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THE EFFECT OF OVARIECTOMY ON WOMEN'S PERIODONTAL STATUS: A PILOT STUDY

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ABSTRACT

Objective: To determine the effect of bilateral oophorectomy on the periodontal status of otherwise healthy women when compared with normal controls.

Study Design: Mixed-method study.

Place and Duration of Study: Riphah International University, Islamabad, from Apr to Sep 2016.

Methodology: A total of 24 women with and without oophorectomy procedures were recruited. Twelve women who has undergone radical hysterectomies at least 6 months prior to the evaluation were recruited for this investigation. These women underwent a comprehensive oral examination with detailed documentation of their periodontal status following a thorough medical/dental history. An age- and sex-matched control population underwent a similar examination.

Results: Statistically significant results were noted for probing, color, consistency, texture and contour of gingiva with the p-value of 0.007, 0.001, 0.002, 0.005 and 0.037 when the results were compared with the control population.

Conclusion: Bilateral oophorectomy does not compromise the periodontal health of otherwise healthy women.

Keywords: Menopause, Oral health, Ovariectomy, Periodontitis.

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INTRODUCTION

Hysterectomy is a gynecological surgical procedure that requires removal of the uterus, occasionally ovaries, and other associated organs. Over 78% of the hysterectomy procedures in women over the age of 45 are accompanied by bilateral ovariectomy/oophorectomy. Indications for this procedure includebenign tumors, ovarian cancer, severe endometriosis, bilateral tubo-ovarian abscess, familial breast-ovarian cancer syndrome and severe premenstrual syndrome¹. It is estimated that one in three women in the United States, and one in five women in the United Kingdom undergo this procedure before reaching 60 years of age². A Indian study has reported a prevalence of 6% in women³. Another study conducted in Gujrat, India documented a higher incidence of hysterectomies that is 20.7/1000 women- year at a mean age of 36 years⁴. Although baseline statistics from Pakistan are not available, hysterectomy coupled with oophorectomyis one of the most frequently performed surgical procedure in women, due to complaints of menorrhagia and fibroids5.

Bilateral oophorectomy results in low estrogen levels in the body. This causes temperature intolerance, depressive illnesses, increased susceptibility to urinary tract infections and weight gain. Long term deficiency

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of estrogen predisposes women to cardio-vascular diseases, and Alzheimer disease⁶. Estrogen plays a fundamental role in skeletal growth and bone homeostasis, thus predisposing women undergoing this procedure to osteoporosis⁷.

The symptoms associated with oophorectomy and menopause should be similar as both result in estrogen deficiency. It is also known that menopauseassociated estrogen deficiency can result in burning mouth syndrome, xerostomia, taste alterations, mucosal changes, periodontitis, decreased bone mineral content of alveolar bone, and neurological disorders8. In addition, desquamative gingivitis can be caused by endocrinal imbalance, menopause, hysterectomy or ovariectomy9. While limited information is available about the dental implications of oophorectomy, we do know that post-menopausal women are 4 times more likely to develop osteoporosis leading to systemic and local bone loss than men¹⁰. Estrogen levels are in a tight balance; higher levels can cause gingivitis while low levels potentiate alveolar bone loss leading to periodontitis⁷. Hormone replacement therapy helps in preserving the oral health in estrogen deficient patients¹¹.

This creates a need for dentists to be aware of the dental implications of estrogen deficiency in females. Since little is known about the estrogen-deficient state as a result of bilateral oophorectomy, this study was planned to evaluate the effects of this procedure on the periodontal health of otherwise healthy women.

METHODOLOGY

A mixed-method study was designed to study the effects of bilateral oophorectomy on oral health. This study was approved by the Ethical Review Board at Riphah International University (ref. no. IIDC/IRC/2019/10/003), prior to data collection from April to September 2016. Since no figures were available from Pakistan, we took the maximum prevalence of hysterectomy from an Indian study; 6%³. This was coupled with a confidence interval of 95% and a margin error of 5% rendering a sample size of 45. We set our benchmark for the pilot investigation for 15. However, it was difficult finding participants that satisfied our inclusion criteria so were forced to settle for 12.

Twelve consenting females were enrolled in the study group through a convenience sampling technique. Inclusion criteria included pre-menopausal women who had undergone oophorectomy procedures between the range of 6 months to 10 years. Maintenance of good oral hygiene through regular brushing, flossing and routine dental visits was also required. Patients over the age of 45, women taking hormone replacement therapy and poor oral hygiene status were excluded from the sample. All patients with significant medical histories were also excluded to minimize confounding factors. The control population consisted of age and sex-matched females who had not undergone oophorectomies.

