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RESEARCH ARTICLE

HUMAN URINARY RNA EXOSOME: OPTIMIZING METHODS OF ISOLATIONS AND SAMPLE PREPARATION FOR TRANSCRIPTOME

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ABSTRACT

Introduction: Human urine is potential bio-fluid to study as a diagnostic biomarker methods. There are substances that secreted from metabolism residue and damaged cell, including genetic substances that cast away through urine, and also RNA (Ribonucleic Acid). Recently, RNA (coding-ncRNAs) has been developed for diagnosis method because it could represent profile expression in the cell. Furthermore, RNA urinary isolation methods is important to be established to get reliable biomarker non-invasive compared to tissue biopsy. In fact that optimization method for isolation RNA from urine is not clear. So that, the optimization and stability storage study are needed to be used as reference standard protocol. This study performed to know the optimization methods of RNA isolation from urine samples and RNA concentration stability storage for transcriptomic (non-coding RNA) analysis.

Methods: Each sample was collected as many 15 mL in the morning and treated with lysis solution from different manufacturers (Qiagen, Ambion, Geneid, control without buffer). ANOVA Statistic analysis was performed to know significant difference between methods used.

Results: RNA stability measuring of RNA and DNA observed on day 1, 3, 5, 7, 9, 11, and 13-day by P-value > 0.01. at the same time, RNA stability storage is known to decrease consistently by 0.1-1 ng each day. Quantifikasi miRNA could be done from urine samples.

Conclusion: There is no significant difference between all the methods used.

Keyword: urine, lysis buffer, RNA isolation, stability

Introduction

The last few decades study with urine was not much done yet. Urine sample expected can be a non-invasive biomarker on several types of disease so as can replace some gold standard diagnosis like tumour biopsy. Some study has indicated that a heterogeneous population of nanosized structures (microvesicles, apoptotic vesicles and exosomes) secreted and found all cell types of biological fluids (Morrissey et al., 2015; Kind et al., 2007; Bosso et al., 2008).

The exosome is small carrying (30-120 nm) various molecular constituents of their cell of origin, including proteins and RNAs (mRNAs, miRNAs and non-coding RNAs) that represented tissue specific. Many types of cell have capacity to secreting exosome, including reticulosis (Pan, B-T. and Johnstone, R.M.,

1983), dendritic cell (Thery, C et al., 1996), B cell (Raposo, G. et al., 1996), T Cell (Blanchard, N et al., 2002), Mast Cell (Raposo, G. et al., 1997), Epitel cell (Van Niel, G et al., 2001) and tumour cell (Mears, R et al., 2004). miRNAs exosome can be stable in blood, urine, and body fluids, and exosome can reflect tissue or origin cell in the presence of protein specific of the surface (Simmons, M. and Raposo, G., 2009; Mathivanan, S.et al., 2010; and Gross, J.C. et al., 2012).

In this study, we have performed the activity and stability of ribonuclease from the urinary sample. which can be found in almost all living organisms, is quite stable and immediately contaminates RNA degradation samples. RNA is less thermodynamically stable material than DNA because the 2'-OH group is present in the ribose ring, resulting in hydrophilic bonds directed towards the 5'-3 'phosphodiester bond. Temperature rise and elevation of pH can cause RNA damage. Beside it, we have compared the four groups using different commercial lysis buffer ambion (Cat no. 10608970A), GeneAid (Cat no. MK 11107), Qiagen (Cat no. 127154224) and without lysis buffer to know potential methods to isolate and storage.

The activity of ribonuclease, While many consider the temperature of -80o C as the standard in storage. At Biochemistry and Molecular Biology Laboratory of Gadjah Mada University Medical School, we assume that RNA is best kept at ultra-low temperatures, so a temperature of -80o C has been continuously used to preserve Sample RNA. The objective of this study was to know the most optimal method of isolating RNA in urine and to know the stability of RNA concentration on deep freeze storage.

Material and Methods

Sample collection and Exosome Isolation

Urine samples from 16 human urine have been collected in the morning with at the rate 1,1 mL using tube collection 15 mL and centrifuged at 10.000 x g for 5 minutes. Exosome isolation was performed using miRCURRY Exosome isolation kit – cells urine and CSF, 12-80 rxns (cat no. 3001012 Exiqon, Denmark). All the procedures were followed the manufacture recommendation.

RNA Isolation

Four methods were used to know the most potential methods for isolation RNA from urine. They were Buffer lyses ambion (Cat no. 10608970A), GeneAid (Cat no. MK 11107), Qiagen (Cat no. 127154224) and without lysis buffer. 100 µL samples were a vortex for 15 seconds. Incubation for 10 minutes and centrifuge for 300 x g for 1 minutes at the temperature 20°C. 100 µL Supernatant was used as a template RNA isolation. Isolation RNA used miRCURY RNA Isolation Kit Bio-fluids (Cat no. 300112 Exiqon Denmark). The Results of total RNA have been measured using Nano-drop GE NanoVue Plus. All the procedures were followed the manufacturer's recommendation.

Synthesis cDNA

Synthesis cDNA used Universal cDNA synthesis kit II, 8-64 rxns (Cat no. 203301, Exiqon Denmark). Total RNA was used as a

template, then cDNA concentration calculated using by Nanodrop GE Nano Vue Plus.

RNA Stability test

To determine the stability of RNA in -80oC storage, concentration RNA samples were calculated on: day 3rd, 5th, 7th, 9th, 11th, and 13th-day using by Nanodrop (NanoVue GE).

qPCR and data analysis

qPCR analysis of miRNA gene expression was performed using qPCR CFX 96 Thermocycler (Bio-Rad). Quantification used SYBR Green miRCURY LNATM microRNA PCR Excellent Each SYBR® Green Master mix concentred (Exiqon, Cat no. 203402). All procedure followed the manufacture's recommendation. All data statistical was determined using SPSS, Graph Pad to know significance difference methods that used.

Results and Discussion

RNA isolation from urine samples

This study using urine samples has not been widely performed. Isolate RNA from urine samples have some advantages for diagnosis and drug development. We have done to approach to look at predictive markers based on non-coding RNA from urine exosome PCA. All type of the cell-secreted microvesicles include: (1) prostasom with size 150-500 nm, produced by epithelial cells of prostate ducts which are the normal components of seminal fluid and play a role in male fertility (Burden et al., 2006); and (2) exosomes of 30-100 nm, special nanovesicles with cup-shaped morphology (Mitchell et al., 2009). Cells can communicate via membrane transfer by secretion of exosomes/microvesicles (Ratajczak J. et al., 2006). Nucleic acids have been identified in exosomes, ie mRNA, microRNA (miRNA) and other non-coding RNA (ncRNA) (Sato-Kuwubara, Y. et al., 2015). Many cells have capacity to release exosome, including reticulocytes (Pan, BT and Johnstone, RM, 1983), dendritic cells (Thery, C et al., 1996), B cells (Raposo, G. et al., 1996) T cells (Blanchard, N et al., 2002), mast cells (Raposo, G. et al., 1997), epithelial cells (Van Niel, G et al., 2001) and tumor cells (Mears, R et al. , 2004). Exosomes miRNAs are stable in blood, urine, and body fluids, and exosomes reflect the tissue or cell origin. (Simmons, M. and Raposo, G., 2009; Mathivanan, S.et al., 2010; and Gross, JC et al., 2012). RNA Exosome is more stable than RNA extracted from whole urine (Kevin C, et al, 2010). Microvesicles from exosome resist to RNase and DNase digestion and still protect the nucleic acids contained within them (Zhou, et al. 2006). Unlike whole cells, microvesicles (exosome) are quite resistant to freeze-thawing, and nucleic acids can be extracted from the urinary exosomes following freeze-thawing (Russo et al., unpublished data). So that isolating RNA from urine exosome is more suitable for transcriptome (RNA) isolation.

miRCURYTM Exosome Isolation Kit (EXIQON) used to isolate exosomes from urine samples. Subsequently, RNA was isolated from urine exosomes with three different lysis buffer (Ambion, Geneaid, Qiagen) as additional buffer and control with no additional buffer. after that RNA was synthesized into cDNA. RNA dan cDNA concentrations measured with nanodrop and analyzed with Anova

Table 1. The results of RNA isolated concentration measurements

Treatment	RNA concentration (ng/µl)
Without lysis buffer	5.0
Ambion	6.8
GeneAid	6.3
Qiagen	8.0

Table 2. The measurements of cDNA concentrations from RNA synthesis results

cDNA			
Without lysis buffer	Lysis Buffer		
	Ambion	Genaid	Qiagen
345			
338.5	371.5	357.5	337.5
351.5	364.0	359.5	381.0
307.5	379.0	379.0	358.5

Table 3. One Way ANOVA Analysis optimization of RNA isolation method results

Anova: Single Factor

SUMMARY

Groups	*Count*	*Sum*	*Average*	*Variance*
Without Buffer	3	15.1	5.033333	0.723333
Ambion	3	21.2	7.066667	2.443333
Genaid	3	19	6.333333	5.453333
Qiagen	3	23.9	7.966667	2.843333

ANOVA

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	13.83333	3	4.611111	1.608995	0.262309	7.590992
Within Groups	22.92667	8	2.865833			
Total	36.76	11				

Based on result Qiagen has been a higher mean score of RNA concentration (8.0 ng/µl), then second is ambion with RNA concentration 6,8 ng/µl, Genaid 6,3 ng/µl and without additional buffer 5,0 ng/µl RNA. The mean of concentration data analysis has been performed with ANOVA.

Anova statistical analysed indicating P-value (>) 0.01, its mean that the concentration showed at each group of RNA isolation method using 4 treatments have no different significant value. A lysis buffer is a buffer solution used for the purpose of breaking open cells for use in molecular biology experiments that analyze the compounds of the cells. Most lysis buffers contain salts (e.g. Tris-HCl or EDTA) to regulate the acidity and osmolarity of the lysate. Sometimes detergents (such as Triton X-100 or SDS) are added to break up membrane structures (Posch, 2014). Lysis buffer is an important thing in isolating RNA step because get an optimal lysis buffer to break up the membrane in exosome, can get a better concentration of total RNA.

