

Diagnostic Test of Combination of Wall Bladder Thickening Ultrasound and Lekosit Esterase on Clinical Cystitis

Ana Majdawati¹, Inayati Habib², Suryanto³

1. Muhammadiyah University Yogyakarta, Radiology Departement, Yogyakarta, Indonesia

2. Muhammadiyah University Yogyakarta, Microbiology Departement, Yogyakarta, Indonesia

3. Muhammadiyah University Yogyakarta, Pathology Clinic Departement, Yogyakarta, Indonesia

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Abstract

Combination wall bladder thickening on ultrasound and lekosit esterase decades often used as an adjunctive diagnostic in some cystitis cases. Purpose of this research was to determine how sensitivity and specificity of combination wall bladder thickening on ultrasound and lekosit esterase in sufferers with clinical cystitis. Method of this research is diagnostic test to determine the sensitivity and specificity of combination wall bladder thickening on ultrasound and lekosit esterase in sufferers of gold standard with cystitis clinical is bacteriological urine (urine midstream streak plate method). The results of sensitivity and specificity of this research is 80,33% and 76,92%. This value is higher than sensitivity and specificity ultrasound or lekosit esterase separately. Combination of examination is very important for skreening clinical diagnosis of cystitis. Ultrasound helps knowing the clinical causes of non infection cystitis, such as obstruction of bladder due to fibrosis, cystokele, mucous wall bladder abnormalities as there are masses, trabekulasi, prostate hypertrophy, neurogenic bladder and stone. Lekosit esterase is a parameter of the process inflammation in bladder. The Conclusion is research has a good sensitivity and specificity so that enforcement needed in diagnosis of cystitis.

Keywords: ultrasound of the wall bladder thickening, lekosit esterase, sensitivity, specificity, cystitis

1. Introduction

Cystitis is an inflammatory reaction of wall bladder caused by several things which is the most common cause of bacterial infection that followed another mikroorganisme as fungi, viruses and parasites. Cystitis is the most common cause of gram-negative bacteria such as *Escherichia coli* (80%), *Acinetobacter calcoaceticus*, *Klebsiella pneumonia* and gram-positive bacterial such as *Staphylococcus aureus* often occurred at infants, children and increases in the elderly. The incidence of cystitis in female more often than male (female: male ratio = 2 : 1), because the female urethra is shorter and its location near the anorectal (1,2,3)

The symptoms of cystitis do not typical and some without symptoms. Common symptom is dysuria, hematuria, heartburn or burning when urinating. There are also other symptoms as suprapubic pain, difficult to urinate, tenesmus, nocturia and even secondary nocturnal enuresis, prostatismus (difficulty starting urination and less heavy flow of urinate), pain urethra, ureter and renal colic (1,3).

Diagnosis of cystitis is often proposed by some clinician (internist, pediatric or urologist), among which the examination of leukocyte esterase (LE) and ultrasound (4,5). The ultrasound of bladder has been made include the measurement of wall thickness for cases related to abnormalities in the bladder. Some studies indicate that there is a relationship between bladder wall thickness with cystitis due to inflammation of the mucosa and the musculus detrusor. Echostruktur of mucosal bladder differences with echostruktur detrusor muscle (5). The positive Leukocyte esterase results has a significant relationship to the number of neutrophils, either in one piece or lysis indicating the inflammatory process in cystitis. On examination of the urine strip (or strips dipstick dye) the amount of leukocyte esterase urine based leukocytes will produce a color change reaction which gives information about the concentration of substances present in urine and read semiquantitatively (6). The diagnosis of bacterial cystitis is surely to be found bacteria in the urine culture. Level of significance of the number of bacteria in urine is greater than 100,000 / ml urine (7). Some the questions that arise, whether the sensitivity and specificity of the combined of the wall bladder thickening on ultrasound and LE high enough as a diagnostic support case Cystitis? The diagnosis of cystitis can be enforced by the combined size of the wall thickening in ultrasound and LE, when the sensitivity and specificity of the above examination has high value. This can help enforcement of early diagnosis and treatment of cystitis can be immediately done.

