analyzed for serum estradiol levels in every patient by chemiluminescence immunoassay method using Siemens Advia Centaur XP and UniCel DxI 600 Access Immunoassay System in Department of Microbiology, Bangabandhu Sheikh Mujib Medical University. Data were analyzed statistically by using Statistical Package version for Social Science (SPSS-26 version) and presented as table and figure, P-value  $P < 0.05$  was accepted as level of significance.

## RESULTS

A total of 60 patients with surgical menopause and natural menopause who fulfilled the selection criteria were included in this study. Patients, who were divided into two groups, Group A (Consisted of 30 surgical menopausal women) and group B (Consisted of 30 natural menopausal women).

**Table I: Demographic characteristics of the study patients (N=60).**

Demographic characteristics	Group A (n=30)		Group B (n=30)		p value
	n	%	n	%	
Age (years)					
44-46	7	23.3	5	16.7	
47-49	15	50.0	14	46.7	
50-52	8	26.7	11	36.7	
Mean±SD	48.0	±2.3	48.6	±1.9	<sup>a</sup> 0.275 <sup>ns</sup>
Range (min-max)	44.0	-52.0	46.0	-52.0	
Educational status					
SSC	5	16.7	6	20.0	
HSC	15	50.0	19	63.3	<sup>b</sup> 0.328 <sup>ns</sup>
Graduate	10	33.3	5	16.7	
Occupational status					
Housewife	11	36.7	13	43.3	
Employee	10	33.3	8	26.7	<sup>b</sup> 0.823 <sup>ns</sup>
Others	9	30.0	9	30.0	

ns= not significant

<sup>a</sup>P value reached from unpaired t-test

<sup>b</sup>P value reached from chi square test

Table I shows that 15(50.0%) of the patients belonged to age 47-49 years in group A and 14(46.7%) in group B. The mean age was found 48.0±2.3 years in group A and

48.6±1.9 years in group B. Half (50.0%) of the patients had completed HSC education in group A and 19(63.3%) in group B. 11(36.7%) patients were housewives in group A and 13(43.3%) in group B. Age, educational and occupational status were not statistically significant ( $p > 0.05$ ) between two groups.

**Table II: Distribution of the study patients according to postmenopausal symptoms (N=60).**

Postmenopausal symptoms	Group A (n=30)		Group B (n=30)		p value
	n	%	n	%	
Hot flush	16	53.3	8	26.7	0.035 <sup>s</sup>
Vaginal dryness	11	36.7	8	26.7	0.405 <sup>ns</sup>
Dyspareunia	9	30.0	8	26.7	0.774 <sup>ns</sup>
Dysuria	11	36.7	7	23.3	0.260 <sup>ns</sup>
Urinary incontinence	9	30.0	8	26.7	0.774 <sup>ns</sup>
Mood swing	11	36.7	9	30.0	0.584 <sup>ns</sup>

Cognitive aging & dementia	3	10.0	2	6.7	0.500 <sup>ns</sup>
Muscle & joint pain	15	50.0	10	33.3	0.190 <sup>ns</sup>
Anxiety & irritability	6	20.0	4	13.3	0.488 <sup>ns</sup>
Change in sexual desire	4	13.3	7	23.3	0.317 <sup>ns</sup>

s= significant, ns= not significant  
P value reached from chi square test

statistically significant ( $p < 0.05$ ) but other postmenopausal symptoms were not statistically significant ( $p > 0.05$ ) between two groups.

Table II shows that 16(53.3%) patients were found hot flushes in group A and 8(26.7%) in group B. Which was

**Table III: Distribution of the study patients according to time of onset (in years) of postmenopausal symptoms (N=60)**

Postmenopausal symptoms	Time of onset (years)		p value
	Group A (n=30)	Group B (n=30)	
	Mean±SD	Mean±SD	
Hot flush	0.88±0.34	1.00±0.38	0.441 <sup>ns</sup>
Vaginal dryness	0.91±0.30	1.12±0.23	0.117 <sup>ns</sup>
Dyspareunia	1.00±0.35	1.19±0.26	0.228 <sup>ns</sup>
Dysuria	0.82±0.34	1.14±0.24	0.051 <sup>ns</sup>
Urinary incontinence	0.78±0.26	1.00±0.38	0.180 <sup>ns</sup>
Mood swing	0.73±0.26	1.00±0.43	0.100 <sup>ns</sup>
Cognitive aging & dementia	1.33±0.29	1.25±0.35	0.789 <sup>ns</sup>
Muscle & joint pain	0.80±0.32	1.10±0.46	0.066 <sup>ns</sup>
Anxiety & irritability	0.83±0.41	1.13±0.25	0.231 <sup>ns</sup>
Change in sexual desire	0.88±0.48	0.93±0.34	0.843 <sup>ns</sup>

ns= not significant  
P value reached from unpaired t-test

mood swing, cognitive aging & dementia, muscle & joint pain, anxiety & irritability and change in sexual desire were not statistically significant ( $p > 0.05$ ) between two groups.

