

CORRELATION OF ESTRADIOL WITH MONOCYTE CHEMOTACTIC PROTEIN-1 (MCP-1) URINES LEVELS ON MENOPAUSAL WOMEN WITH OVERACTIVE BLADDER

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Abstract

This research supposed to be assessing the correlation between Estradiol levels and urine levels of Monocyte Chemotactic Protein-1 (MCP-1) in menopausal patients with Overactive Bladder at H Adam Malik General Hospital Medan. This research was an observational analytic study with a case series research design to assess the correlation between Estradiol levels and urine urine Monocyte Chemotactic Protein-1 (MCP-1) in postmenopausal women with overactive bladder. The sample was all menopausal female paramedics with overactive bladder at H Adam Malik General Hospital Medan who met the inclusion and exclusion criteria using non-probability methods with consecutive sampling technique. All data collected is then analyzed. Data were analyzed using the Pearson correlation test if the data were not normally distributed and the Spearman test if the data were not normally distributed. A p value of less than 0.05 was considered significant with 95% CI. From the results of the study found the characteristics of OAB patients. primipara, sekundipara and multipara 1 (2.9%), sekundipara 13 (38.2%) and 20 (58.8%). Based on normoweight and overweight as many as 6 (17.6%) and 28 (82.4%), menopause, 2-3 years, 4 years, and 5 years respectively 20 (58.8%), 12 (35, 3%), and 2 (5.9%), age, 40-49 years and 50 - 59 years, respectively 2 (5.9%) and 32 (94.1%). the value of urinary MCP 1 was based on a mild, moderate, OABSS score of 65.14 ± 96.11 ; 34.10 ± 46.15 ; 41.28 ± 61.59 from the spearman correlation test found a very strong negative correlation correlation coefficient -0.682 ; $p < 0.001$. The mean urine urine estradiol sample was 24.26 ± 5.73 (154-37.8). urine MCP 1 value based on a mild, moderate OABSS score of 92.81 ± 4.44 ; 108.53 ± 10.21 ; 156 ± 10.21 ; Spearman correlation test obtained a correlation coefficient value of 0.856 ; $p < 0.001$. Estradiol correlation with urine Monocyte Chemotactic Protein-1 (MCP-1) in postmenopausal women with overactive bladder r value -0.658 . There is a negative correlation between Estradiol levels and urine urine Monocyte Chemotactic Protein-1 (MCP-1) in menopausal women with overactive bladder

Keywords: Overactive bladder, OAB, Monocyte Chemotactic Protein-1, MCP-1, Menopause.

I. INTRODUCTION

The elderly population globally is predicted to continue to increase. According to the World Health Organization (WHO) 2007, it is estimated that 25 million women worldwide will experience menopause every year and Asia is the region with the highest menopausal women in the world, menopause often occurs at the age of 45-50 years.¹

Overactive bladder (OAB) is a condition of urinary urgency with or without incontinence, and is usually accompanied by frequency and nocturia.¹ Overactive bladder has a high prevalence and is estimated to be around 10.7% of the entire world population (around 455 million people). The prevalence increases with increasing age, estimated to increase by around 41% in men and 31% in women > 75 years.² The prevalence of overactive bladder reported in the study of Zhu et al is around 10-15%.³

Prostaglandins and urinary cytokines are proposed as OAB markers. Prostaglandin E2 (PGE2) is more widely studied and is considered superior to NGF (Nerve growth factor) as a discriminatory marker.⁴ Recent investigations of urine chemokinin in OAB patients show an increase in MCP-1 and some pro-inflammatory cytokines, mean urinary cytokine / chemokine levels are higher in wet OAB than in dry OAB, showing a linear relationship between the severity of symptoms and cytokine levels. Specific cytokines play an important role for the pathophysiology of OAB through the process of regulating the upper part of the communication gap of intersellular intersections and connexin expression.⁵

Bilal et al study in 2017, conducted research on 26 patients and found that the median value of MCP-1 in the control group without symptoms of OAB was 60, whereas in the case group after receiving therapy the median value of MCP-1 was 29.3 which significantly decrease from the initial value of 154.8. In the study of Bilal et al, in 2019 conducted in 29 patients with 10 controls it was found that, the level of MCP-1 in controls was 48.02 while in the OAB group found levels of MCP-1 of 209.25 in wet OAB and 185.25 in dry

OAB. There is an increased risk of overactive bladder in menopausal women and there is evidence from previous studies of the effect of decreasing estradiol playing a role in the occurrence of increased inflammatory mediators and causing high levels of MCP-1 in overactive bladder individuals.⁶

Based on these facts, researchers are interested in examining the correlation between levels of Estradiol in the blood as a marker of risk of inflammation with MCP-1 levels in the urine of menopausal women with overactive bladder at H Adam Malik General Hospital Medan.