We performed quantification miRNA using miR-21, miR-22, miR-19a and miR-19b. The results of miRNA expression can be seen in figure 1 and 2. Quantification expression of miRNA can be able to detect from urine samples.

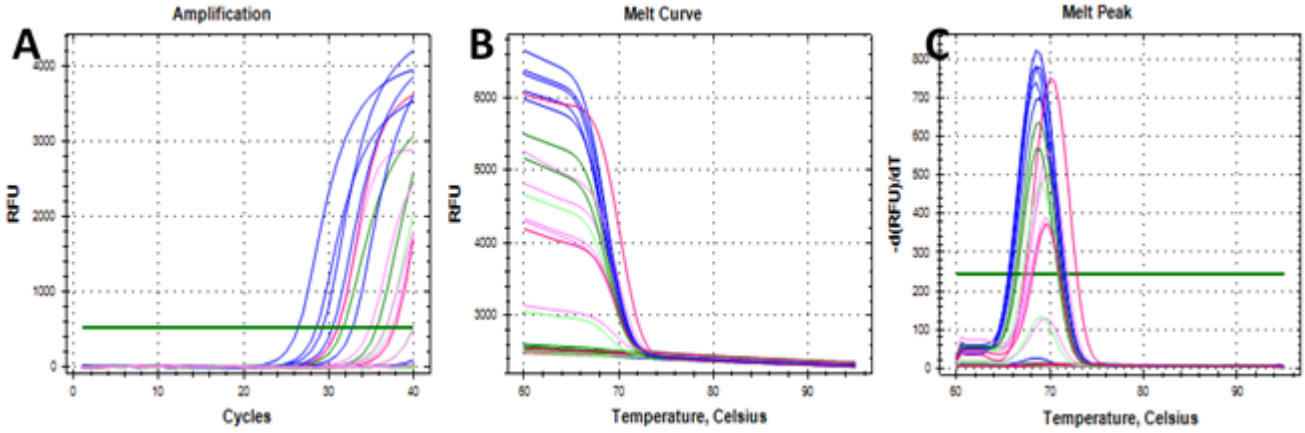
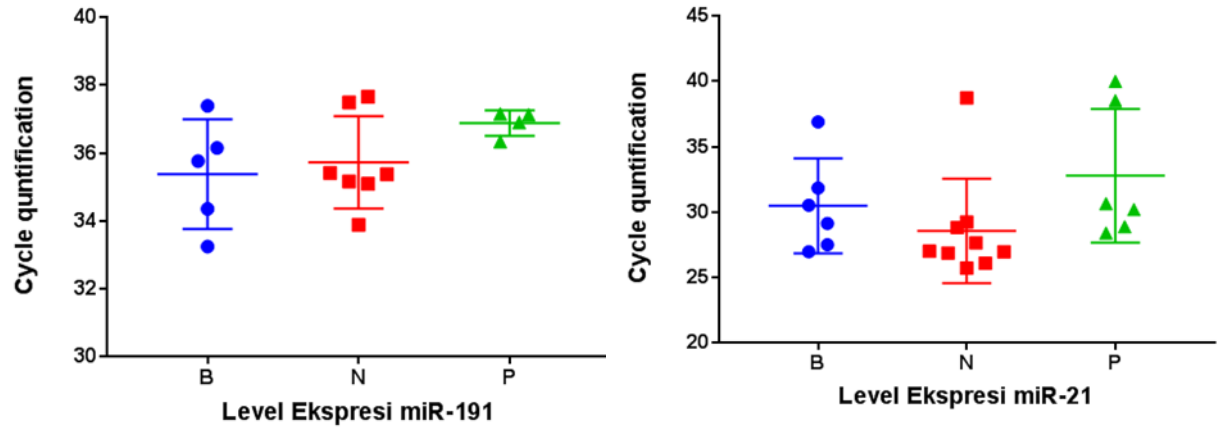


Figure 1. miRNA quantification used qPCR Biorad CFX-96 manager including miR-19a, miR-19b, miR-21 and miR-22 from urine samples. A. Amplification cycle, B. Melt Curve, C. Melt Peak.

Four types distribution of miRNA cycle quantification (cq) (figure 2) indicated that consistently stable in each type of samples. miR-191, miR-21, miR- 22 and miR-19b formed a spread pattern with mean cq between 30-34.



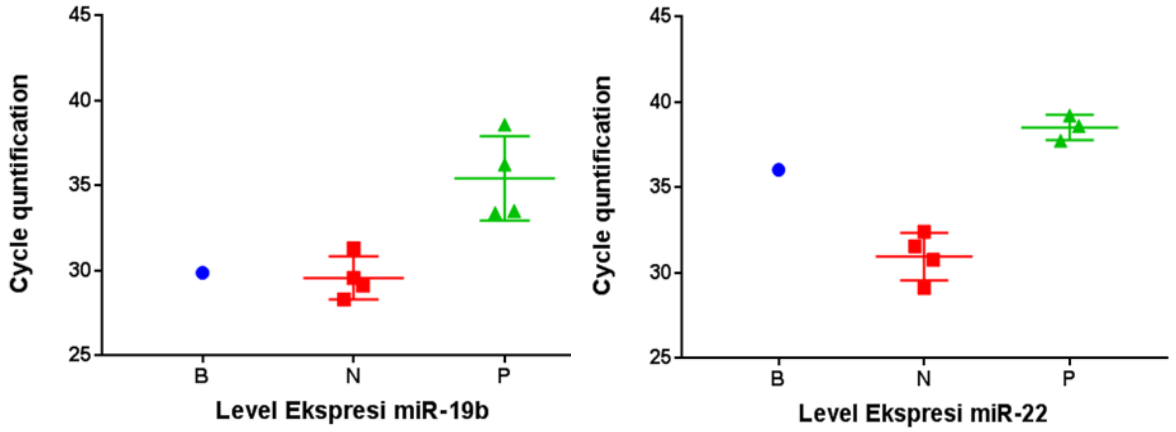


Figure 2. cycle quantification distribution of miRNA used qPCR with targeting miRNA-191, 21, 19b and miR-22. The results indicated that mon-coding RNA (miRNA) can be detected from urine samples.

RNA Stability in Storage

Subsequently, total RNA was storage deep freeze storage (-800C). Then to compare stability of the RNA concentration from 4 different treatment method, RNA concentration was measured every two days for thirteen days

Table 4. Result of RNA concentration measurement

Average of RNA concentration measurements per 2 days							
Treatments	**Day 1**	**Day 3**	**Day 5**	**Day 7**	**Day 9**	**Day 11**	**Day 13**
Without *lysis buffer*	5.0	6.2	5.5	5.4	5.0	5.0	3.9
Ambion	6.8	8.27	5.3	5.8	5.0	5.7	6.1
GeneAid	6.3	7.0	5.6	6.8	3.8	7.4	3.2
Qiagen	8.0	10.3	7.4	6.9	5.1	5.7	4.5

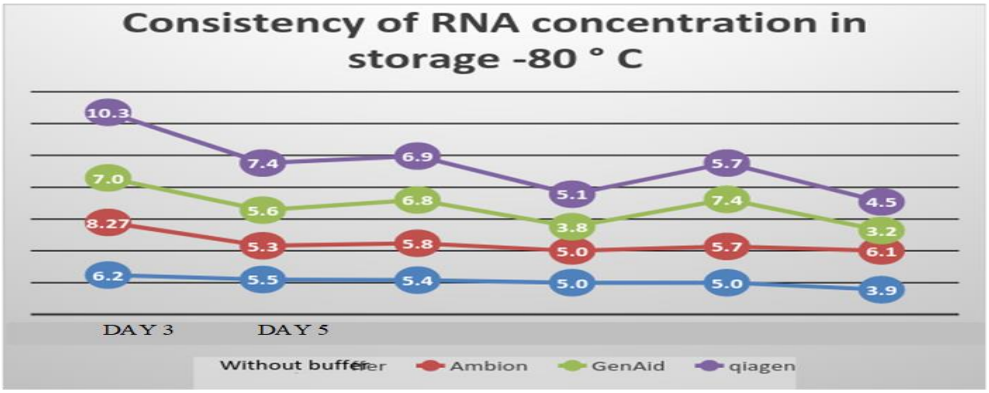


Figure 3. Graphic consistency of RNA concentration on the duration of shelf life

Table 4 and Figure 1 show that RNA samples that stored at -80° C little bit decreased in concentration in all treatment. RNA has bad stability compared to DNA, because of 2'Hydroxyl (-OH) group of RNA nucleotides that make it easily degraded. (sumber ?). Deep freeze storage can inactive any endogenous enzyme degradation of RNA, such as RNase, Helicase, etc (Houseley, et al., 2009).

Table 5. Decreased score of RNA concentration

Difference in RNA Concentration on Storage -80°C				
Day	**Without *lysis buffer***	**Ambion**	**GeneAid**	**Qiagen**
Hari 5	-0.7	-2.97	-1.4	-2.9
Hari 7	-0.1	+0.5	+1.2	-0.5
Hari 9	-0.4	-0.8	-3	-1.8
Hari 11	0.0	+0.7	-3.6	+0.6
Hari 13	-1.1	0.4	-4.2	-1.2

Table 6. One Way ANOVA Analysis, reduction of RNA concentration from each treatment

Anova: Single Factor						
SUMMARY						
Groups	*Count*	*Sum*	*Average*	*Variance*		
Without Buffer	5	-2.3	-0.46	0.203		
Ambion	5	-2.17	-0.434	2.35478		
GenAid	5	-11	-2.2	4.7		
Qiagen	5	-5.8	-1.16	1.743		
ANOVA						
Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*

Between Groups	10.30714	3	3.435712	1.526851	0.2459	5.292214
Within Groups	36.00312	16	2.250195			
Total	46.31026	19				

Based on One-Way ANOVA test shows that degradation of RNA concentration from 4 different methods almost smilar, has no significant value (p-value > 0.01) (Table 6). This result shows that deep freeze storage cannot totally stop RNA degradation but it can slow down RNA degradation. So this study recommend that RNA isolation method without additional lysis buffer treatment is better way, it will be cheaper and efficient to isolate RNA from urine samples

Conclusion

RNA isolation without additional lyses buffer is successfully conducted without buffer treatment. There are no different results between buffer and without buffer treatment showed by RNA concentration and degradation score in deep freeze storage. Therefore, isolation exosome RNA from urine sample can be better conducted without additional lysis buffer, it is more efficient and economical .

