

Urinary glycosaminoglycans levels in women with urinary tract infection and non urinary tract infection

H P Pasaribu^{1*}, A Hanifa, R Z Tala¹, E Ardiansyah¹, R Y Simanjuntak¹ and I H Effendy¹

¹Department of Obstetrics and Gynecology, Haji Adam Malik General Hospital, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

*Corresponding author: partogipasaribu@yahoo.com

Abstract. UTI is an infection that occurs in the urinary tract due to the proliferation of a microorganism. Female is fourteen times more vulnerable to UTI than male, because their urethra is shorter. Bladder epithelium is coated with a thin layer of glycosaminoglycans which act as a non-specific anti-adherence factor and nonspecific defense mechanisms against infection and can be found in the urine. An analytic study with cross sectional approach was conducted in 46 patients (23 with UTI and 23 non UTI) from June 2016 to determine differences in levels of urinary glycosaminoglycans between two groups. Urine samples were taken and tested for UTI and non UTI strips test. Laboratory examination of urine GAGs levels using ELISA kit for Human Glycosaminoglycans, then tabulated and analyzed using SPSS. The result showed no significant differences in the characteristics of women between two groups. There are significant differences in the mean levels of urinary GAGs in women with UTI compared with Non-UTI (69.74 ± 21.34 ; 21.39 ± 2.61 mg/l; $p < 0.001$). There was no significant relationship between the sexual status and UTI incidence, with low odds ratio values and no significant difference in the mean of urinary glycosaminoglycans level based on sexual status.

1. Introduction

Urinary Tract Infection (UTI) is an infectious disease commonly found in all age groups. But, some groups of people are more prone to UTIs than others. UTI is broadly defined as an inflammatory response against bacterial invasion of the urothelium, which usually associated with bacteriuria and pyuria. Bacteriuria is the presence of bacteria in the urine. UTI can happen anywhere along the urinary tract. Women are fourteen times more prone to suffer from UTI than men. UTIs are more common in women who are sexually active and after menopause.[1,2]

Strong evidence was found that among infectious diseases in the urinary tract such as UTI, cystitis and painful bladder syndrome, interstitial cystitis that pathophysiology associated with the early stages of the disease lose the mucus layer of glycosaminoglycans (GAGs), which is the beginning of the inflammatory process. Bladder epithelium is coated with a thin layer of GAGs that act as non-specific anti-adherence factors and non-specific defense mechanism against infection and can be found in the urine. Injured and not healed GAGs layers can cause bladder epithelial damage and chronic neurogenic inflammation.[3]



2. Materials and Methods

2.1. Location, time and population

This was a cross-sectional study to know the difference of GAGs in patients with Urinary Tract Infections (UTI) and non-Urinary Tract Infection (Non-UTI). The research was conducted in RSUP H. Adam Malik, and RSU Pirngadi Medan from June 2016 until the number of samples was fulfilled. The populations were all inpatient and outpatient women in RSUP Dr. H. Adam Malik and RSU Pirngadi Medan, with Urinary Tract Infection as a diagnosis or complaint. The samples were part of the population whom GAGs levels were measured. Samples were chosen by using a randomized sampling technique based on the inclusion and exclusion criteria.

2.2. Data collection

After having an explanation of the research purpose, benefits, procedures, and signed agreement to participate, interviews were conducted by using questionnaires to determine the researcher required data. As much as 20cc mid-stream urine was taken from the participant for urine test strips UTI and non-UTI, then levels of GAGs were measured by using ELISA kit for Human Glycosaminoglycan (GAGs), which will be examined in the laboratory. Data were collected and analyzed statistically.

2.3. Ethics

Ethical clearance was approved by Ethical Committee of Medical Faculty, Universitas Sumatera Utara. Informed consents were obtained from all test participants.

2.4. Data analysis

Data analysis and statistical tests were computerized. The results of the research will be presented in frequency distribution table. To analyze the differences in the levels of GAGs, a statistical test was conducted with unpaired t-test for normal distribution data. If the data were not normally distributed, Mann-Whitney test would be conducted with a confidence level of 95% ($\alpha = 0.05$).

3. Results

Based on table 1, the characteristics of research subjects based on age in the UTI women group were mostly at the age of 26-30 years (56.5%) whereas in the Non-UTI group, most were at the age of 20-25 years (56.5%). By education level, UTI women group were mostly low-educated (56.5%) as well as in Non-UTI group (52.2%). Based on sexual status, the UTI women group were most sexually active (73.9%) as well as in Non-UTI group (60.9%). Based on employment, the samples in UTI women group are mostly employed (52.2%) whereas in the Non-UTI group, most are unemployed (65.2%). Based on the statistical test by Chi-Square test, there were no significant differences between the UTI women characteristics with non-UTI women characteristics ($p > 0.05$).

Table 1. Characteristics of research subjects by age, education, sexual status, and employment.

Characteristic	Cases (UTI)		Control (Non UTI)		Total	%	P ^a Value
	N	%	N	%			
Age (years)							
• 20-25	10	43.5%	13	56.5%	23	50%	0.376
• 26-30	13	56.5%	10	43.5%	23	50%	
Education							
• Low	13	56.5%	12	52.2%	25	54,3%	0.767
• High	10	43.5%	11	47.8%	21	45,7%	
Sexual Status							0.345

• Active	17	73.9%	14	60.9%	31	67,4%	
• Inactive	6	26.1%	9	39.1%	15	32,6%	
Employment							
• Employed	12	52.2%	8	34.8%	20	43,5%	0.234
• Unemployed	11	47.8%	15	65.2%	26	56,5%	

^aChi-Square test

From table 2, it was found that the level of urine glycosaminoglycans was not normally distributed, so that the Mann-Whitney test was conducted to determine the differences between the mean of urine glycosaminoglycans level on women with UTI and Non-UTI. The mean of urine glycosaminoglycans level on women with UTI was 69.74 ± 21.34 mg/l the mean of urine glycosaminoglycans level on women with non-UTI was 21.39 ± 2.61 mg/l. Statistically, there was a significant difference on the mean of urine glycosaminoglycans level on women with UTI and Non-UTI. The hypothesis of this research, which stated that there were significant differences in urine glycosaminoglycans level on women with Urinary Tract Infection and Non-Urinary Tract Infection, is accepted.