Medical and dental history was taken from the sample population. Oral hygiene habits were inquired and preliminary oral hygiene status was assessed. Current oral symptoms, if any, color, consistency, texture and contour of gingiva, plaque index, bleeding on probing, pocket depth (CPITN), calculus (OHI-S), presence or absence of plaque retentive factors, gingival recession, furcation involvement, tooth mobility, clinically visible bone loss and xerostomia were recorded during the clinical oral examination. For detail scoring /coding of indices as shown in table-I. For evaluation of clinical bone loss, measurements were taken from cemento-enamel junction to alveolar bone crest.

Data was tabulated and analyzed using SPSS-22. The p-value \leq 0.05 was considered significant at 95% confidence interval. Descriptive analysis was done and Fisher's exact test was applied for all the parameters under study for comparison between the two groups.

RESULTS

This pilot studyincluded a total of 24 females with the mean age of 38.6 ± 3.4 year. Twelve (50%) women had undergone bilateral at least 6 prior to

this visit. Twelve (50%) healthy women were taken as healthy controls. Following the coding used as per proforma, the only parameters that showed statistically significant difference between study group and control group were bleeding on probing, color, consistency, texture and contour of gingiva with the *p*-value of 0.007, 0.001, 0.002, 0.005 and 0.037 respectively (table).

DISCUSSION

To the best of our knowledge, human studies on the effects of surgically induced estrogen deficiency, or oophorectomy on oral health are deficient in the literature. However, a few animal studies show an association between the estrogen deficiency and periodontal health. Most of these studies include experimentation on rats, as the structure of periodontal tissues of rats and humans are similar. The experimentally induced skeletal changes as a result of oophorectomy in rats are similar to those seen in post-menopausal women¹².

Amadei et al, documented that experimentally induced periodontitis is observed in ovariectimized (OVX) rats after 90 days indicating that long-term estrogen deficiency results in the ligature induced alveolar bone loss¹³. Our results however do not support this notion. We were unable to identify statistically significant differences in terms of periodontal health and clinical bone loss. Only non-specific parameters like bleeding on probing, color, consistency, texture and contour of gingiva showed statistically significant difference between our sample and control groups. Since these parameters do not support a definitive diagnosis of periodontal disease, they are only considered as oral alterations of estrogen deficiency. Therefore making a strong association between oophorectomy and oral health status was difficult to determine.

In accordance with our results, a study conducted by Anbinder *et al*, in 2006 performed radiographic and macroscopic analysis in OVX rats. This study did not find a correlation of estrogen deficiency and periodontal health status¹⁴. Our results werealso consistent with a study done by Marques *et al*. They conducted a histometric evaluation of the furcation region in lower molars andfound no significant bone loss. Similarly, Orrico *et al*, showed no difference between OVX rats and control group in periodontal bone loss based on radiographic and densitometric analysis^{15,16}.

In contrast to our results, arat experimentation conducted by Xin-Chen *et al*. Demonstrated that oophorectomy resulted in the deterioration of the alveolar bone microarchitecture, alveolar crest height reduction,