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ABBREVIATIONS ORIGINALITY AUTHOR CONTRIBUTIONS

Study design: Tirta Wardana, Sofia Mubarika Haryana and Indwiani Astuti, Data acquisition, management and sample collection: R Danarto. Data Analysis: Angga Dwi Prasetyo, Joni Kristanto, Richardus Hugo, Santoso Pradana Putra. Manuscript writing: Angga Dwi Prasetyo, Joni Kristanto, Richardus Hugo, Santoso Pradana Putra, Tirta Wardana. Project supervisors : Sofia Mubarika Haryana and Indwiani Astuti.

CONFLICT OF INTEREST

The authors state that there is no conflict of interest in this study.

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RESEARCH ARTICLE

IDENTIFICATION OF STUDENT'S PERCEPTIONS ABOUT MEDICAL SKILLS LEARNING SYSTEM OF URINE CATETER INSERTION AT MEDICAL FACULTY OF MATARAM UNIVERSITY

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ABSTRACT

Background: Mastery of students in medical skills is a very important aspect that will bridge the gap between clinical competence and knowledge of procedures. Based on the 2012 Indonesian Doctor Competency Standards, urinary catheter installation skills have 4A competencies, which means that a primary care doctor graduate must be able to do it independently. Students' perceptions of the learning system and learning environment will be the basis for maximizing and varying the learning system and environment. The Covid-19 pandemic is one of the obstacles for students in learning, especially in the field of medical skills. Where the learning system which was originally an offline method turned into online learning. Currently, the Faculty of Medicine, University of Mataram is also facing online learning skills. This study aims to determine student perceptions of the urinary catheter insertion skill learning system at the Faculty of Medicine, University of Mataram.

Methods: This research is a descriptive analytic study with a cross-sectional research design in the fifth and seventh semester students of the Medical Education Study Program, Faculty of Medicine, University of Mataram. Sample filling out a questionnaire about the perception of medical skills urinal insertion. Furthermore, the search for the relationship between the learning method with the results of the main exam and whether there are differences in perceptions with the student skills learning method.

Results: From 196 respondents consisting of men (34.7%) and women (65.3%), semester V (51%) and semester VII (49%) with an age range of 19-23 years. Good perception of medical skills in inserting a urinary catheter is seen from the percentage of motivational factors (96.9%), instructors (89.8%-100%), self-awareness (99%-100%), learning atmosphere (81.1%-100%). 96.9%), facilities and infrastructure (43.4%-89.3%), self-confidence (57.7%-99.5%), and clinical learning environment (89.8%). The bad perception is only found in the difference between learning on the mannequin and the patient (56.6%). The results of the bivariate study using the chi-square test found that there was no relationship between the learning method of urinary catheter insertion skills and the results of the main exam for students ($p > 0.05$), $p = 0.474$, and there was no significant difference between the level of perception and the skills learning method. student medical.

Conclusion: All students have a good perception of the medical skills learning system for urinary catheter insertion. There is no relationship between learning methods and students' main exam results. And there was no significant difference between the level of perception and the student's medical skills learning method.

Keyword: student perception, medical skills, urinary catheter insertion

INTRODUCTION

Insertion of a urinary catheter is an action performed by inserting a catheter into the bladder through the urethra which aims to help needs of elimination and as a collection of examination materials (1).

Based on the 2012 Indonesian Doctor Competency Standards, medical skills in urinating have competency 4A, which means that a primary care doctor graduate must be able to do it independently. In addition, doctors must also master all theories, principles, indications, contraindications, and complications that can arise from these medical skills (2).

Perception aspects in learning activities are currently starting to get attention with the objectives of learning activities. Students' perceptions of the learning system and learning environment will be the basis for maximizing and varying the learning system and environment (3).

Student perceptions have a relationship with student learning outcomes. According to research conducted by Ahmed et al, it is stated that students who have higher learning achievement show a more positive perception of their learning activities, while students who have low learning achievement show a negative perception of their learning activities (4).

Mastery of medical skills is a very important aspect that bridges between knowledge of procedures and clinical competence. Medical skills learning helps ensure that all students acquire the necessary mastery of the techniques and are judged correctly before they are applied directly to real patients (5).

Currently, the Covid-19 pandemic is becoming one of the major health crises for every individual from all nations, continents, races, and socioeconomic groups. The responses needed, such as social isolation, advice to stay at home, in the community, and the closure of educational institutions suddenly changed the life of learning. Students are one of the individuals who have felt the impact of the Covid-19 pandemic. This pandemic has become one of the difficulties for students in their learning. Where the learning system that was originally face-to-face in a campus environment or practice area turned into online or daring learning, be it lectures or activities related to practice.

From some of these problems, researchers want to conduct research at the Faculty of Medicine, University of Mataram to develop a learning system for urinary catheter insertion techniques. The results of this study can be used as initial information to improve the effectiveness of the urinary catheterization skill learning system for the following year.

METHODS

The research method used in this research is descriptive analytic research with a cross-sectional research design, which was conducted on fifth semester students and seventh semester students of the Medical Education Study Program, Faculty of Medicine, University of Mataram. Sampling was carried out by total sampling technique, a sampling technique where the number of samples was the same as the affordable population, which

met the inclusion criteria and did not include the exclusion criteria.

Inclusion criteria in this study were fifth semester students and seventh semester students of the Mataram University Medical Education Study Program who were willing and still active in lectures, were or have taken part in urinary catheter insertion medical skills activities. The exclusion criteria for this study were students who were not present during the study or did not fill out the questionnaire completely, and stated that they had resigned in the midst of data collection activities. This research has received approval from the Health Research Ethics Commission of the University of Mataram.

The variables in this study were the medical skills learning system for urinary catheter insertion, the semester where the study was conducted, the student's perception level, and the student's test results in the medical skills exam for urinary catheter insertion. The data was obtained by using a questionnaire. Furthermore, the data will be analyzed descriptively, and the Chi-Square test is performed. Statistical data analysis in this study using SPSS software.

RESULTS

Characteristics of Research Respondents

Characteristics of respondents in this study include the sex of the semester, test results, and age.

Table 1 Characteristics of Research Respondents

Karakteristik	Jumlah(n)	Persentase (%)
Jenis Kelamin		
Laki-laki	68	34,7
Perempuan	128	65,3
Semester		
VII (offline)	96	49
V (online)	100	51
Hasil Ujian		
Lulus	186	94,9
Tidak Lulus	10	5,1
Usia		
19 tahun	11	5,6
20 tahun	78	39,8
21 tahun	93	47,4
22 tahun	11	5,6
23 tahun	3	1,5

Based on Table 1, it was found that from 196 samples in this study, the number of male respondents was 68 students (34.7%) and female respondents were 128 students (65.3%). Respondents in semester VII were 96 people (49%) and semester V were 100 people (51%). The number of respondents who did not pass the main exam was 10 people (5.1%), while those who passed were 186 people (94.9%). With ages ranging from 19-23 years.

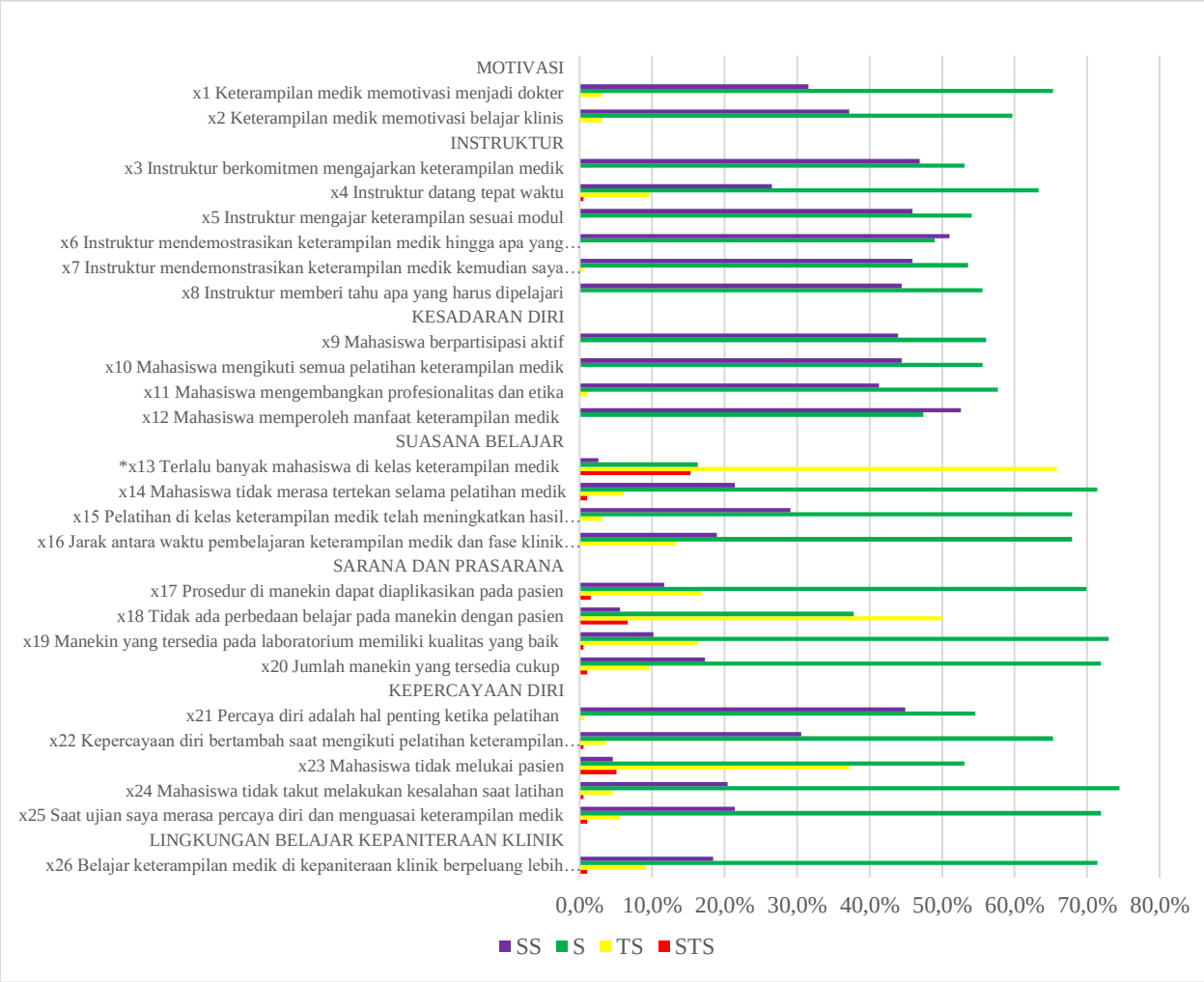

Figure 1 Level of Student Perception About Medical Skills Learning System Urinary Catheter Insertion

The motivation factor consists of 2 statement items. In statement number 1 regarding medical skills training for urinary catheter insertion motivating to become a doctor, respondents had a good perception of 96.9% and a bad perception of 3.1%. In statement number 2 regarding medical skills training for urinary catheter insertion motivating to study clinical courses, respondents had a good perception of 96.9% and a bad perception of 3.1%.