Table III shows that time of onset of hot flush, vaginal dryness, dyspareunia, dysuria, urinary incontinence,

**Table IV: Distribution of the study patients according to serum estradiol level (N=60)**

Serum estradiol level (pg/ml)	Group A (n=30)		Group B (n=30)		Mean difference	p value
	n	%	n	%		
≤10.0	19	63.3	1	3.3		
10.1-20.0	11	36.7	19	63.3		
20.1-30.0	0	0.0	6	20.0		
>30.0	0	0.0	4	13.3		
Mean±SD	10.6	±3.0	20.3	±8.0	-9.7	0.001 <sup>s</sup>
Range (min-max)	6.4	-18.7	10.0	-35.0		

s= significant  
P value reached from unpaired t-test

Table IV shows that 19(63.3%) patients had serum estradiol level ≤10.0 pg/ml in group A and 1(3.3%) in group B. The mean serum estradiol was found 10.6±3.0 pg/ml in group A and 20.3±8.0 pg/ml in group B. The difference was statistically significant ( $p < 0.05$ ) between two groups.

## DISCUSSION

The mean age was 48.0±2.3 years in group A and 48.6±1.9 years in group B. The difference was statistically not significant ( $p > 0.05$ ) between two groups. Kaur *et al.*<sup>[5]</sup> found that the mean age was 47.46±2.61 years in surgical menopause and 48.42±2.60 years in natural menopause. The difference was not statistically significant ( $p > 0.05$ ) between two groups.

In present study, educational status and occupational status of all the subjects were almost similar in both

groups and no statistically significant ( $p>0.05$ ) differences were observed among them. So, they were matched for educational status and occupational status.

Garg *et al.*<sup>[6]</sup> reported that menopause is associated with many symptoms such as hot flashes and night sweating, which are the cardinal symptoms of menopause. Other symptoms include vaginal dryness, dyspareunia, urinary symptoms (incontinence, frequency, urgency), sexual dysfunction and sleep disturbance. They also suffer from anxiety, headache, depression, irritability, mood swings, forgetfulness, sudden tear, irregular heartbeat, loss of skin tone and muscle weakness.

In present study, vaginal dryness, dyspareunia, dysuria, urinary incontinence, mood swing, cognitive aging & dementia, muscle & joint pain, anxiety & irritability, change in sexual desire were not found statistically significant ( $p>0.05$ ) between two groups but 16(53.3%) patients were found to experience hot flushes in group A and 8(26.7%) in group B which was statistically significant ( $p<0.05$ ).

Kaur *et al.*<sup>[5]</sup> which reported that 68% experiencing hot flushes in surgical menopause group & 46% in natural menopause group and 48% women had mood swings in surgical menopause group & 28% in natural menopause group and this difference is statistically significant ( $p<0.05$ ). Greater percentage of women experiencing hot flushes and mood swings in surgical menopausal women as compared to women in natural menopausal group, have also observed in Naik Raviraj *et al.*<sup>[7]</sup>

In our study, time of onset of hot flush, vaginal dryness, dyspareunia, dysuria, urinary incontinence, mood swing, cognitive aging & dementia, muscle & joint pain, anxiety & irritability and change in sexual desire were not statistically significant ( $p>0.05$ ) between two groups.

In every woman's life menopause is an event characterized by the reduced production of hormones by the ovaries specially estrogen and this effect are more pronounced following surgical menopause. In the present study, the mean estradiol level was decreased in surgical menopausal than natural menopausal women. The mean serum estradiol level was found  $10.6\pm 3.0$  pg/ml in group A and  $20.3\pm 8.0$  pg/ml in group B. The difference was statistically significant ( $p=0.001$ ) between two groups. Kabir *et al.*<sup>[8]</sup> have found similar result with lower level of serum estradiol in surgical menopausal group (16.73 pg/ml) when compared to natural menopausal group (26.57 pg/ml). NaikRaviraj *et al.*<sup>[7]</sup> have shown similar result with the mean level of estradiol in surgical menopause group to be  $10.72\pm 2.30$  pg/ml and  $18.18\pm 2.59$  pg/ml in natural menopause group and this difference is statistically significant ( $p<0.001$ ). Kaur *et al.*<sup>[5]</sup> have observed the mean level of serum estradiol in surgical and natural menopausal to be  $20.49\pm 3.16$  pg/ml and  $27.41\pm 5.08$  pg/ml and this difference is statistically significant ( $p<0.0001$ ).