Cpitn No pocket (0)	Table: Different parameters under study.					
Cpitn No pocket 5mm (1) Pecket 4-5mm (2) 5 (41.7) (43.3) 5 (41.7) (43.3) 0.105 Plaque Index No calculus (0) Pecket 4-5mm (3) 2 (16.7) (3 (25.0) 3 (25.0) 0.397 Plaque Index Supra 10 rd more than 1/3rd tooth surface0 (1) (5 (41.7) (3 (25.0)) 5 (41.7) (3 (25.0)) 0.397 Gingival Recession Supra 10 rd more than 1/3rd tooth surface0 (1) (0) (7 (58.3)) 1 (8.3) (18.3) 1 (8.3) (18.3) Furcation Involvement Extension to MG junction (0) (0) (7 (58.3)) 10 (83.3) (2 (16.7) (2 - 10.4) 0.461 Furcation Involvement Extension to beyond MG junction (1) (1) (2 (16.7) (2 (16.7) (2 - 10.4)) 2 (16.7) (2 - 10.4) 0.461 Furcation Involvement In clinical furcation (9) (10 (83.3) (10 (19.1)) 1 (19.17) (19.17) 0.461 Furcation Involvement In clinical furcation (9) (10 (83.3) (10 (19.1)) 1 (19.17) (19.17) 0.461 Furcation Involvement In clinical furcation (9) (10 (10 (83.3) (10 (19.1)) 1 (19.17) 0.317 Furcation Involvement In clinical furcation (9) (10 (10 (10 (10 (10 (10 (10 (10 (10 (10		Variables (Code)	Case, n (%)	Controls, n (%)	<i>p</i> -value	
Pocket 1-5mm (2)	Cpitn		\ /	\ /	0.105	
Pocket > Form (3)				5 (41.7)		
Plaque Index		\ \ /	4 (33.3)	-		
Plaque Index			-	-		
Supra Ol/3rd to 2/3rd or isolated flecks of sub. (2)	Plaque Index		\ /		0.397	
Supra or Supra or Subra or						
No extension to MG junction (0)				1 (8.3)		
Gingival Recession Extension to or beyond MG junction (1) 3 (25.0) 2 (16.7) 0.461 Bone or soft tissue loss present, partial root coverage (2) 2 (16.7) - - With gross flattening, no root coverage (3) - - - no clinical furcation (0) 8 (66.7) 11 (91.7) 0.317 Bone loss up to 1/3rd width (1) 4 (33.3) 1 (8.3) 0.317 Mobility Normal < Imm (0)		1 /		-		
Bone or soft tissue loss present, partial root coverage (2) 2 (16.7) - -	Gingival Recession			` /	0.461	
Bone or Sort Itsset loss present, partial roor coverage (2) 2 (16.7) -			3 (25.0)	2 (16.7)		
Furcation Involvement Furcation Involvement Bone loss up to 1/3rd width (1) 4 (33.3) 1 (8.3) Bone loss up to 2/3rd width (2) Through and through defect (3) Mobility Up to Imm horizontal (1) 2 (16.7) 1 (8.3) 1 (191.7) Up to Imm horizontal (1) 2 (16.7) 1 (8.3) 1 (100.0) Greater than Imm horizontal (2)		Bone or soft tissue loss present, partial root coverage (2)	2 (16.7)	-		
Bone loss up to 1/3rd width (1) 4 (33.3) 1 (8.3)			-	-		
Bone loss up to 2/3rd width (2)	Furcation Involvement	no clinical furcation (0)	8 (66.7)	11 (91.7)	0.317	
Bone loss up to 2/3rd width (2)		Bone loss up to 1/3rd width (1)	4 (33.3)	1 (8.3)		
Mobility		Bone loss up to 2/3rd width (2)	-	-		
Mobility Up to 1mm horizontal (1) 2 (16.7) 1 (8.3) 1.000 Greater than 1mm horizontal (2) - - - greater than 2mm horizontal or vertical (3) - - - No bleeding (0) 10 (83.3) 6 (50.0) - - Tenous red line along gingival sulcus (1) - 6 (50.0) - <td>Through and through defect (3)</td> <td>-</td> <td>-</td>		Through and through defect (3)	-	-		
Contour of gingiva Contour	Mobility	Normal <1mm (0)	10 (83.3)	11 (91.7)	1.000	
Creater than 1mm horizontal (2) - - -		Up to 1mm horizontal (1)	2 (16.7)	1 (8.3)		
No bleeding (0)		Greater than 1mm horizontal (2)	-	_		
No bleeding (0)		greater than 2mm horizontal or vertical (3)	-	-		
Tenous red line along gingival sulcus (1)	Bleeding on Probing		10 (83.3)	6 (50.0)	0.007	
Profuse bleeding (2)			-	6 (50.0)		
Xerostomia Absent 4 (33.3) 6 (50.0) 0.680 Burning Mouth Absent 8 (66.7) 6 (50.0) 0.680 Burning Mouth Absent 10 (83.3) 12 (100.0) 0.478 Syndrome Present 2 (16.7) - - Clinical Bone Loss Absent 10 (83.3) 12 (100.0) 0.478 Present 2 (16.7) - - - Present 2 (16.7) - - - Color of Gingiva Inflamed red 10 (83.3) - - 0.001 Pale gingiva -			-	†		
Xerostomia Absent 4 (33.3) 6 (50.0) 0.680 Burning Mouth Absent 8 (66.7) 6 (50.0) 0.680 Burning Mouth Absent 10 (83.3) 12 (100.0) 0.478 Syndrome Present 2 (16.7) - - Clinical Bone Loss Absent 10 (83.3) 12 (100.0) 0.478 Present 2 (16.7) - - - Present 2 (16.7) - - - Color of Gingiva Inflamed red 10 (83.3) - - 0.001 Pale gingiva -		Delayed Bleeding (30-60sec) (3)	2 (16.7)	-		