The instructor factor consists of 6 statements in numbers 3 to 8. In statement number 3 about the instructor's commitment to teaching, all respondents have a good perception. In statement number 4 about the instructor coming on time, respondents have a

good perception of 89.8% and a bad perception of 10.2%. In statement number 5 about instructors teaching skills according to the module, all respondents have a good perception. In statement number 6 about the instructor demonstrating medical skills in inserting a urinary catheter until the students understand what I have to do, all respondents have a good perception. In statement 7 about the instructor demonstrating medical skills in inserting a urinary catheter before I did, the respondent had a good perception of 99.5% and a bad perception of 0.5%. In statement number 8 about the instructor telling what to learn, all respondents have a good perception.

The self-awareness factor consists of 4 items in statements number 9 to 12. In statement number 9 about respondents having to actively participate in medical skills classes, all respondents have a good perception. In statement number 10 about students participating in all training in medical skills in urinary catheter insertion, all respondents have a good perception. In statement number 11 about students developing an ethical professionalism approach in the medical skills class, respondents have a good perception of 99% and 1% have a bad perception. In statement number 12 regarding medical skills training for urinary catheter insertion is useful, all respondents have a good perception.

The learning atmosphere factor consists of 4 statements in statements number 13 to 16. In statement number 13 about the atmosphere in the class is not too crowded, respondents have a good perception of 81.1% and 18.9% have a bad perception. In statement number 14 about respondents not being depressed during the training, respondents have a good perception of 92.8% and 7.2% have a bad perception. In statement number 15 about training in medical skills class urinary catheter insertion has increased self-study outcomes, respondents have a good perception of 96.9% and have a bad perception of 3.1%. In statement number 16 regarding the distance between the learning time and the clinical phase is correct, respondents have a good perception of 86.7% and a bad perception of 13.3%.

The facilities and infrastructure factor consists of 4 statement items in number 17 to 20. In statement number 17 regarding medical skills in inserting a urinary catheter that is learned with a mannequin can be applied directly to patients, respondents have a good perception 81.6% and a bad perception 18.4% . In statement number 18 about there is a difference between learning medical skills in placing a urinary catheter on a mannequin with patients, respondents have a good perception of 43.4% and 56.6% have a bad perception. In statement number 19 regarding the quality of the urinary catheter mannequin in the medical skills laboratory, it is good, respondents have a good perception of 83.2% and 16.8% have a bad perception. In statement number 20 regarding the number of urinary catheter mannequins in the medical skills laboratory, respondents have a good perception of 89.3% and 10.7% have a bad perception.

The self-confidence factor consists of 5 items in statements number 21 to 25. In statement number 21 about self-confidence is important when they perform medical skills in inserting a urinary catheter, respondents have a good perception of 99.5% and a bad perception of 0.5%. In statement number 22 regarding medical skills training for urinary catheter insertion, it increases their confidence, respondents have a good perception of 95.9% and 4.1% have a bad perception. In statement number 23 about not having to be afraid that they will hurt the

patient, respondents have a good perception of 57.7% and 42.3% have a bad perception. In statement number 24 about feeling not afraid if they make a mistake during medical skills training for urinary catheter insertion, respondents have a good perception of 94.9% and a bad perception of 5.1%. In the statement about the time of the exam they feel confident and master the medical skills of inserting a urinary catheter, respondents have a good perception of 93.3% and 6.7% have a bad perception.

The clinical learning environment factor consists of 1 item in the statement number 26. In the statement number 26 about studying clinical clerkships it provides better opportunities to learn medical skills, respondents have a good perception of 89.8% and 10.2% have a bad perception.

Table 2 Relationship between learning methods and student main exam results

Metode/ sistem Pembelajaran	Ujian Utama		Nilai p
	Lulus	Tidak lulus	
Offline	90	6	
Online	96	4	0,474
Jumlah	186	10	

In this study also conducted a search for the relationship between the learning method of medical skills in inserting a urinary catheter with the results of the main student exam using the chi-square test, in this study there was no significant relationship because the p value was > 0.05 (0.474).

Table 3. Relationship between students' perception level and learning method

Tingkat persepsi	Metode/sistem Pembelajaran		Nilai p
	Offline	***Online***	
Baik	96	100	
Tidak baik	-	-	-
Jumlah	96	100	

Overall, there was a good perception of all respondents on each of the factors studied, so that with this there was no significant difference in the online and offline method of learning medical skills of urinary catheter insertion with the level of student perception in the study.

DISCUSSION

The results of this study indicate that students' perceptions of learning medical skills in urinary catheter insertion can be seen from several factors. These factors are motivation, instructor, self-awareness, learning atmosphere, facilities and infrastructure, self-confidence, and clinical clerkship learning environment.

Motivation has a relationship with the personality and positive attitudes of students in terms of perseverance, social intelligence, discipline and gratitude (6). Based on this research, the majority of respondents think that medical skills increase motivation to become a doctor and motivation to learn other clinical subjects. This is in line with previous research conducted by Hashim et al., which was conducted on 137 respondents (7). Strong motivation in the learning process of a

medical student is needed for academic success and self-improvement (6).

The instructor's ability to teach affects students' perceptions of learning medical skills. In this study, the majority of respondents had a good opinion of the instructor's ability. This ability includes the ability to demonstrate medical skill procedures correctly and a commitment to teaching responsibly, so that respondents feel they get a good picture and are able to carry out the procedures that have been exemplified. Research conducted by Erikson showed that the better the instructor's ability to teach, the better the respondent's perception of medical skills. A good instructor's teaching ability accelerates the absorption of material in a shorter time so that respondents' perceptions will be better and respondents will feel more benefit from learning medical skills (8).

In this study, respondents had good self-awareness such as following all medical skills, being professional, actively participating and considering medical skills useful for respondents. The research conducted by Flavian shows that stable self-awareness will be very useful in the progress and learning process of students in various aspects of life. Good self-awareness has an effect on increasing student academic achievement (9).

The learning atmosphere describes the quality of learning and affects student learning outcomes. A conducive learning atmosphere is characterized by comfortable instructor and student interactions so that it increases student enthusiasm and confidence in participating in lessons (10). In the study, a comfortable learning atmosphere was formed from good interactions between respondents and their medical skills group friends and instructors. This is in line with previous research conducted by Saputra and Lisiswati that a conducive learning atmosphere will be created from the attitude and way the instructor delivers the material, the interaction between friends in the medical skills group and the enthusiasm of a medical skills group in learning these skills (11).

In this study, respondents believed that the procedures learned on mannequins could be applied directly to patients. This is in line with research conducted by Erikson that medical skills facilities and infrastructure affect perceptions of medical skills. The better the facilities and infrastructure provided, both here defined as both in terms of quality and quantity of the mannequins themselves, the more the benefits of medical skills training obtained by students will be maximized (8). However, in this study, respondents also thought that there was a difference between learning medical skills on mannequins and actual patients. This research is in line with previous research conducted by Lavanya and Kalpana, that mannequins should be more realistic. In addition, mannequin skin is different from human skin, it is not even possible to tell whether there is perforation or embolism (12).

Students who are more confident in their ability to apply more knowledge, skills and skills in taking on new challenges related to how to treat patients (13). In this study, respondents think that self-confidence is important in learning medical skills, namely to increase respondents' self-confidence. This is in line with research conducted by Erikson that the level of self-confidence affects the perception of medical skills, where respondents with high self-confidence will feel that medical skills have benefits for them and vice versa (8).

In this study, respondents thought that the clinical clerkship learning environment provided better opportunities to learn medical skills. This is in line with previous research conducted by Nielsen et al. stated that learning skills in clinical clerkships provides students with better opportunities when compared to medical skills laboratories (14). However, in this study, respondents also thought that learning medical skills was not enough if it was only done at the clinical clerkship. This is in line with previous research by Sandika that learning medical skills is needed at all levels of education so as to make it easier for students to master medical skills (15).

In this study, it was found that there was no relationship between the medical skills learning method and the student's main exam results. This is in accordance with previous research which states that there is no evidence that offline learning is better than online learning (16).

Another study also shows that student performance is better when learning online than when learning using offline methods. The same research also states that the best performance of students is using a blended learning learning system, where offline and online learning elements are combined in the teaching and learning activity system. Combining offline and online learning systems can be beneficial for students and instructors, because students and instructors can carry out efficient teaching and learning activities, while maintaining the effectiveness of learning outcomes (17).

CONCLUSION

There was no relationship between the learning method of medical skills of urinary catheter insertion and the results of the examinations obtained by students, this also applies to the relationship between the semester of learning and the results of students' medical skills exams. In addition, there was no significant difference in the online and offline methods of learning medical skills with urinary catheter insertion and the level of student perception.