This finding was in agreement with the study of many other researchers of different countries.<sup>[9,10]</sup> On the contrary, some researchers found no significant changes in estradiol level in surgical menopausal women in comparison to natural menopausal women.<sup>[11-13]</sup>

In group A, thirteen (68.4%) patients experienced hot flush when serum estradiol level was  $\leq 10.0$  pg/ml and 3(27.3%) patients when serum estradiol level was 10.1-20.0pg/ml. Which was statistically significant ( $p<0.05$ ) between two groups. Hot flush had 5.78 (95% CI 1.89% to 42.77%) times more likely to developed, when serum estradiol level is  $\leq 10.0$  pg/ml.

## CONCLUSIONS

This study revealed serum estradiol level was significantly decreased in surgical menopause than natural menopause. It is recommended, surgical menopausal women should be informed that they are at higher risks of hormonal imbalance which may develop earlier than natural menopause and encouraged for hormone replacement therapy and other supplements as required.

## ACKNOWLEDGEMENTS

The authors express their gratitude to ICMH authority for research grant and the department of Obstetrics and Gynecology, Institute of Child and Mother Health (ICMH), Matuail, Dhaka for all technical support. The authors also gratefully acknowledge the Department of Microbiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), for laboratory facilities.

## REFERENCES

1. Prabha YS, Ashalata K, Babu P, Kumari P, Nagamani M. A study of bone markers (serum calcium, serum phosphorus and serum alkaline phosphatase) in post-menopausal women in east Godavari District, Andhra Pradesh, India. *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 2015; 14: 1-3.
2. Brett KM. Can hysterectomy be considered a risk factor for cardiovascular disease?. *Circulation*, 2005; 111(12): 1456-8.
3. Simoes RD, Baracat EC, Szjenfeld VL, Lima GR, Goncalves WJ, Bortoletto CD. Effects of simple hysterectomy on bone loss. *São Paulo Medical Journal*, 1995; 113(6): 1012-6.
4. Chan CC, Ng EH, Ho PC. Ovarian changes after abdominal hysterectomy for benign conditions. *The Journal of the Society for Gynecologic Investigation: JSGI*, 2005; 12(1): 54-7.
5. Kaur N, Malla VG, Gupta S. Serum estradiol level and postmenopausal symptoms in surgical and natural menopause. *Int J Reprod Contracept Obstet Gynecol*, 2017; 6: 3920-3.
6. Garg R, Rawat R, Pathak M, Lalitha G, Rajwansi R. Menopausal symptoms among postmenopausal women of North India: A cross-sectional study. *J South Asian Fed Menop Soc*, 2015; 3(1): 3-5.

7. Naik Raviraj R, Chandel Rittu S, Abichandani Leela G. Comparison of Serum Estradiol levels in Surgical and Natural menopause. *IOSR Journal of Pharmacy and Biological Sciences*, 2014; 9(1): 65-7.
8. Kabir F, Jahan N, Sultana N, Akter R. Lipid profile status in surgical menopause. *Journal of Bangladesh Society of Physiologist*, 2011; 6(2): 127-33.
9. Moiety FM, Salem HA, Mehanna RA, Abdel-Ghany BS. Comparative study on induction and effects of surgical menopause in a female rat model: a prospective case control study. *International journal of clinical and experimental medicine*, 2015; 8(6): 9403-11.
10. Laughlin GA, Barrett-Connor E, Kritiz-Silverstein D, von Muhlen D. Hysterectomy, oophorectomy, and endogenous sex hormone levels in older women: the Rancho Bernardo Study. *The Journal of Clinical Endocrinology & Metabolism*, 2000; 85(2): 645-51.
11. Abdelazim IA, Abdelrazak KM, Elbiaa AA, Farghali MM, Essam A, Zhurabekova G. Ovarian function and ovarian blood supply following premenopausal abdominal hysterectomy. *Przegląd menopauzalny Menopause Review*, 2015; 14(4): 238.
12. Kotsopoulos J, Shafrir AL, Rice M, Hankinson SE, Eliassen AH, Tworoger SS, et al. The relationship between bilateral oophorectomy and plasma hormone levels in postmenopausal women. *Hormones and Cancer*, 2015; 6(1): 54-63.
13. Cai Y, Sun H. Clinical research of effects of retaining the uterine blood supply hysterectomy on ovarian function. *InBIO Web of Conferences*, 2017; 8: 1-5.