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RESEARCH ARTICLE

EVALUATION OF SALIVARY URIC ACID LEVELS AS A NOVEL BIOMARKER IN THE ASSESSMENT OF ORAL HEALTH STATUS AMONG WOMEN AT DIFFERENT STAGES OF THEIR LIFE CYCLE

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Abstract

Hormonal fluctuations throughout a woman's lifespan profoundly influence both systemic and oral health. Key physiological phases namely puberty, menstruation, pregnancy and menopause heighten susceptibility to oral infections. These hormonal variations can significantly affect a woman's overall quality of life. Saliva, being a readily accessible biofluid offers important diagnostic insights for the assessment of various pathological conditions related to hormonal changes.The aim of this study was to evaluate the salivary uric acid levels as a novel biomarker in assessment of oral health status among women at different stages of their life cycle.

Methodology: The study protocol was approved by the institutional ethical committee and informed consent was obtained from all participants. Assessment of oral health status was done using simplified oral hygiene index and DMFT index.Clinical evaluation was carried out and appropriate score as per WHO was recorded.Saliva samples were collected from the study participants and were sent to a bio chemistry laboratory for evaluation of uric acid levels. The data obtained was entered on a Microsoft excel spreadsheet and statistically analyzed.

Results: The results of this study demonstrated that the salivary uric acid level was the highest in menopausal women followed by non menstruating, menstruating and pregnant women. The DMFT score was the highest among menopausal women and the oral health status was fair in comparison to a good oral health status observed among menstruating women and non menstruating women. This could suggest that there is a significant correlation between salivary uric acid level and oral health status among women. However further studies will be needed to investigate and promote greater insights with regard to the health needs of women.

Conclusion:A comprehensive approach to women's health encompassing menstruation, pregnancy, and menopause, should be regarded as a fundamental component of the healthcare system. Salivary biomarkers such as uric acid can be used for assessment of oral health status among women. However, continued research is

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essential to develop deeper insights and advance understanding in these areas.

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Introduction:

The oral cavity represents a complex environment characterized by a variety of structures and tissue types that work together to maintain oral health.[1] Saliva is predominantly composed of water (99.5%). It also contains essential proteins (0.3%), trace organic compounds such as urea and uric acid (0.2%), and various inorganic substances.[2]Saliva plays a pivotal role in oral health through several mechanisms such asprotectionof the mucosal surfaces,lubrication, maintaining oral homeostasis, preserving the integrity of dental tissues,facilitating enamel remineralization, neutralizing acidic plaque, washing off of food debris and providing antibacterial effects.[3]

Hormonal fluctuations significantly impact a women's health.The different phases such as puberty, menstruation, pregnancy and menopause play a significant role in theoverall healthof a woman. Each of these stages involves distinct hormonal changes that can influence both systemic and oral health.[4]Variations in hormone levels can affect oral mucosal health, alter salivary parameters, increase susceptibility to oral infections and cause changes in oral microbiota. These fluctuations may in turn impact their overall oral health and quality of life.[5]

Saliva is a readily accessible biofluid that offers valuable insights into both physiological and pathological conditions.[6]Additionally saliva holds significant potential as a diagnostic tool for identifying biomarkers associated with dental caries.[7] Recent research underscores the importance of salivary uric acid in maintaining biofilm, pH balance and antioxidant properties.[8] The ongoing discovery, validation and interpretation of saliva-based biomarkers are crucial for establishing oral fluids as reliable diagnostic tool.[9]This highlights its potential for enhancing oral health assessment and developing more effective intervention strategies to maintain oral health.

Despite extensive research the impact of hormonal changes on properties of saliva at different phases of women's lifecycle remains unexplored. Not many studies have been done to assess the impact of menstruation, pregnancy and menopause on the alteration in the physiochemical properties of saliva and oral health status. Therefore the present study was conducted to evaluate the salivary uric acid and oral health status among non-menstruating, menstruating, pregnant and menopausal women in Mangalore city.

Methodology:

The research protocol was approved by the Institutional Ethical and Research committee. A cross sectional study was conducted to compare and evaluate oral health status and effect of menstruation, pregnancy and menopause on the physiochemical properties of saliva among women. Healthy pregnant women in their third trimester reporting for antenatal checkup to the department of obstetrics and gynaecology at A J institute of Medical Sciences, Mangalore were included. Menstruating women with in first three days of menstruation (with normal cycle of 28-30 days), menopausal women with history of menopause of more than one year and a control group of non menstruating women who have a regular menstrual cycle of 28 -30 days but are not menstruating at the time of salivary sample collection were included in the study.

Patients with a history of any systemic diseases, or on antimicrobial therapy since two months or during the study, Patients under medication which can alter salivary parameters, or showing clinical signs of xerostomiawere excluded from the study.