Respondents in the study mostly had good perceptions of the statement components such as motivation factors, instructors, self-awareness, learning atmosphere, facilities and infrastructure, self-confidence and clinical learning environment, both with online and offline learning methods. The perception is not good, which is only found in the factors of facilities and infrastructure, namely the difference in learning in mannequins and patients.

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RESEARCH ARTICLE

RELATIONSHIP OF AGE AND URINATING BEHAVIOR WITH THE INCIDENCE OF OVERACTIVE BLADDER (OAB) IN FEMALE NURSES AT RISA SENTRA MEDIKA MATARAM HOSPITAL

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ABSTRACT

Introduction: Overactive bladder (OAB) is a chronic syndrome that has a major influence on the quality of life of sufferers. OAB is a prevalent disease, with a general incidence of 16.5%. Female nurses are more likely to get OAB because of their working conditions and poor urinating behavior. Because the risk of infection is greater due to the short urethra in female nurses, so researchers aim to find out the incidence of OAB sufferers in female nurses of the surgical section at Risa Hospital by using OABSS.

Method: This research is a correlative analytical study with a cross sectional design. Cross sectional research is a study whose measurement of variables is done only once at a time.

Result: In this study, 56 samples met the criteria as study subjects, 16 samples had OAB (28.6%) and the rest did not experience OAB. The sample of OAB was divided into 13 mild OAB (23.2%) and 3 moderate OAB (5.4%). The average score of the urinating behavior is 0.47. The average age of respondents was 32 years, with the most age being 28 years.

Conclusion: The prevalence of OAB cases in female nurses in the study was 16 samples (28.6%). Respondents with OAB had an average of worse urination habit scores. Respondents with OAB had a higher average age. The urinating behavior has a very weak opposite correlation with the incidence of OAB in female nurses. Age has a very weak correlation with the incidence of OAB in female nurses.

Keyword: OAB, age, urination habits, Female nurse

Introduction

Urinary bladder is an organ which contain our urine until internal and external stimulations triggers us to urinate. Urinating or micturition process relies on the role of brain cortex, pons, spinal cord, peripheral autonomic nerve, somatic nerve, and sensory nerve as well as anatomical component of lower urinary tract. Malfunction in these components can cause overactive bladder (OAB). General symptoms of OAB is caused by instability in the urinary bladder.

OAB is a chronic syndrome which significantly affects the quality of life for people who suffers from this condition. This syndrome can disrupt the patient's daily activity .[1] The prevalency of OAB is 16,5% which indicates that this condition is not a rare condition .[2,3] OAB's main symptoms increases the urge to urinate. This syndrome is

correlated with incontinentia, increased micturition frequencies, and nocturia .[2,4]

OAB is more often found in women than in men, yet with increasing age, especially people older than 60 years old, this condition is more prevalent in men. OAB in men under 45 years old has a prevalency of 8,5% while in men over 55 years old, the numbers spiked to 21,8%. Another research reportet that there is a significant increase in the prevalency of OAB in men older than 75 and women older than 60 years old (Eapen and Radomski, 2016). OAB is also possible to develop in the productive age. In fact, OAB is more often found in people aged 35-45 years old than in people in 20-22 and 23-27 years old (Palma et al., 2013). Poor urinating behavior also can cause OAB such as diet-induced irritation in the bladder, lack of water, abnormal body mass index (BMI), infrequent micturition, and smoking .[5]

Based on the above explanation, the author is interested in investigating the correlation of age and urinating behavior with the incidence of OAB on Female nurse in Risa Sentra Medika Hospital Mataram.

Research Methods

This research is a correlative analysis research with a cross-sectional design. A cross sectional research design is a research in which the measurements of the variables is only done once in one timeframe. This research utilizes two questionnaires which are Overactive Bladder Symptom Score (OABSS) and Urinating behavior questionnaire in Risa Sentra Medika Hospital Mataram. The inclusion criteria is a Female nurse in Risa Sentra Medika Hospital Mataram and agreed to be the participant of this research. Total sampling method is used in this research in which all the reachable subject is included in the research.

Results

Sample characteristics

56 samples of Female nurse in Risa Sentra Medika Hospital Mataram were included. This research found 16 samples with OAB (28,6%) and the rest of them does not have OAB. 13 out of 16 samples with OAB is categorized as mild OAB (23,2%) while 3 of them categorized as moderate OAB (5,4%). The average score of the urinating behavior questionnaire were 0,47 while the average age of the participants were 32 years old with the most prevalent age is 28 years old.

OABSS Questionnaire Answers

Based on the collected OABSS Questionnaire Answer, in the afternoon urinating frequency question, 40 samples (71,4%) stated that they urinated ≤ 7 times in the afternoon, 15 samples (26,8%) urinated 8-14 times, and 1 sample (1,8%) urinated ≥ 15 times. While in the night urinating frequency question, 13 samples (23,2%) stated that they doesn't urinate in the night, 34 samples (60,7%) urinated 1 time, and 8 samples (14,3%) urinated 2 times.

Urinating Behavior Questionnaire Answers

Based on the collected Urinating Behavior Questionnaire answers, 37,5% of the participants stated that "I urinate when there were little or no urge to urinate before going to bed", 62,5% of the participants stated "I worry about the hygiene of public toilet" in the preference aspect, 18,8% stated "I postpone

urinating when I'm busy" in the postponing to urinate aspect, and 6,3% each stated "I strain myself to start urinating". "I strain myself to keep urinating", and "I strain myself to finish urinating earlier".

Overview of Urinating Behavior and Age on the incidence of Overactive Bladder

Incidence of OAB	**Average urinating behavior score**
OAB	48,2
Tidak OAB	46,1

The average score of urinating behavior score in OAB samples is higher in comparison to the non-OAB samples.

	OAB	**Non-OAB**
	Value	
Mean	32,5	31,7
Median	33,5	32
Modus	28	28
Minimum	26	24
Maximum	38	42

Age comparison of OAB and non-OAB samples. OAB samples showed an older average age than that of non-OAB samples (32,5 years old and 31,7 years old). The most prevalent age is 28 years old.

Variable	OAB			
	No	Mild	Moderate	Severe
Urinating behavior **(mean)**	0,47	0,45	0,49	-
Age **(mean)**	31,43	32,09	34	-

The average score of urinating behavior is 0,47 in non-OAB samples, 0,45 in mild OAB samples, and 0,49 in moderate OAB samples. Average age of non-OAB samples were 31,43 years old, 32,09 years ld in mild OAB, and 34 years old in moderate OAB.

Variable		**OAB**
Urinating behavior	p-value	0,388
	Correlation coefficient	– 0,118

	(r)	
Age	p-value	0,330
	Correlation coefficient (r)	0,133

p-value is considered significant if p < 0,05
Correlation coefficient (r) is considered:

- Very weak bila r = 0,0 s.d. 0,2
- Weak bila r = 0,2 s.d. 0,4
- Moderate bila r = 0,4 s.d. 0,6
- Strong bila r = 0,6 s.d. 0,8
- Very strong bila r = 0,8 s.d. 1

Negative r value means a negative correlation.

Statistical analysis between urinating behavior and OAB resulted in the p-value of 0,388 with the correlation of -0,118. These result indicates that there were very little correlation between those two variables and statistically insignificant. Statistical analysis between age and the incidence of OAB resulted in the p-value of 0,330 with the correlation 0,133. These result indicates that there were very little correlation between the two and satistically insignificant.

Discussion

OAB syndrome is a chronic condition which hugely affects the quality of life of the patient. OAB can affect the performance of everyday tasks and also social function such as working. This is because of the fact that the symptoms of OAB is the increasing urge to urinate and also increasing frequency and nocturia, with or without incontinentia, and also with or without urinary tract infections. Research regarding OAB in the United States of America reported a high prevalency of OAB with 16,5% out of 33 million patients across all countries. Similar study which conducted in Europe showed the average age of OAB patients was over 40 years old with an increasing prevalence with increasing age. This number can be higher because most of the patients were undiagnosed because of the pudency to acknowledge it's symptoms and also doesn't feel that this condition is bothering them hence didn't seek for care . One of the at-risk population is nurse. OAB can cause occupational stress in Female nurse.

In this study, it was found that the prevalence of OAB in Female nurse was 28,9%. Similar result was also found in Female nurse population in China with a prevalence of 27,57% and the most prevalent age is under 35 years old . A study conducted by Xu et al. found a higher prevalence in his study with 32% of the population .[7] The average age of OAB patients were 32,5 years old. A study conducted by Zhang et al. and Xu et al. showed a similar result with 31,1 years old and 30,2 years old .[6,7] OAB is most prevalent in the age of 28 years old and Xu et al., in his study, also found a similar result with the most prevalent age group is 26-30 years old.[7-9]

This research found that most of the Female nurse who suffers from OAB has a particular concern on the hygiene of the public toilet. This concern is thought to cause them to avoid using the public toilet and, therefore, hold their urge to urinate until they get home. A study regarding participant's behavior regarding the use of public toilet has showed

that the utilization of public toilet gave a negative experience on it's user. Several participants also showed fear and worries regarding public toilet usage. Several factors which affect someone in avoiding the use of public toilet is privacy reasons and also it's hygiene .[9] This results is different from a result of a study conducted by Xu et al. in which he stated that most Female nurse would rather postpone her urge to urinate. Xu et al. found that 51,7% of the samples were concerned with the hygiene of the public toilet, while 33,3% is avoiding it. Another study showed that 75% of women is concerned in the hygiene of the public toilet and this concern is related with the position during urinating. This position is also called hovering which lowers the urine flow rate because of the low relaxation of the pelvic floor muscles.