II. RESEARCH METHODOLOGY

This research was an observational analytic study with a cross sectional study design to assess the correlation between levels of Estradiol and Monocyte Chemotactic Protein-1 (MCP-1) urine in menopausal women with overactive bladder at H. Adam Malik General Hospital Medan from April 2019 till the sample size fulfilled (32 people)

Framework

After obtaining approval from the Ethics Committee of the Medical Faculty, University Sumatera Utara, a sample was taken at H Adam Malik General Hospital Medan. The paramedics who participate in the research sample according to the inclusion and exclusion criteria were given informed consent. Then through interviews the age at menopause, parity, duration of menopause was asked, then BMI was determined by calculating height and weight, then grouped: underweight = <18.5, normal = 18.5 - 22.9, overweight = 23,0 - 24.9, obese \geq 25.0. Followed by taking as much as 3 cc of blood from the vein mediana cubiti for examination of estradiol and Monocyte Chemotactic Protein-1 (MCP-1) from urine. Subsequently sent to the integrated Clinical laboratory Medical Faculty USU Medan.

Statistical analysis

The data collected will be analyzed descriptively to assess the frequency distribution of research sample characteristics based on age, parity and BMI. Then proceed with inferential analysis to analyze the correlation of Estradiol levels with MCP-1 levels of urine of menopausal women with OAB using Spearman's correlation test if the data are not normally distributed. The results of this study were conducted with a significance level $p < 0.05$ and all results are presented in the frequency distribution table.

III. RESULTS AND DISCUSSION

The following are the results of the characteristics of the research subjects based on age, parity, menopause duration, BMI and OABSS.

Table 1. Characteristics of Research Subjects

Characteristics	OAB	
	N	%
Age		
40-49 years old	2	5,9
50-59 years old	32	94,1
Parity		
Primipara	1	2,9
Secundipara	13	38,2
Multipara	20	58,8
Menopause Duration		
2-3 years old	20	58,8
4 years old	12	35,3
5 years old	2	5,9
BMI		
Normoweight	6	17,6
Overweight	28	82,4
OABSS		
Mild (< 5)	14	41,2
Moderate (6-11)	14	41,2
Severe (> 12)	6	17,7
Total	34	100

Table 1. above explains that based on parity, primipara, secundipara and multipara patients were obtained 1 patients (2.9%), 13 patients (38.2%) and 20 patients (58.8%) respectively. Based on BMI, there were 6 (17.6%) and 28 (82.4%) patients with normoweight and overweight. Based on the duration of menopause,

2-3 years, 4 years, and 5 years were 20 patients (58.8%), 12 patients (35.3%), and 2 patients (5.9%). Based on age, 40-49 years and 50 - 59 years respectively 2 patients (5.9%) and 32 patients (94.1%).

Table 2. MCP-1 Urine and Estradiol Levels in Menopausal Women

	Mean	SD	Median	Min	Max
Estradiol	24,26	5,73	25,8	15,4	37,8
MCP-1 Urine	107,53	24,8	97,2	78,3	176

Based on table 2, the mean level of Estradiol in postmenopausal patients with OAB is 24.26 with SD 5.73, median 25.8 and min-max values of 15.4-37.8. The mean levels of MCP-1 in menopausal patients with OAB were 107.53, SD 24.8 with a median value of 97.2; min-max 78.3-176.

Table 3. Correlation of estradiol levels in menopausal women with OAB with OABSS Score

OABSS score	n	Estradiol				R	P
		mean	SD	Median	Min-Max		
Mild	14	27,3	6,11	27,55	26-292		
Moderate	14	21,8	6,15	22,35	17-194	-0.682*	0.001**
Severe	6	15,4	1,59	16,25	15-167		

* Spearman's correlation test

** T-test independent

Based on table 3. obtained values of estradiol based on mild, moderate, severe OABSS scores were 27.3 ± 6.11 , 21.8 ± 6.15 ; 15.4 ± 1.59 respectively. Based on the Spearman's correlation test, it was found a very strong negative correlation between OABSS score with estradiol levels with a correlation coefficient of -0.682 and p value <0.001.