A sample size of 132 based on convenience sampling technique was calculated using G* Power software version 3.1. The minimum number of subject required in each group was 33. The nature of the study was explained and a written informed consent was obtained from all the study participants.

Assessment of oral health status

The Simplified Oral Hygiene Index (OHI-S by Greene and Vermillion) was used. The dental status was assessed by clinical evaluation for the presence of dental caries, filled, missing teeth and fixed dental prosthesis. The periodontal status was determined by examining for the presence of gingival bleeding, periodontal pockets and the depth of the periodontal pockets. The severity of the loss of attachment and the probing measurements was recorded. The teeth

were examined for the presence of enamel fluorosis, dental erosion and dental trauma. The oral mucosa was examined for the presence of any lesion. The appropriate score as per WHO for each criterion was recorded.

Assessment of salivary uric acid levels

Saliva collection was done between 9:00 am and 12:00 noon to avoid diurnal variation. The patients were advised not to eat, drink, one hour before and during the entire procedure. Unstimulated whole salivary samples were collected by spitting method. 5-6 ml of saliva was collected in a graduated test tube through a glass funnel.

Subjects were made to sit comfortably on the dental chair and after a few minutes of relaxation the procedure for collection of saliva was carried out. The saliva samples were then sent to a private bio chemistry laboratory for estimation of salivary uric acid level. The data obtained was entered on a Microsoft excel spreadsheet and statistically analyzed.

The statistical analysis was done using SPSS 23.0. The categorical variables were represented in frequency and percentage. The numerical variables were presented using mean and standard deviation. Comparison of multiple groups was performed using repeated measures of ANOVA. Pairwise comparison was done using Bonferroni Test. A p-value less than 0.05 was considered statistically significant.

Table 1:- Showing mean age of the women in the four groups.

AGE	N	Mean	Std. Deviation
Non- menstruating women (control group)	33	27.121	5.538
Menstruating	33	23.212	1.616
Pregnant	33	26.667	5.035
Menopausal women	33	55.879	6.122

The data indicated that for non-menstruating women (control group), the mean age was 27.121 ± 5.538 years. Menstruating women had a mean age of 23.212 ± 1.616 years. For pregnant women, the mean age was 26.667 ± 5.035 years and menopausal women had a mean age of 55.879 ± 6.122 years.

Figure 1:- Representing the mean age of the women.

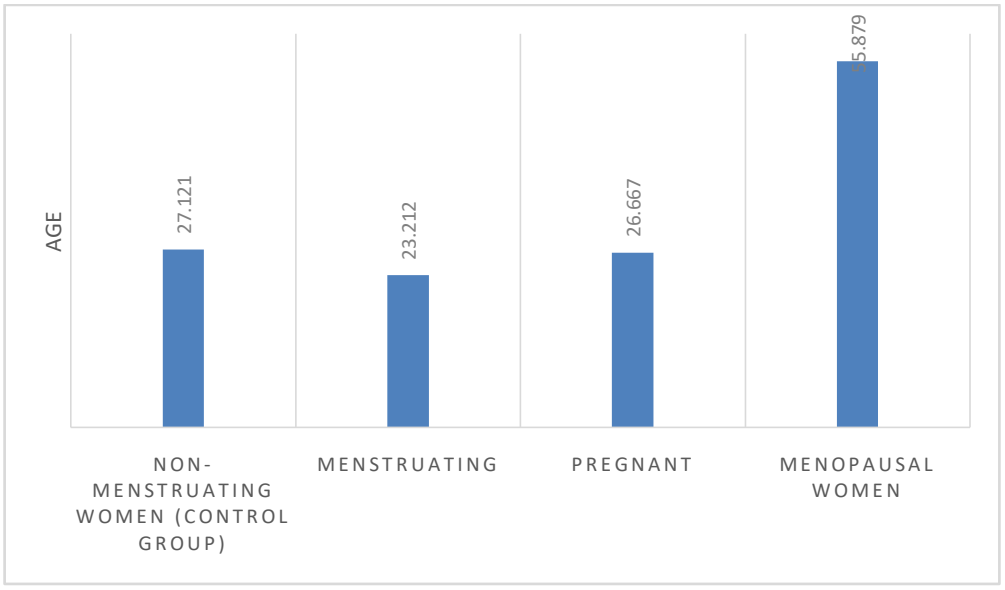

Table 2:- Showing uric acid levels of the women in the four groups.