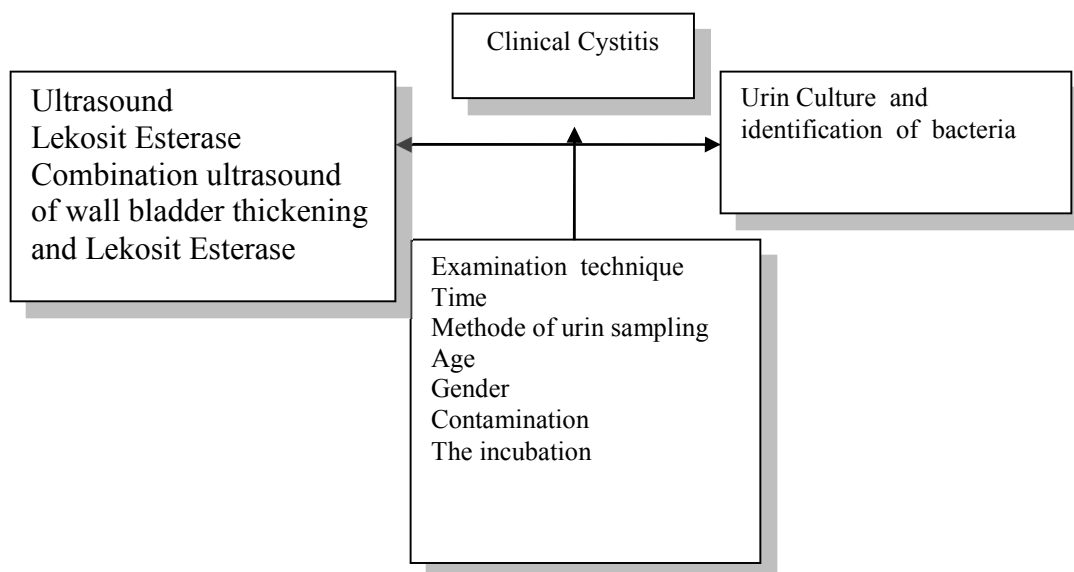


Figure 1 The research framework

2. Research Methods

This study was to determine the sensitivity and specificity of the combined wall bladder thickening on ultrasound and LE in patients with cystitis. The gold standard of this research is bacteriological urine culture with diagnostic test with 2 x 2 table. The implementation of this research from April to November 2011 in PKU Muhammadiyah Yogyakarta Hospital and a clinic doctors in private practice at Kulon Progo. The sample 100 patients that inclusion and exclusion criteria. Inclusion criteria : 1) age 18-60 years with clinically Cystitis (at least 2 clinical symptoms) were fill an informed consent as research subjects ; 2) . Bladder mass , congenital anomalies or an enlarged prostate ; 3) . not pregnant ; 4) . not undergoing radiotherapy or chemotherapy due to the bladder or prostate malignancy . Exclusion criteria , found a mass in the bladder on ultrasound. Clinical symptoms of cystitis are dysuria , often feels the urge to urinate (frequency) , cloudy urine or redness and subfebril fever

Lekosit esterase examination done in the laboratory of PKU Muhammadiyah Hospital and culture of urine in the Laboratory of Microbiology, Medical Faculty of Muhammadiyah University Yogyakarta. Ultrasound of bladder, LE and urine culture reviewed by experts. Tools and materials research are 1). Ultrasound with probes from 3.5 to 7 M.Hz curve shape; 2). leukocyte esterase reagent strip commercial urine; 3). bacteriological urine and identification of bacteria that cause UTIs; 4) urine samples; 5). computer, stationery and paper. The research variables: 1). independent variable which consists of a combination of wall thickness on ultrasound and LE is normal and abnormal. 2). dependent variable, that urine culture (mid stream) is normal and abnormal. Bladder wall thickness is the measure of the mucosa lining the detrusor muscle with transabdominal ultrasound in transverse and longitudinal section. Used probe frequencies from 3.5 to 5 mHz with bladder filled with water 80% (150-200 ml). Levels of leukocyte esterase, an enzyme that is present in primary granules of neutrophils were measured semiquantitatively. Positive results indicate the presence of neutrophil cells in the urine. Figures Germs, is the number of bacteria from urine culture cystitis sufferers. Positive results when the bacteria are found in significant amounts, unit of colony forming units / ml (cfu / ml). Identification of Bacteria: a type of bacteria that grow and are determined based microscopic and biochemical tests.