Table 2. The differences in urine glycosaminoglycans level of women with urinary tract infection and non urinary tract infection.

Research Group	Glicosaminoglycans level (mg/l)				P ^a Value
	n	Mean	SD	Median	
UTI	23	69.74	21.34	67.8	0.001
Non-UTI	23	21.39	2.61	21.3	
Sum	46				

Mann-Whitney Test

As shown in table 3, Chi-square test was conducted to determine the relationship between sexual statuses with UTI incidence. Based on statistical analysis by chi-square test, there was no significant relationship between sexual statuses with UTI incidence ($p < 0.345$). From the table, it was known that the odds ratio value was 1,821. It meant that a patient with sexually active status has the possibility to suffer UTI by 1.8 times.

Table 3. The relationship between sexual statuses with UTI incidence.

Sexual Status	Case (UTI)		Control (Non-UTI)		P Value	OR
	n	%	n	%		
Active	17	73.9	14	60.9	0.345	1.821
Inactive	6	26.1	9	39.1		

Table 4 indicates that according to the sexual status, sexually active women group has higher urinary glycosaminoglycans level as 74.2588 ± 20.62071 mg/l compared with sexually inactive with urinary glycosaminoglycans level 56.9500 ± 19.44580 mg/l. But statistically, there was no significant difference on the mean of women urinary glycosaminoglycans who suffered UTI based on sexual activity.

Table 4. The differences of mean of glycosaminoglycansurine level on women UTI based on sexual statuses.

Sexual Activities	Glicosaminoglycans level (mg/l)				P Value
	N	Mean	SD	Median	
Active	17	74,2588	20,62071	74,30	0,123

Inactive	6	56,9500	19,44580	49,85
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4. Discussion

The results of this research found no significant difference between the UTI women characteristics with non-UTI women characteristics ($p > 0.05$). This explains that characteristics of age, education level, sex, and employment status have no influence on levels of GAGs. The literature states that UTIs are more often found in women who are sexually active and after menopause. In this research, the women were still in the reproductive and premenopausal state.

Protective factors that counter UTI in women is the estrogen-dependent mucous membranes formation of GAGs in the bladder. This mucus has a function as an antimicrobial. During menopause, estrogen levels decline, and this protection system disappeared so that women who had experienced menopause will be prone to UTI. Protection against UTI is formed by the urine nature which is acidic and then acts as an antibacterial. Bladder epithelial layer also serves as a defense mechanism against infection. This layer also specifically regulate bladder function and contribute to the pathogenesis of various bladder diseases.[3,4,5]

Results of laboratory analysis of the urinary GAGs levels showed that the mean GAGs level of women with UTI group was 69.74 ± 21.34 mg/l. It was higher than the mean GAGs level in women with Non-UTI group (21.39 ± 2.61 mg/l). Statistical test showed a significant difference between the mean levels of GAGs in women with UTI and non-UTI groups. This explains the GAGs level was significantly increased in the urine of women with urinary tract infections.

The bladder has a variety of natural defense mechanism against infection. Bacteria are taken out by the bladder through the urine. Low urine pH inhibits the bacteria growth. Urothelium also maintains bladder from infection by recognizing and preventing bacteria adhesion. GAGs layer, umbrella cells, tight junctions, which covers the top layer of the urothelium, form the highly impermeable epithelial surface. GAGs have a role in the immune system stimulation by triggering the activation and leukocytes movement to inflammatory tissue. GAGs also act as chemokines carrier and growth factors.[6,7]

GAGs layer also known as the mucosal layer, is an important factor in cellular permeability. It is composed of GAGs layer and proteoglycans which cover the surface of the lumen urothelium. Damage to this layer causes urothelial cells exposure which is located in the base and may cause bladder dysfunction.[6]

The same research results reported by George Gray, who conducted research on 662 samples and found increased levels of GAGs in 14 samples.[9]

In the Le Phuc Thuy and colleagues research, the normal value of total urinary GAGs in adults is 1.8 ± 0.6 g / mol creatinine with 16 people samples.[10]

David C. Wei conducted research for measurement of GAGs in 20 normal individuals and 25 patients with UTI, then found the levels of GAGs in normal individuals is 19.9 ± 2.5 , and the GAGs levels in patients with UTI is 30.4 ± 5.1 . [11]

While Gousse A et al., who conducted research on 14 patients with UTI and 4 normal individuals, found GAGs levels in normal individuals are 39.5 ± 11.2 $\mu\text{g}/\text{mg Cr}$, while the GAGs levels in a patient with UTI are 75 ± 15.4 $\mu\text{g}/\text{mg Cr}$. Yara et al. conducted a measurement of GAGs in 25 normal individuals where they found the levels of GAGs are 20.16 – 22.50 mg/L.[12]

5. Conclusion

Statistically, there was no significant difference found between UTI women characteristics and non-UTI women characteristics ($p > 0.05$). The difference in mean levels of urinary glycosaminoglycans was statistically significant in UTI women than in non-UTI women.

There was no significant relationship between the sexual status and UTI incidence ($p > 0.05$), with low odds ratio values and no significant difference in the mean of urinary glycosaminoglycans level based on sexual status.

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