A study conducted by Kowalik et al. showed a correlation between the preference of their house with urinary tract functions. This study which conducted in the USA investigate the urinating behavior of women showed that many of it's sample has a bad urinating behavior. Almost all respondents stated that they concernec about the hygiene of the public toilet. Most of them strongly avoid using the public toilet, urinate before going out of their house, and try to hold their urge to urinate until they arrived at their house. Similar behavior is also found in this study which most of the sample postpone their urge to urinate while being busy working and straining themselves to be able to urinate faster. A study similar to this one showed that 26% of their sample strongly limit their use of public toilet .[10] They also often do hovering while urinating. Besides of the hygiene reasons, they also concerns about the quality of the public toiolet and also privacy. It is found that women who limits their use of public toilet is more often to have bad urinating behavior and lower urinary tract symptoms .[11]

This study doesn't found any significant result. This insignificancy is thought to be caused by internal and external factors. Internal factors are the small amount of sample dan the high possibility of recall bias because of the nature of the questionnaire while external factors are other factors that are also affects the incidence of OAB in Female nurse such as occupational stress and BMI .[12,17] Other internal factors that can be considered is anxiety. One systematic review showed a significant correlation between anxiety and the incidence of OAB. Several studies that were included in this systematic review has found a coexistence between lower urinary tract symptoms and anxiety, obsessive compulsive disorder (OCD), dan attention deficit/ hyperactivity disorder (ADHD). Hence, psychiatric nurse is also a confounding factor that affect the result of this study .[13]

The use of behavioral change intervention has been used since a long time ago in the management of urgency, incontinentia, and other symptoms of OAB. One of the example is bladder drill. Bladder drill is an intervention made to increase the interval between urinating to create a normal urinating frequency and normalize the function of the bladder. Bladder training is a modified version of bladder drill which done gradually on an outpatient basis. Bladder training has been found to be able to decrease the incidence of incontinentia in older women. Multicomponen behavioral training (MBT) is a form of bladder training which focuses on the exercise of pelvic floor muscles. MBT has a profound focus on the change in physiological response of the bladder and pelvic floor muscles and not really focusing on the urinating behavior. A systemati review which published

in 2002 investigated the effect of behavioral changes in the symptoms improvement in OAB patients. The included studies of this systematic review utilizes bladder drill in OAB patients for 7 until 10 days. These patients has a precise and nurse-monitored urinating schedule. In severe urgency cases, bladder drill can be accompanied by anticholinergic therapy. A study by burgio in 2002 reported a cure rate of 82-86% which showed that a proper urinating behavior can help to improve the condition of patients with OAB .[14]

A randomized controlled trial done in USA reported a similar result in men. It was found that behavioral change therapy can improve the symptoms of OAB better than pharmacological therapy alone and in some aspects has a similar result with combination therapy (behavioral change therapy and pharmacological therapy) .[14]

A meta-analysis that was also done in USA investigated the correlation between bad urinating behavior because of occupational reasons with the incidence of lower urinary tract symptoms in women. It was found that prolonged infrequent urinating behavior is a bad urinating behavior. Such a behavior can be caused by occupational reasons such as heavy-lifting occupation, occupation with huge burden, a hot/cold work environment, and work that requires the worker to use a particular outfit or uniform which limits their ability to urinate. In that study, it was found that nurses has a huge burden and a very high prevalence of lower urinary tract symptoms .[15] Another study also found a similar result which several particular occupation has a relatively fast pace therefore causing the worker to postpone their urge to urinate. The availability, or rather unavailability, of toilet in the workplace is also another condition that causing OAB. A study in Female nurse has found that Female nurse only urinates 0-2 times in 8 work hours .[16]

Besides the modification of urinating behavior and bladder training, a review hypothesized that modifying the lifestyle factors can helps decreasing the incidence of OAB. Smoking and consuming bladder irritant such as alchohol, caffeine, and carbonated beverages can also caused OAB while consuming a sufficient amount of mineral water can lower the incidence of OAB .[17]

This study also didn't dound a significant result between age and the incidence of OAB. This result is different from the result reported by Zhu et al. who found a significant result between age and the incidence of OAB (p=0,00). This difference is thought to be caused by internal and external factors which has been discussed earlier. Similar result was also found by a study conducted in UsA which found that with increasing age, the possibility of developing lower urinary tract symptoms is also increased. Age is thought to be correlated with sphincter deficiency and an increase in the prevalence of OAB. Urothelium and suburothelial space can detects the fullness of the bladder by releasing acetylcholine and adenosine triphosphate which can bind to a receptor in cajal interstitial cell. This neurotransmitter is increasing along with increased age. The excessive release of neurotransmitter will cause excitation in the afferent nerve which then caused a detrusor hypersensitivity and spontaneous contraction. This mechanism is thought to have significant role in the development of the urgency in OAB patients .[16,17]

The limitation of this study is that the confounding variables such as occupational stress was not analyzed. Besides that, because of the nature of retrospective study design,

there is a possibility of recall bias in which the participants of the study is forgotten some aspects in the questionnaire. The author of this study was also not able to meet directly with the participants because of COVID-19 pandemic condition therefore the author was not able to demonstrate how to fill the questionnaire properly.

Conclusion

The prevalence of OAB case in Female nurse in this study is 16 samples (28,6%). The OAB samples is further categorized into mild OAB with 13 samples (23,2%) and 3 moderate OAB with 3 samples (5,4%). Samples with OAB has an worse average score in the urinating behavior questionnaire in comparison to the non-OAB samples. OAB samples also showed a higher average age in comparison with non-OAB samples (32,5 and 31,7). The most prevalent age in OAB sample was 28 years old. Urinating behavior has a negative and insignificant correlation with the incidence of OAB in Female nurse with a p-value of 0,388 and correlation coefficient of -0,118. These results indicates that there was a negative correlation between urinating behavior and the incidence of OAB which statistically insignificant. Age has a positive yet also insignificant correlation with the incidence of OAB in Female nurse with a p-value of 0,330 and correlation coefficient of 0,133. These result indicates that there was a positive correlation between age and the incidence of OAB which statistically insignificant.

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CASE REPORT

Percutaneous Nefrolitotomy in Duplex Collecting System

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ABSTRACT

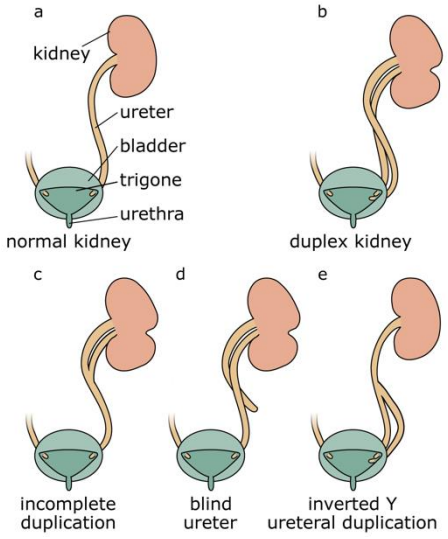
Duplex renal collecting systems are a common congenital abnormality. One of the complications of this is renal calculi. Management of renal calculi in this patient is complex. We describe a patient with renal calculus in duplex collecting system whom was performed PCNL.

Keyword: Duplex Collecting System, Stone, PCNL

Background

Duplex collecting system is one of the most common anomalies of the urinary tract. Its prevalence is 1 in 125 births. Child patients with duplicated kidneys and ureters usually present recurrent episodes of urinary tract infections (UTIs) or ureteral obstruction.[1]

Duplex collecting system have four classification[1,9], those are (1) duplex kidney (complete duplication produces a duplex kidney with two poles that drain into two ureters), shown in figure b; (2) incomplete duplication leads to a Y-shaped ureter (figure c); (3) Blind ureter which one of them not draining into the bladder (figure d); (4) inverted Y-ureteral duplication (rare case), whose two ureters fuse before entering the kidney (figure e).



Picture 1. Classification of duplex kidney

The management of staghorn calculi continues to remain a challenge despite the advances in instrumentation and technology. The various options available in the treatment of staghorn calculi include percutaneous nephrolithotomy (PCNL) monotherapy, single-tract PCNL with flexible nephroscopy, multi puncture PCNL, combinations of PCNL and extra corporeal

shockwave lithotripsy (ESWL), and open surgical options. PCNL offers high stone clearance rate and it is a safe in anomalous kidney. In that condition, PCNL is feasible procedure similar to normal kidney but requires careful preoperative planning and one has to be vigilant for all possible intra and post-operative complications.[2]

Case Report

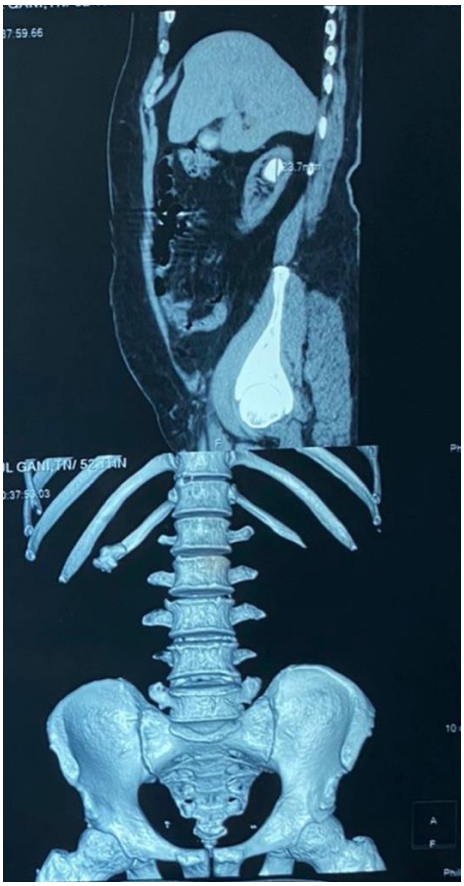
A 53-year-old male complained pain on the right flank for several weeks. No complained of dysuria, LUTS or gross haematuria. He has had several episodes of UTIs in the past. He has history of hypertension and chronic kidney disease.

On physical examination, the general condition was good, blood pressure was 180/90, pulse rate was 75/minute, respiratory rate was 18/minute, and temperature was 37.6^{o}C. No abnormalities in the patient general physical examination. On right flank palpation, patient complained pain but no mass being detected. There was no tenderness in the left flank area. External genitalia examination was normal too. On laboratory examination, haemoglobin 11.2 g/L, leukocytes count 9.62x103/µL, platelets count 214x103/µL, urea 146 mg/L, and creatinine 4.4 mg/L.