Xerostomia Absent 4 (33.3) 6 (50.0) 0.680 Burning Mouth Syndrome Absent 10 (83.3) 12 (100.0) 0.478 Clinical Bone Loss Absent 10 (83.3) 12 (100.0) 0.478 Clinical Bone Loss Absent 10 (83.3) 12 (100.0) 0.478 Present 2 (16.7) - - Normal color 2 (16.7) 12 (100.0) 0.0478 Pale gingiva - - - 0.001 Pale gingiva - - - - - 0.001 Consistency of Gingiva Normal firm and resilient 6 (50.0) 7 (58.3) - 0.002 - Edematous - 5 (41.7) 0.002 -			-	-		
Burning Mouth Absent 10 (83.3) 12 (100.0) 0.478	Xerostomia		4 (33.3)	6 (50.0)	0.680	
Syndrome Present 2 (16.7) - 0.4/8 Clinical Bone Loss Absent 10 (83.3) 12 (100.0) 0.478 Color of Gingiva Normal color 2 (16.7) 12 (100.0) 10 (83.3) - 0.001 Pale gingiva - - - - - - 0.001 Consistency of Gingiva Normal firm and resilient 6 (50.0) 7 (58.3) - 0.002 Edematous - 5 (41.7) 0.002 -		Present	8 (66.7)	6 (50.0)		
Syndrome Present 2 (16.7) - 0.478 Clinical Bone Loss Absent 10 (83.3) 12 (100.0) 0.478 Color of Gingiva Normal color 2 (16.7) 12 (100.0) 0.001 Inflamed red 10 (83.3) - 0.001 Pale gingiva - - Consistency of Gingiva Normal firm and resilient 6 (50.0) 7 (58.3) Edematous - 5 (41.7) 0.002 Fibrotic 6 (50.0) - - Stippled attached gingiva & interdental papilla - 7 (58.3) 12 (100.0) Texture of gingiva Peeling of surface (desquamative) - - - Peeling of surface (desquamative) - - - - Leathery (hyperkeratotic) - - - - Nodular (drug induced enlargement) - - - Contour of gingiva Gingival enlargement - - - McCall's Festoon (recession) 5 (41.7) - -	Burning Mouth	Absent	10 (83.3)	12 (100.0)	0.478	
Present 2 (16.7) -		Present	2 (16.7)	_		
Present 2 (16.7) -	Clinical Bone Loss	Absent	10 (83.3)	12 (100.0)	0.478	
Color of Gingiva Inflamed red Pale gingiva 10 (83.3) - 0.001 Consistency of Gingiva Normal firm and resilient 6 (50.0) 7 (58.3) - Edematous - 5 (41.7) 0.002 Texture of gingiva Stippled attached gingiva & interdental papilla - 7 (58.3) - Loss of stippling: 12 (100.0) 5 (41.7) 0.005 Leathery (hyperkeratotic) - - - Nodular (drug induced enlargement) - - - Normal scalloped 7 (58.3) 12 (100.0) - Contour of gingiva Gingival enlargement - - - McCall's Festoon (recession) 5 (41.7) - -		Present	2 (16.7)	_		
Pale gingiva	Color of Gingiva	Normal color	2 (16.7)	12 (100.0)	0.001	
Pale gingiva		Inflamed red	10 (83.3)	-		
Consistency of Gingiva Normal firm and resilient 6 (50.0) 7 (58.3) Edematous - 5 (41.7) 0.002 Fibrotic 6 (50.0) - Stippled attached gingiva & interdental papilla - 7 (58.3) Loss of stippling: 12 (100.0) 5 (41.7) Peeling of surface (desquamative) - - Leathery (hyperkeratotic) - - Nodular (drug induced enlargement) - - Normal scalloped 7 (58.3) 12 (100.0) Gingival enlargement - - McCall's Festoon (recession) 5 (41.7) -		Pale gingiva	-	-		
Edematous	Consistency of Gingiva		6 (50.0)	7 (58.3)	0.002	
Fibrotic 6 (50.0) -		Edematous	-			
Stippled attached gingiva & interdental papilla		Fibrotic	6 (50.0)	-		
Loss of stippling: 12 (100.0) 5 (41.7) Peeling of surface (desquamative) - - 0.005 Leathery (hyperkeratotic) - - - Nodular (drug induced enlargement) - - Contour of gingiva O.037 Contour of gingiva O.037 Leathery (hyperkeratotic) - - - Normal scalloped 7 (58.3) 12 (100.0) Gingival enlargement - - - McCall's Festoon (recession) 5 (41.7) -	Texture of gingiva	Stippled attached gingiva & interdental papilla	-	7 (58.3)	0.005	
Texture of gingiva Peeling of surface (desquamative) - - 0.005 Leathery (hyperkeratotic) - - - Nodular (drug induced enlargement) - - Normal scalloped 7 (58.3) 12 (100.0) Gingival enlargement - - McCall's Festoon (recession) 5 (41.7) -			12 (100.0)			
Leathery (hyperkeratotic)			-	-		
Nodular (drug induced enlargement)			-	-		
Contour of gingiva Normal scalloped 7 (58.3) 12 (100.0) Gingival enlargement - - McCall's Festoon (recession) 5 (41.7) -			-	-		
Contour of gingiva Gingival enlargement 0.037 McCall's Festoon (recession) 5 (41.7) -			7 (58.3)	12 (100.0)	0.037	
McCall's Festoon (recession) 5 (41.7) -			-	-		
	Contour of gingiva		5 (41.7)	_		
		Stillman's cleft (puffy swollen)	-	_		