URIC ACID LEVELS	Mean	Std. Deviation	F value	p value
Non- menstruating women (control group)	.330	.552	2.866	0.039*
Menstruating	.230	.113		
Pregnant	.188	.082		
Menopausal women	.388	.246		

The data here indicates that for non-menstruating women (control group), the mean uric acid level was 0.330 ± 0.552 mg/dL. Menstruating women had a mean uric acid level of 0.230 ± 0.113 mg/dL. Pregnant women had a mean uric acid level of 0.188 ± 0.082 mg/dL and Menopausal women had a mean uric acid level of 0.388 ± 0.246 mg/dL. The F value of 2.866 and p value of 0.039 suggests that the differences in uric acid levels among the groups are statistically significant.

Figure 2:- Representing mean uric acid levels of the women.

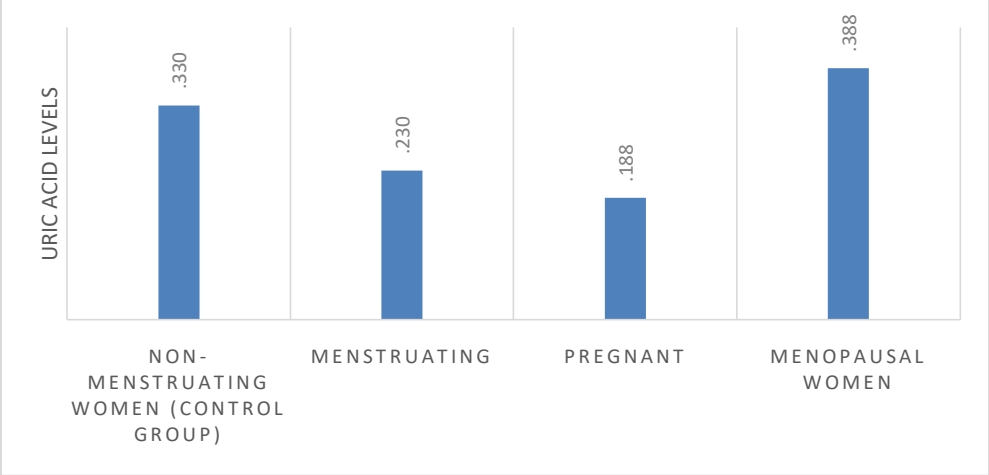

Table 3:- Showing pairwise comparison of Uric Acid Levels.

URIC ACID LEVELS		Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Non-menstruating women (control group)	Menstruating	.10000	.07634	1.000	-.1046	.3046
	Pregnant	.14242	.07634	.386	-.0622	.3470
	Menopausal women	-.05758	.07634	1.000	-.2622	.1470
Menstruating	Pregnant	.04242	.07634	1.000	-.1622	.2470
	Menopausal women	-.15758	.07634	.246	-.3622	.0470
Pregnant	Menopausal women	-.20000	.07634	.059	-.4046	.0046

This table showedthat there is statistical significance only in the pair pregnant and menopausal women with $p<0.05$.

Table 4:- Showing DMFT index score of the women in the four groups.

DMFT INDEX SCORE	Mean	Std. Deviation	F value	p value
Non- menstruating women (control group)	.104	.052	2.501	.0620
Menstruating	.115	.040		
Pregnant	.104	.034		
Menopausal women	.129	.044		

The DMFT index scores indicated that non-menstruating women (control group) had a mean score of 0.104 ± 0.052. Menstruating women had a mean score of 0.115 ± 0.040. Pregnant women also showed a mean score of 0.104 ±

0.034. In contrast, menopausal women exhibited the highest mean score of 0.129 ± 0.044. The F value of 2.501 and p value of 0.062 suggested that they were not statistically significant at the 0.05 level.

Figure 3:- Representing mean DMFT index score of the women.

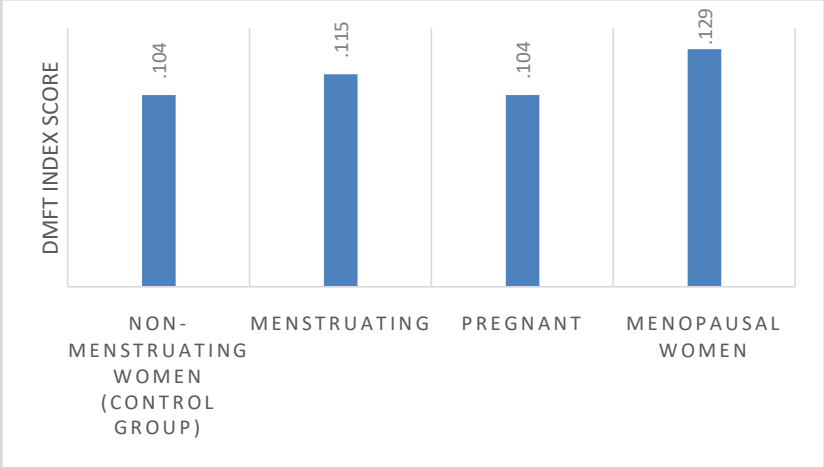

Table 4:- Showing crosstabulation of oral hygiene score and group.