Table 4. Correlation of MCP-1 levels in menopausal women with OAB with OABSS Score

OABSS Score	n	MCP 1				R	P
		Mean	SD	Median	Min-Max		
Mild	14	92.81	4,44	91,80	85-102		
Moderate	14	108,53	10,21	107,50	91-123	0.856*	0.001**
Severe	6	156	10,21	160	132-176		

* Spearman's correlation test

** T-test independent

Based on table 4.4. MCP-1 urine values were obtained based on mild, moderate, severe OABSS scores were 92.81 ± 4.44 ; 108.53 ± 10.21 ; 156 ± 10.21 ; respectively. Based on Spearman's correlation test, it was found that there was a very strong positive correlation between the OABSS score and MCP-1 with a correlation coefficient of 0.856 and p value <0.001.

Table 5. Correlation of estradiol and MCP-1 urine levels in OAB menopausal women with OABSS Score

Mean	SD	Median	Min	Max	R	Nilai p**	
Estradiol	24,26	5,73	25,8	15,4	37,8	-0.682*	0.001*
MCP-1 Urine	107,53	24,8	97,2	78,3	176	0.856*	0.001**

* Spearman's correlation test

** T-test independent

Based on table 5. the value of Estradiol and MCP 1 urine based on OABSS scores were 24.26 ± 5.73 (15.4-37.8) and 107.53 ± 24.8 (78.3-176), respectively. Based on Spearman's correlation test, a very strong negative correlation was found between the OABSS score and the estradiol level with a correlation coefficient -0,682 and p value <0.001, and there was a very strong positive correlation between the OABSS score and the MCP-1 urine levels with a correlation coefficient of 0.856 and a p value <0.001.

Table 6. Correlation of Estradiol and MCP-1 urine levels in Menopausal women with OAB

	Mean	SD	Median	Min	Max	Nilai r*	P**
Estradiol	24,26	5,73	25,8	15,4	37,8	-0.658*	0.001**
MCP-1	107,53	24,8	97,2	78,3	176		

* Spearman's correlation test

** T-test independent

Based on table 6. Estradiol and MCP 1 urine values were obtained based on OABSS scores were 24.26 ± 5.73 (154-37.8) and 107.53 ± 24.8 (78.3-176), respectively. Based on Spearman's correlation test, it was found that a very strong negative correlation between estradiol and MCP-1 urine levels with a correlation coefficient value -0.658 and p value <0.001.

Based on the table in this research it was found that based on parity, primiparous, secundipara and multipara patients obtained 1 patient (2.9%), 13 patients (38.2%) and 20 patients (58.8%) respectively. Based on BMI, there were 6 patients (17.6%) and 28 patients (82.4%) patients with normoweight and overweight. Based on the duration of menopause, 2-3 years, 4 years, and 5 years were 20 patients (58.8%), 12 patients (35.3%), and 2 patients (5.9%). Based on age, 40-49 years and 50 - 59 years respectively 2 patients (5.9%) and 32 patients (94.1%). Based on izmir research, it was found that the majority of women suffering from OAB were 51 years old with a mean value of 51.2 ± 11.1 and prevalence rate of OAB is 42.8%. Based on parity, they obtained nulliparous samples, parity below 3 and parity above 3 respectively 128 people (17.8%), 442 people (61.5%) and 149 people (20.7%). This is consistent with the results of our research with a number of samples with multiparity was 36 (94.7%).⁷ Overactive bladder (OAB) is a group of symptoms of urinary urgency conditions, usually with frequency and nocturia, with or without urinary incontinence (UI) urgency.⁸