decline in the bone formation rate and increased osteoclast activity¹⁷. Similarly, Duarte et al, reported a higher inter-radicular bone loss in OVX rats. They also found that estrogen replacement or calcitonin therapy cannot protect against this bone loss¹⁸. A three dimensional micro-computed tomographic analysis revealed a combination of experimental periodontitis and oophorectomy induced systemic bone loss particularly in mandible and femoral region¹⁹. These results were verified by Dai et al, and Liu et al, studies20,21. In another OVX rat study, Romualdo et al, demonstrated the elevation of interleukin 1 beta, tumor necrosis factor alpha, interleukin 6, MMP-8, and MMP-13 in apical periodontitis. They concluding that hypoestrogenic state exacerbates inflammation and degradation of extracellular matrix components leading to development of apical periodontitis²². A study done by Andriy and Inna in 2019 also showed progression of inflammatory and destructive process in the periodontium worsens within 3-5 years after total ovariectomy²³. A review determined that estrogen effects the normal bone mass and density. It also found that estrogen levels lead to loss of keratin, thinning of gingival tissues, redness, soreness and decreased salivary gland function²⁴. Limited work is done on this topic warrants further research to facilitate such women in their dental problems.

The limitations of our study include asmall sample size, lack of radiographs for evaluation of bone loss and no follow ups. Future recommendations include a larger sample size accompanied by radiographic analysis to assess changes in bone. Longitudinal studies on human subjects rather than experimental rat models can allow us to compare periodontal health of women before and after the oophorectomy procedure. This can help us ascertain the effect of the procedure better. If we find that such a correlation does exist, patients who have undergone oophorectomy should be advised to maintain good oral hygiene and referred to endocrinologist for hormone replacement therapy (HRT) to maintain their estrogen levels in blood. Regular visits to dentist should also be observed.

CONCLUSION

There was no statistically significant difference between medically OVX human subjects and control group regarding oral health status. Hence this study concluded that medically OVX human subjects do not show signs of periodontitis or alveolar bone loss after 6 months of the procedure.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

REFERENCES

- Hendrix SL. Bilateral oophorectomy and premature menopause. Am J Med 2005; 118(Suppl-12B): 131-35.
- Al-Kadri HM, Al-Turki HA, Saleh AM. Short and long term complications of abdominal and vaginal hysterectomy for benign disease. Saudi Med J 2002; 23(7): 806-10.
- 3. Shekhar C, Paswan B, Singh A. Prevalence, sociodemographic determinants and self-reported reasons for hysterectomy in India. Reprod Health 2019; 16(1): 118-22.
- Desai S, Campbell OM, Sinha T, Mahal A, Cousens S. Incidence and determinants of hysterectomy in a low-income setting in Gujarat, India. Health Policy Plan 2017; 32(1): 68-78.
- 5. Majeed T AR, Mahmood Z, Mahmood H. Audit of Gynaecolo-