		GROUP				Total	Chi square	p value
		Non-menstruating women (control group)	Menstruating	Pregnant	Menopausal women			
ORAL HYGINIENE SCORE	Good	29	32	13	8	82	74.798	p<0.001
		87.9%	97.0%	39.4%	24.2%	62.1%		
	Fair	3	1	20	14	38		
		9.1%	3.0%	60.6%	42.4%	28.8%		
	Poor	1	0	0	11	12		
		3.0%	0.0%	0.0%	33.3%	9.1%		
Total		33	33	33	33	132		
		100.0%	100.0%	100.0%	100.0%	100.0%		

The table depicted, majority of 29(87.9%) non menstruating women had good oral hygiene score. 32(97%) menstruating women had good oral hygiene score. 20(60.6%) pregnant women and 14(42.2%) menopausal women had fair oral hygiene score. It showed significant difference with p<0.001 and chi square value 74.798.

Discussion:

Women undergo various hormonal changes throughout their lives, which can significantly impact their oral health. These hormonal fluctuations influence the body's response. Hormones such as estrogen and progesterone play a crucial role in the health of the oral tissues.[4] Elevated levels of these hormones lead to vasodilatation and increased capillary permeability, resulting in greater fluid and white blood cell migration to oral tissues. This heightened response makes the oral tissues more susceptible to infections. Additionally, high hormone concentrations can alter the oral microbiome and augment the nutrient supply for microbial growth.[10]

It has been suggested that saliva's primary defense mechanism involves its antioxidant system. This encompasses a variety of components such as salivary peroxidase, salivary uric acid, and several minor enzymes.[11]The reference value of Uric acidmay range between 1.5–7.0 mg/dL.[12]Uric acid has been considered as the major antioxidant present in human saliva. It may also function as a biomarker for a spectrum of systemic conditions. Thus in this study we have assessed the salivary uric acid levels.

The results of thisstudy demonstrated that the salivary uric acid level is the highest in menopausal women followed by non menstruating, menstruating and pregnant women.

The elevated uric acid levels observed could be related to increased oxidative stress. The collective ability of these components to counteract oxidative stress is known as the total antioxidant capacity (TAC).[13–15]Uric acid being a keysalivary antioxidantit accounts for approximately 85% of the TAC of both unstimulated and stimulated saliva.[16]

Age-related increases in serum uric acid levels among women have been documented. A study of 3,013 female residents of Tecumseh as well as another study involving 254 women in the UK, reported that serum urate levels began to rise around the ages of 50 to 54.[17,18] Similarly, a study conducted on 18,324 Japanese women found a persistent increase in uric acid levels up to age 70 and beyond. These observations could show a link between hormonal changes during menopause as a potential factor for rise in uric acid levels.[19] Furthermore, a case series revealed asubstantial majority of female gout cases were identified after menopause. Additional factors such as renal function, the use of diuretics, and hypertension were also attributed to increase in uric acid levels.[20]In addition, the results of this study observed that the DMFT index was the highest among menopausal women and the oral health status was fair in comparison to a good oral health status observed among menstruating women and non menstruating women.

During menopause there is an increase in salivary progesterone levels. This is known to be associated with oral dryness. Also menopausal changes causeestrogen deficiency that leads to monocytes and macrophages producing greater pro-inflammatory cytokines.[21]These significant physiological changes among menopausal women could be the reason for remarkable decrease in the salivary pH and salivary flow rate. The pertinent change in the salivary flowrate and pH could be credited to the high values of DMFT and decreased oral hygiene status in menopausal group.[22]

There is also a noteworthy evidence of disruptions of the redox system that has been observed in the saliva of patients with high dental caries.This striking alteration in antioxidant and pro-oxidant parameters, as well as biomarkers of oxidative damage can be associated to an increase in salivary uric acid level, which is considered as a major salivary antioxidant.[23,24]Moreover, an increase in oxidative damage of the salivary biomarkers such as uric acid coupled with a decrease in antioxidant capacity has been linked to the progression of dental caries and this could suggestthe significantcorrelation between menopause and increase in DMFT as well as decreased oral health status among menopausal women.[25]However further studies will be needed to investigate and promote greater insights with regard to the health needs of women.

Conclusion:

A comprehensive perspective on women's health needs related to menstruation, pregnancy, and menopause should be considered an integral component of the healthcare system. Further research is necessary to explore and advance our understanding of a woman’s health.Thereby fostering more informed and effective approaches to women's health care.

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