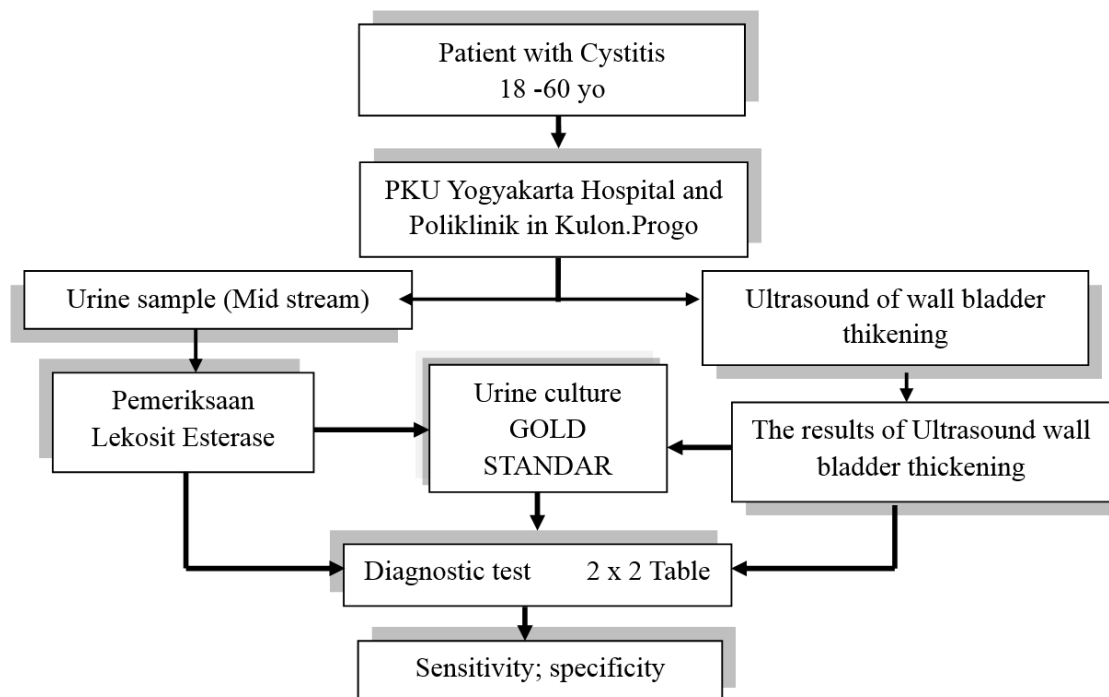


Figure 2 The course of study

3. Results and Discussion

3.1. Results

Table 1. Characteristics subjects of the research

NO	Description	Classification	The total number of	%
1	Gender	Man	40	40
		Woman	60	60
2	Age	≤ 20 yo	6	6
		20-50 yo	55	55
		> 50 yo	39	39
3	Clinical Symptoms	Dysuria	69	69
		Suprapubik pain	15	15
		Hematuria	5	5
		Frequency	11	11
4	Lekosit esterase	Normal (≤ 25)	42	42
		Abnormal (> 25)	58	58
5	Ultrasound	Normal (≤ 0,5 cm)	41	41
		Abnormal (> 0,5)	59	59
6	Ultrasound + LE	Normal	58	58
		Abnormal	42	42
7	Bacteriology Urine	Positive (Cystitis)	61	61
		Negatif	39	39

Table 2. Pattern bacteria cause cystitis

NO	Bacteria	Total number	ULTRASOUND
1	<i>E.coli, Staphylococcus Sp, Streptococcus Sp</i>	16	positive
2	<i>E.coli, Salmonella Sp, Klebsiella Sp</i>	6	positive
3	<i>E.coli, Staphylococcus Sp, Salmonella</i>	1	negative
4	<i>E. coli, Staphylococcus Sp, Candida</i>	15	Negative 5; positive 10
5	<i>E.coli, Klebsiella Sp, Candida</i>	1	positive
6	<i>E.coli, jamur/candida</i>	2	2 (negative)
7	<i>E.coli, Streptococcus Sp</i>	8	4 (positive 4; negative 4)
8	<i>E.coli</i>	2	positive
9	<i>Staphylococcus Sp, Streptococcus Sp, Candida</i>	4	positive
10	<i>Staphylococcus Sp, Streptococcus Sp</i>	1	positive
11	<i>Staphylococcus Sp</i>	1	positive
12	Candida/Fungi	4	negative

Table 3. 2x2 table of diagnostic test combination ultrasound of wall bladder thickening and lekosit esterase

		Urine Culture	
		+	-
Ultrasound	+ LE	49	9
	-	12	30

Sensitivity : $49/61 \times 100\% = 80,33\%$ Spesifisity : $20/24 \times 100\% = 76,92\%$

3.2. Discussion

Total sample of 100 patients with cystitis consisting 40 men (40%) and 60 women (60%). This is in accordance with the theory which incidence of cystitis in women more often than men because the distance of the bladder by osteum urethra externa is shorter in women than men and women are easily contaminated with the genitalia from anorectal (3,6). The incidence of reproductive age much of cystitis that is between 20-50 years in which sexual activities at this age are still active. This is in accordance with the number of the subject of this research is the most aged between 20-50 years (3).