- gical Hysterectomies. Pak J Med Health Sci 2013; 7(3): 684-87.
- Friedlander AH. The physiology, medical management and oral implications of menopause. J Am Dent Assoc 2002; 133(1): 73-81.
- Robinson JL, Johnson PM, Kister K, Yin MT, Chen J, Wadhwa S. Estrogen signaling impacts temporomandibular joint and periodontal disease pathology. Odontol 2020; 108(2): 153-65.
- 8. Mutneja P, Dhawan P, Raina A, Sharma G. Menopause and the oral cavity. Ind J Endocrinol Metab 2012; 16(4): 548-51.
- Sambashivaiah SCS, Bilichodmath S, Subbaiah R. Desquamative Gingivitis as a Clinical Manifestation in Endocrinal Imbalance-A Case Report. Ind J Stomatol 2011; 2(1): 49-52.
- Abraham A, Pullishery F. The Effect of Menopause on the Periodontium-A Review. J Dent Med Sci 2015; 14(4): 79-82.
- 11. Hariri R, Alzoubi EE. Oral manifestations of menopause. J Dent Health Oral Disord Ther 2017; 7(4): 306-309.
- 12. Johnston BD, Ward WE. The ovariectomized rat as a model for studying alveolar bone loss in postmenopausal women. Biomed Res Int 2015; 2015(1): 635023-26.
- 13. Amadei SU, Souza DM, Brandao AA, Rocha RF. Influence of different durations of estrogen deficiency on alveolar bone loss in rats. Braz Oral Res 2011; 25(6): 538-43.
- Anbinder AL, Prado Mde A, Spalding M, Balducci I. Estrogen deficiency and periodontal condition in rats: a radiographic and macroscopic study. Braz Dent J 2006; 17(3): 201-207.
- 15. Orrico SR, Goncalves D, Galeazzi ST, Giro G, Takayama L, Pereira RM. The influence of loss of bone mass on induced periodontal disease: a radiographic and densitometric study of female rats. J Periodontol 2005; 76(9): 1436-42.
- Marques MR, da Silva MA, Manzi FR, Cesar-Neto JB, Nociti FH, Barros SP. Effect of intermittent PTH administration in the periodontitis-associated bone loss in ovariectomized rats. Arch Oral Biol 2005; 50(4): 421-29.
- 17. Xu XC, Chen H, Zhang X, Zhai ZJ, Liu XQ, Zheng XY, et al. Effects of oestrogen deficiency on the alveolar bone of rats with experimental periodontitis. Mol Med Rep 2015; 12(3): 3494-502.
- 18. Duarte PM, Goncalves PF, Sallum AW, Sallum EA, Casati MZ, Humberto Nociti F. Effect of an estrogen-deficient state and its therapy on bone loss resulting from an experimental periodontitis in rats. J Periodontal Res 2004; 39(2): 107-10.
- Anbinder AL, Moraes RM, Lima GMG, Oliveira FE, Campos DRC, Rossoni RD, et al. Periodontal disease exacerbates systemic ovariectomy-induced bone loss in mice. Bone 2016; 83(1): 241-47.
- Dai J, Ma Y, Shi M, Cao Z, Zhang Y, Miron RJ. Initial changes in alveolar bone volume for sham-operated and ovariectomized rats in ligature-induced experimental periodontitis. Clin Oral Investig 2016; 20(3): 581-88.
- Liu Z, Liu L, Kang C, Xie Q, Zhang B, Li Y. Effects of estrogen deficiency on microstructural changes in rat alveolar bone proper and periodontal ligament. Mol Med Rep 2015; 12(3): 3508-14.
- Romualdo PC, Lucisano MP, Paula-Silva FWG, Leoni GB, Sousa-Neto. Ovariectomy exacerbates apical period-ontitis in rats with an increase in expression of proinflammatory cytokines and matrix metalloproteinases. J Endod 2018; 44(5): 780-85.
- Andriy S, Inna HH. Periodontal status of patients in different periods after total ovariectomy. Modern Science-Moderni Veda 2019; 6(2): 105-10.
- 24. Shapiro LF, Freeman K. The relationship between estrogen, estrogen receptors and periodontal disease in adult women: a review of the literature. NY State Dent J 2014; 80(3): 30-34.

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