Based on this reserach, the value of estradiol and MCP-1 urine levels based on OABSS scores were 24.26 ± 5.73 (154-37.8) and 107.53 ± 24.8 (78.3-176), respectively. Based on the Spearman's correlation test, a very strong negative correlation was found between the OABSS score with estradiol levels with a correlation coefficient of -0,682 and p value <0.001, and there was a very strong positive correlation between the OABSS score and the MCP-1 with a correlation coefficient of 0.856 and p value <0.001. Based on Farhan's research, of 29 women with OAB (18 women with OAB-wet, 11 with OAB-dry) and 10 controls. With an average age of 60.45 (9) years for the OAB group and 55.2 (12) years for the control group (P = 0.153). there was no significant difference in the mean age between women with OAB-dry and OAB-wet (P = 0.223), also compared to controls (P = 0.236). Baseline levels of urine MCP-1 for female patients with OAB were significantly higher than those in controls, with a mean of 210.25 vs 48.02 pg / mg Cr (P <0.001). Additionally, significantly normalized urine MCP-1 levels were highest in patients with wet OAB. There was no significant difference in mean BMI between patients with OAB-dry and OAB-wet (P = 0.214). Using Pearson correlation, the level of urine MCP-1 was significantly correlated with the severity of OAB symptoms in OAB-q (r = 0.03, P = 0.003).⁸

Much evidence shows that the inflammatory process is involved in the pathogenesis of OAB. Ghoniem et al. propose the local inflammation hypothesis as a cause and play a central role in the etiology of OAB. Previous research has shown that an increase in urinary MCP-1 levels is evidence of inflammation in the bladder. In our study, we investigated urinary MCP-1 levels in patients with OAB and using our OABSS score compared severity values based on OABSS and MCP 1. These results provide evidence that women with OAB have higher urinary MCP-1 levels, especially in Indonesia, this shows that chronic inflammation results in greater expression of MCP-1 urine.⁸

Based on table 3. Estradiol and MCP-1 values were obtained based on OABSS scores were 24.26 ± 5.73 (154-37.8) and 107.53 ± 24.8 (78.3-176), respectively. Based on Spearman's correlation test, it was found that a very strong negative correlation between estradiol levels and MCP-1 with the correlation coefficient value -0.658 and p value <0.001. There is a strong correlation between the level of MCP-1 urine and the severity of OAB symptoms. This finding is a major strength of our current study, demonstrating the ability to predict the severity of symptoms with MCP-1 urine levels. The mechanism by which urinary MCP-1 levels are increased in patients with OAB. Stretching of the bladder smooth muscle cells increases the expression of mRNA which leads to increased expression and secretion of urine cytokines. Further investigation and studies are needed to confirm this result, as well as the mechanisms involved in this process. A limitation of this study is the small sample of OAB obtained. A larger sample size will allow for more detailed studies with follow-up of responses.⁸

Urinary MCP-1 against OAB therapy. Overall, the findings of this research can be used as a basis for studying the pathogenesis of OAB in the context of chronic systemic inflammation. The level of urine MCP-1 can be used as a potential tool to monitor disease progression, severity, and to assess the therapeutic effect of treatment, enabling a better understanding of the pathophysiology of OAB syndrome. So from this research we can conclude that, MCP-1 urine is significantly higher in women with OAB and there is a negative correlation between estradiol levels and MCP-1 in relation to OAB. Higher levels of urine MCP-1 can be associated with local inflammatory disorders, which are not associated with obesity and aging. This finding can help to understand the pathogenesis of OAB in the context of chronic inflammation.⁸

IV. CONCLUSION

Based on this study, the majority of characteristics in this research were 50 - 59 years old with 32 people (94.1%), multipara with 20 people (58.8%), overweight with 28 people (82, 4%) and menopause duration of 2-3 years with 20 people (58.8%). Based on this research a very strong negative correlation was found between the OABSS score with estradiol levels with a correlation coefficient of -0.682 and a p value <0.001. Based on this research a very strong positive correlation was found between the OABSS score and the Monocyte Chemotactic Protein-1 (MCP-1) with a correlation coefficient of 0.856 and a p value <0.001. Based on this research it can be concluded that there is a negative correlation between the levels of Estradiol and Monocyte Chemotactic Protein-1 (MCP-1) urine in menopausal women with overactive bladder with $r = -0.658$, this indicates that a decrease in estradiol levels will cause an increase in MCP-1 urine levels in menopausal women with overactive bladder.

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ETHICAL CLEARANCE

For research permission, research approval was obtained from the research subjects and the Ethics Committee of the Medical Faculty, Universitas Sumatera Utara who would conduct a feasibility study on the research proposal.

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