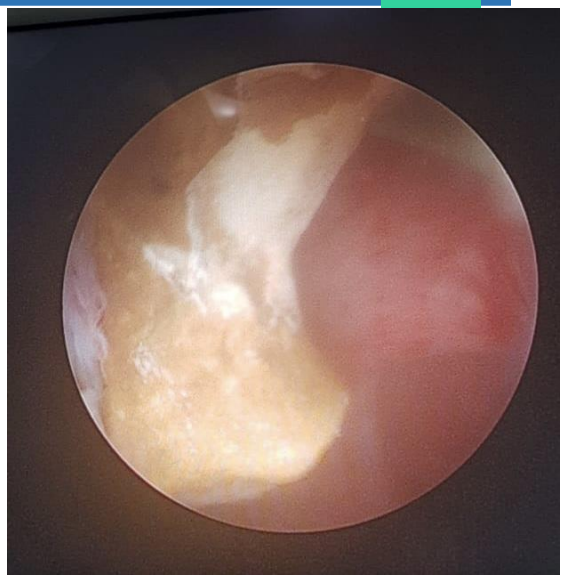
Non contrast abdominal CT-Scan showed staghorn calculi in right kidney whose size was 2.79 x 1.8 cm. No anatomy abnormality was found in CT-Scan. The working diagnosis was right staghorn stone.

We performed percutaneous nephrolitotomy (PCNL) to remove the stones in this patient. Puncture was made via incision on 11th SIC. Incomplete duplex collecting system was found when we performed RPG before puncturing the kidney. The location of the stone was in upper moiety of the kidney. After dilating the wound, we placed amplatz sheath into it, the we inserted the nephroscope. The stone was fragmented with pneumatic lithoclast, and then removed by stone forceps.

No rest stone was seen in nephroscope and X-ray procedure after surgery. A ureteral and urethral catheter were left. Patient was discharged from hospital in good condition two days after surgery. The ureter and urethral catheter was removed before he was discharged. He visited urology clinic seven days after surgery. The wound condition was good, and pain was mild.



Picture 2. Abdominal Ct-scan shows the staghorn calculi in right kidney.



Picture 3: PCNL surgery and the appearance duplex collecting system and staghorn stone in the upper moiety.

Discussion

Urinary tract calculi, one of the most common benign urological diseases, is seen in 12% of patients and has a recurrence rate of approximately 50%. Factors that may play an important role in the increase of urinary tract stone disease include increases in metabolic syndrome, lifestyle changes, dehydration, lack of water intake, and low urine volume.[3]

Indications for surgery on calculus kidney are hydronephrosis due to obstruction, either due to uretheropelvic junction stenosis or stones, and patients with complaints of unbearable pain that can interfere with daily activities. Due to current development, many urological procedures are carried out using non-invasive and minimally invasive techniques, after the introduction of ESWL (*Extracorpal Shockwave Lithotripsy*) and PNL (*Percutaneous Nephrolitotomy*); those are very popular methods due to its fewer postoperative complications than open surgery. ESWL (*Extracorpal Shockwave Lithotripsy*) can be use to treat kidney stones less than 1 cm in diameter, while for kidney stones larger than 2 cm, PNL (*Percutaneus Nephrolithotomy*) is chosen.[4]

While ESWL has the advantage of being non-invasive and avoids the need for general anaesthesia, stone localisation can be difficult due to the overlying bony structures or due to interposed bowel gas. The skin to stone distance is often increased and, even if ESWL was successful in fragmenting the stone, impaired drainage can hinder the passage of the fragments, resulting in reduced Stone free rate. PCNL offered higher stone clearance rates compared to ESWL, but with a higher risk of associated complications. Due to the anatomical variations and abnormal relationship to the adjacent organs (especially bowel), there was an increased risk of iatrogenic injury during percutaneous access in PCNL, and access tracts were often longer.[5,6]

The common congenital renal anomaly present with stone diseases is horseshoe kidney, ectopic pelvic kidney, crossed ectopic kidney (fused or separate), kidney with duplex system, and mal-rotated kidneys. Minimal invasive techniques are advantageous in stone removal due to satisfactory stone clearance, reduced hospital stay, early recovery, and reduced analgesia requirement.[7,8]

Non-contrast CT kidney, ureter and bladder (KUB) is considered to be the gold standard imaging modality for calculi, but in this case it missed the diagnosis of duplex collecting kidney. Actually, CT scan can help determine if an obstruction exists and can aid in assessing the renal parenchyma. Because there was no hydronephrosis and other anatomy abnormalities in this case, contributed to the diagnosis missing.[10]

Abdominal CT scan with contrast can help to determine the abnormalities of the pelvic and calyces, so can diagnose duplex collecting system. As well as excretory urography almost always find anatomic abnormalities in duplex collecting system. Because contrast that filled the pelvicocalyceal system can distinguish the upper and lower moiety. In this case, we found that there was duplex collecting system when we performed

RPG. It was clearly seen that the stone located in upper moiety of the kidney.[10]

On evaluation X-ray after PCNL in this case, we found no rest stone. Stone-free rate after PCNL monotherapy for staghorn calculi is reported to range between 49% to 78%.[11] In another study reported 62,6 %.[12]

Conclusion

One of the most common anomalies of the urinary tract, duplex collecting system of the kidney has a reported prevalence of 1 in 125 births. Minimal invasive techniques are advantageous in stone removal due to satisfactory stone clearance, reduced hospital stay, early recovery, and reduced analgesia requirement. PCNL in anomalous kidney is a safe and feasible procedure similar to normally located kidney but requires careful preoperative planning and one has to be vigilant for all possible intra and post-operative complications.

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CASE REPORT

Horseshoe Kidney

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ABSTRACT

Horseshoe kidneys are identified as having functioning renal masses present on both sides of the vertebral column fused together with ureters that remain uncrossed from the renal hilum to the urinary bladder. The anomaly is characterized by the fusion of the two distinct kidneys at the lower poles (in most of the cases), in the front of the body midline, through an isthmus of functional renal parenchyma or by fibrous tissue. Incidence of horseshoe kidney is 0.25% in general population and more frequent in male (male : female ratio = 2:1).

Keywords: horseshoe kidney, anatomy, embryology, diagnosis, treatment.

Introduction

Horseshoe kidney (HSK) is the most common congenital renal fusion anomaly and is characterised by three morphological anomalies: ectopia, malrotation, and changes in vascular supply. Jacopo Berengario da Carpi was the first person to describe this abnormality during autopsies in 1522. HSK usually consists of two renal masses fused at their lower poles by a parenchymal or fibrous isthmus.1

The isthmus connecting the two renal masses may be positioned in the midline or laterally resulting in asymmetric horseshoe kidney, 70% of which are left dominant, and consists of renal parenchyma in about 80% of cases with the remainder being composed of a fibrous band. In more than 90% of cases, fusion occurs at the lower pole, although fusion may occur at the upper pole in a minority of cases.2

Incidence

Horseshoe kidney is found more commonly in male with ratio to female is 2 : 1. It occurs in 0.25% of the population, or about 1 in 400 individuals. Reported incidence based on radiographic imaging has shown similar results, between 1 in 474 and 1 in 666 individuals.3

Embriology

Embryologically, kidney development is divided into 3 stages: pronephros, mesonephros, and metanephros. The pronephros stage is formed by 7-10 clusters of dense cells in the neck region. The first group forms the vestigial nephrotome, which disappears before the caudal nephrotome is formed. At the end of the 4th week, all signs of the pronephros system disappear. The mesonephros originates from intermediate mesoderm from the upper thoracic to upper lumbar segments. When the pronephric system regresses, the excretory ducts of the mesonephric appear to elongate to form the glomerulus (medial part) and Bowman's loop, both of which are called the mesonephric corpuscles (renal). Lateral part, the ducts converge on the mesonephric duct (wolfian

duct). In the middle of the second month, the medial part of the mesonephros forms the gonads and the ridge formed by these two organs is called the urogenital ridge. The caudal channel remains differentiated. Towards the end of the second month, the cranial portion has largely disappeared. The caudal part in the male remains and contributes to the sex system and in the female it disappears.4

At the time of the metanephrons phase, the metanephric blastema differentiates into a renal nephron, then its function and position become perfect. The metanephric blastema triggers the Wolfian duct and forms the ureteric bud (UB), which in turn fuses the ureter with the kidney. The normal kidney will ascend from the sacrum to the lumbar region which occurs in the six and nine weeks of pregnancy, the ascending kidney will receive a local vascular supply from the surrounding blood vessels.5

Anatomy

The kidneys are normally located in the retroperitoneum between the transverse processes of T12 and L3 with the left kidney slightly more superior than right. Horseshoe kidney is more commonly in a low position because the isthmus does not permit ascent beyond the inferior mesenteric artery. The isthmus of the kidney may not have a separate blood supply or is supplied by a single vessel from the aorta (in 65% of cases), from the common iliac, or inferior mesenteric arteries.1,6