The complaint of most research on the subject of cystitis are dysuria i.e. 69 people (69%), a sense of discomfort or pain, heat before, during and after urination. This happens due to an inflammatory process involving the walls of the bladder that consists of several layers, i.e. the inner wall of the urothelium (epithelium), lamina propria, lamina muscularis (detrussor muscle) and the tunica adventitia. Due to the inflammatory process is in addition to inflicting pain also cause blockage of the urethra from the bladder to the urethra so that steady stream of urine from the bladder less smoothly, It is cause more severe symptoms of cystitis i.e dysuria, frequency, painful suprapubik, hematuri (8).

The results of bacteriological urine cultures from 100 subjects of research, there are 61 patients (61%) are the result of positive and 39 patients (39%) are negative. Based on this research we can see microorganisms cause cystitis most in 61 patients who positive urine culture, based on the order is *Escherrichia coli*, *Staphylococcus Sp.*, *Streptococcus Sp.*, *Candida* and there are several other bacteria, i.e., *Klebsiella Sp.*, *Salmonella sp.* The microorganisms most frequently cystitis from some references are bacteria, followed parasites, fungi and viruses. The bacteria most often causes cystitis is Enterobacteriaceae i.e. *Escherrichia coli*, *Salmonella Sp.*, *Klebsiella Sp.*, and Gram-positive bacteria i.e. *Staphylococcus Sp* and *Streptococcus Sp* (1,3,9).

Subjects with positive urine bacteria culture results as much 61 people and 59 have wall thickened bladder (positive) and 41 patients not thicken (negative). Subject that 39 negative culture urine turned out to be a ultrasound and the results showed thickening of the wall bladder as much as 14 of the subject does not thickening of 25. In this study, thickening of the wall bladder in sufferers of clinical cystitis is not always related to the bacteria that exists in the bladder. It can be inferred that the thickening of the walls bladder is not always the case at all, because of thickening of the wall bladder also influenced by various factors such as age, the body's immune system, the number of colonies of bacteria, bacterial species and invasive nature of the bacteria, the presence of disease/other abnormalities on bladder like uretherocele, the presence of enlarged prostate mass (7).

It is also shown with a combination of ultrasound and LE, out of 61 subjects of the bacteria culture urine are true positive as much as 49 subjects and 12 subjects with negative results. Thirty-nine subjects the

results of bacterial culture negative urine as true negative 30 subjects. Combination of ultrasound and LE assessment obtained sensitivity and spesifisity 80,33% and 76,92%. This value is good enough as a reference supporting examination for cases of cystitis because its value is over 70%. Sufferers of clinical examination performed combined ultrasound and LE who actually bacterial cystitis is around 80,33. The combination of this diagnostic test (LE and ultrasound) in the case of cystitis have specificity 76,92% which means that this test can get rid of a UTI suspek sufferers really negative bacterial cystitis did not suffer as much as 76,92. Preliminary research on there meaningful relationship between thickening bladder ultrasound with LE (10). Lekosit esterase reaction is the initial stage of immunity that will appear after the lysis of membranes lekosit which causes the granule azurofilik in the lekosit cytoplasm will lisis, so that this examination will show positive results (quantitative values > 25). Examination of LE detects esterase in granulositik white blood cells (neutrophils, eosinophils, basophils, and monocytes). Neutrophils are the most frequent lekosit associated with the presence of a bacterial infection. Esterase also on trichomonas and histiosit. Lymphocytes, erythrocytes, bacteria and cells of kidney tissue does not contain esterase. The positive results of the examination of LE most often showed a bacteria as has been discussed previously. infections caused by Trichomonas, Chlamydia, fungi and inflammation of kidney tissue (interstitial nephritis) produces lekosituria without bakteriuria (11).

The results of examination of LE-positive are not always followed by a thickening of the wall bladder ultrasound or urine bacteria culture are positive. This can be caused by several things, including:

1. The time between sampling urine with an examination of urine culture and LE don't along with ultrasound assessment. This led to the results of culture urine and LE are positive and wall bladder in ultrasound not thickened (negatif). This can happen otherwise. Lekosit esterase at the time of the urine is no fresh lead to increased number of lekosit and lisis impact lekosit that will provide the value of the lekosit esterase in quantitative more than 25 (positive results), culture of the urine can give positive results because of the urine are not fresh than bacterial growth can occur (11).
2. in the case of acute bacterial cystitis, The walls bladder is not thickening and measure of wall bladder dont visually on ultrasound, is the number of lekosit urine already began to increase that impact with the value lekosit esterase-positive (20,21). Chronic cystitis can cause pathological changes in the structure of mucosa and the walls of the bladder (detrussor muscle) that cause diffuse thickening (gross wall) and the reduced capacity of the bladder. The thickening measurement of wall bladder can give positive results (12).

Sensitivity and specificity of combination of wall bladder thickening ultrasound and LE in the case of cystitis 73,77% and 64,10%. The value of this sensitivity is good (over 70%), while the value of specificity of ultrasound is a little low (below 70%). The results of the ultrasound with a thick wall which shows normal bladder really is not a case of bacterial cystitis 64,10%. The walls of the bladder that do not thicken the cystitis can be the inflamasiya process is still early, so the wall bladder thickness less than 0.5 cm.

Thickening of the wall of the bladder increases can be caused by several factors, including the presence of abnormalities in the bladder that might not be visible by ultrasound. It cause the occurrence of urethrovesical junction obstruction so that the urine flow so a steady stream of urine is not smooth. Tissue fibrosis formed due to the process of chronic cystitis like as divertikulosis, cystocele that causes the prolapsnya basis of the trigone, infection from outside bladder like Crohn diseases, prostate enlargement and others (8).

Sensitivity and specificity of the LE on suspek cystitis is 78,69% and 74,36%. This value is quite good because more than 70%. The positive results of the examination of LE most often showed a bacteria as has been discussed previously. infections caused by Trichomonas, Chlamydia, fungi that they inflammation of kidney tissue (interstitial nephritis) produces lekosituria without bakteriuria (11)

Combination of ultrasound and LE examination are required because it has better specificity than ultrasound assessment or LE in itself alone. Ultrasound can rule out high enough people with cystitis symptoms that does really not suffer bacterial cystitis with specificity 80,33%. Ultrasound is required to see the cause of the thickening of the walls bladder in the cases that cause by non infectious cases (non bacterial cystitis) that can result in hypertrophy detrussor muscle, dilation of bladder, the mucous disorder (focal thickening of the mucosa of bladder), trabekulasi, divertikel as well as the presence of the masses. In research study by the Khullar, et al conducted that wall thickening of bladder in ultrasound diagnotic test on the case of impaired miksi (include thickening of walls and voiding function) with the standard reference Cystografi, Cystoscopy and uroflowmetri, get the value of the sensitivity and spesifisity high enough that is 84% and 89%. Research results Khullar, et al get the cause of the thickening of the wall bladder due to contraction of the detrussor musculus has increased due to the obstruction of the urethra osteum internum due to fibrosis, cystokele, mucous wall bladder abnormalities as there are masses, trabekulasi, neurogenic bladder, prostate hypertrophy and presence of stones 8,10, 12,13,14).

4. Conclusions and Suggestions

The Conclusions of sensitivity and specificity of combined ultrasound wall bladder thickening and LE in sufferers with clinical cystitis is 80,33% and 76,92%. This value is higher than the value of the sensitivity and

specificity of ultrasound (73,77% and 64,10%) and LE (78,69% and 74,36%) in himself alone. The joint inspection is extremely important for clinical diagnosis of Cystitis skreening against the case of cystitis. Combined ultrasound wall bladder thickening and LE it also has a good point to get rid of the specificity of the diagnosis of the case really is not bacterial cystitis. Wall bladder ultrasound helps to know the clinical causes of UTI/cystitis non bacterial, as due to the obstruction of the urethra osteum internum due to fibrosis, cystokele, mucous wall bladder abnormalities as there are masses, trabekulasi, prostate Hypertrophy, neurogenic bladder and the stone. Bacterial causes of cystitis is most *e. Coli*, *Streptococcus Sp.*, *Staphylococcus Sp* and yeast/Candida.

Suggestions this research many flaws because of the limitations of the existing infrastructure, so the researchers suggest can do similar studies with control some things like below:

This research should be done in one building/hospital so that ultrasound assessment, LE and bacteriological cultures of urine can be easily controlled and avoid the existence of ambiguous results due to the examination of the urine are not fresh (over 4 hours).

1. Ultrasound done by a single person who has done the kappa test and using ultrasound with the same specs so that provide measurement results valid wall bladder thickness, as well as for inspection of LE and bacteriological cultures of urine.
2. Ultrasound conducted by a single person who has undergone a kappa and uses ultrasound with the specification that the same given result of measuring the thickness of a wall bladder, likewise for examination, lekosit esterase and urine culture bacteriology.

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