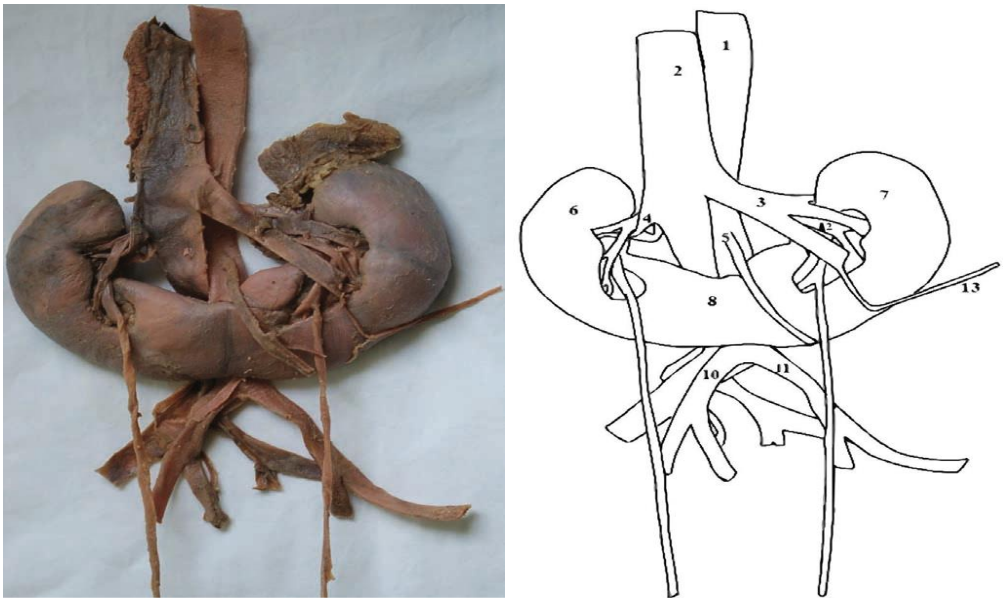

Figure 1 : Panoramic view of the anatomic sample. 1. Aorta; 2. Inferior vena cava; 3. Left renal artery; 4. Right renal artery; 5. Inferior mesenteric artery; 6. Right kidney; 7. Left kidney; 8. Isthmus; 9. Ureters; 10. Right common iliac artery; 11. Left common iliac artery; 12. Renal arteries for the isthmus; 13. left gonadal artery (reflected).6

Symptoms

Horseshoe kidneys are often asymptomatic, and so are often identified incidentally. Sometimes it is diagnosed after finding of a midline mass in the lower abdomen. In other patients the symptoms emerged due to renal obstruction, stones or infections. The

most common presenting symptoms in children are those related to urinary tract infection. About one third of the cases were found incidentally during radiological examination and only 60% of the patients were demonstrating complained symptoms.7

Evaluation

In recent years, ultrasonography has become the first imaging procedure performed in the evaluation of pathologic urinary tract conditions.8

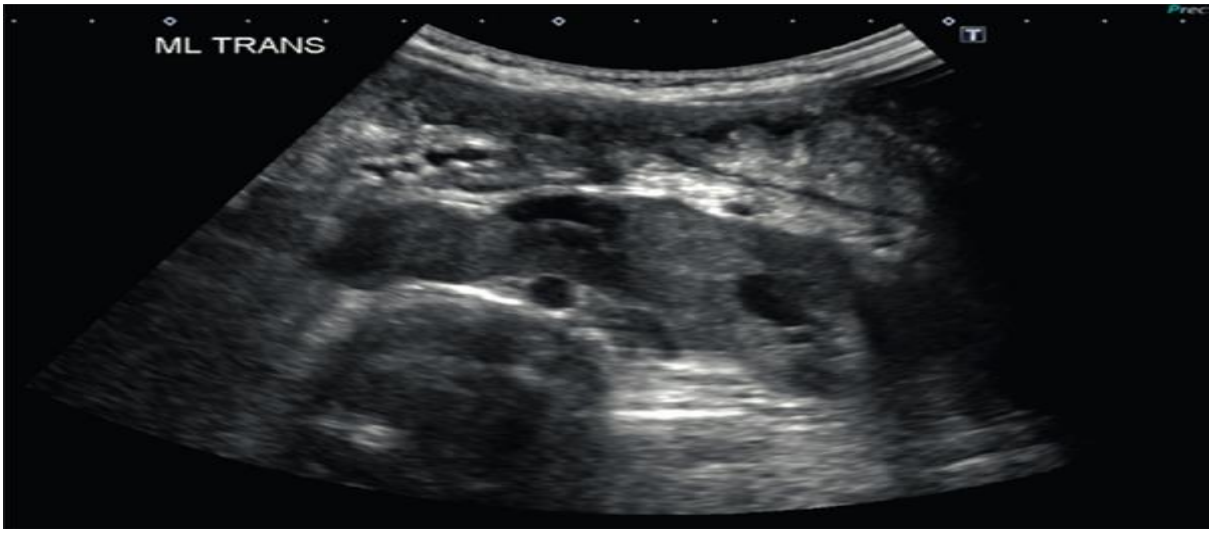

Figure 2 : Newborn with cloacal anomaly. Abdominal sonogram shows horseshoe kidney with mild dilation of the right and left collecting system. Note right side with anterior renal pelvis.3

CT scan are the best for demonstrating the anatomy and can detect accessory vasculature and surrounding structures.9

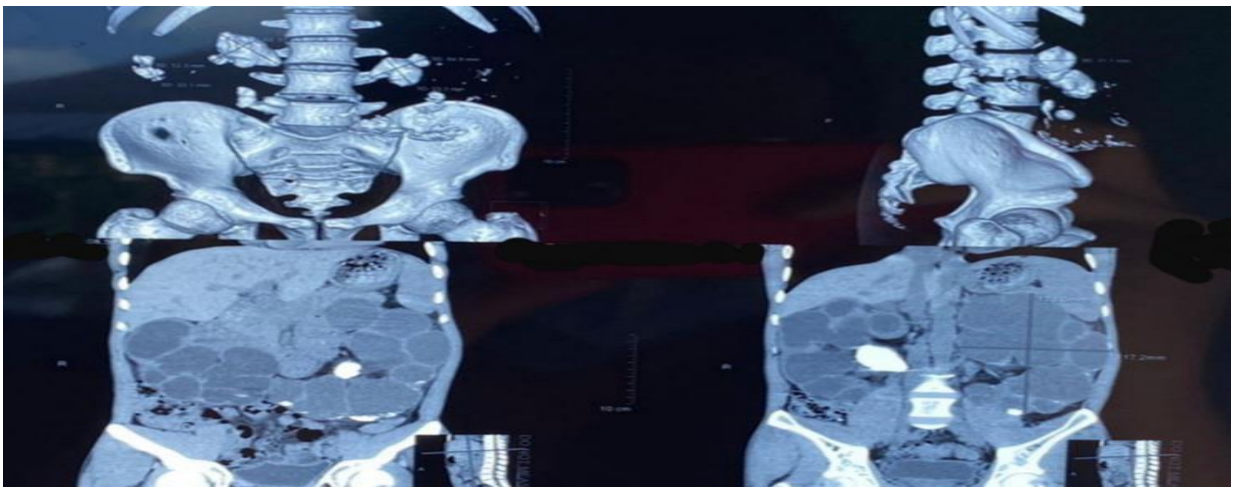

Figure 3: CT of an adult male with horse shoe kidney shows severe hydronephrosis and staghorn stones. Red arrow points to inferior isthmus of the kidneys, which separates left and right kidney. (Private collection)

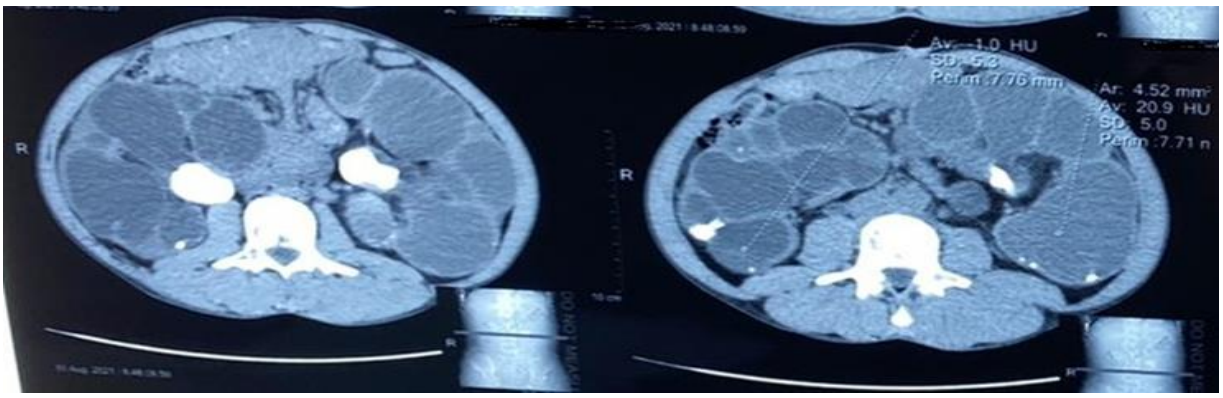

Figure 4: CT of an adult male with horse shoe kidney shows severe hydronephrosis and staghorn stones. Stone in renal-pyelum (red arrow) points to postero-medial, while in normal kidney stone points to antero-medial. (Private collection)

Treatment

Medical treatment may be necessary if complications are identified (renal stones or infections). PCNL is suggested as the first-line treatment method for staghorn stones in patients with Horseshoe Kidney. In 1973, Fletcher and Kettlewell reported the first PCNL in horseshoe kidney. From then on, percutaneous puncture of the Horseshoe Kidney has been found to be relatively safe because of favourable calyceal orientation and vascularity. PCNL showed a better stone-free rate (SFR) 81% to 87% than ESWL, and it was found that the risk of arterial bleeding did not increase in Horseshoe kidney compared with normal kidneys. Percutaneous puncture in horseshoe kidney is relatively safe, especially performed by passing through the superior poles. Janetschek and Kuanzel pointed out that the puncture should be made below the 12th rib on the posterior axillary line with caudad angle of puncture.10

Conclusion

Horseshoe kidney is the most common congenital renal fusion anomaly and is characterised by three morphological anomalies: ectopia, malrotation and changes in vascular supply. Horseshoe kidneys are often asymptomatic, and so are often identified incidentally. Sometimes it is diagnosed after discovery of a midline mass in the lower abdomen. CT scan are the best for demonstrating the anatomy and can detect accessory vasculature and surrounding structures. PCNL is suggested as the first-line treatment method for staghorn stones in patients with horseshoe kidney.

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CASE REPORT

Paraphimosis in Circumcised Old Man

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ABSTRACT

Introduction: Paraphimosis is an emergency uncommon condition in which penile foreskin retracted to proximal and cannot be returned to its normal anatomic position.This condition occurs when the uncircumcised or partial circumcised male penis retracted for an extended period of time. In Indonesia, many men had been circumcised in the past not by doctor nor nurse, but traditional physician. They performed partial circumcision, so there was still foreskin covers part of glans penis that can cause paraphimosis.

Method: We report one case, partial circumcised 60 years old man, came to Namira Islamic Hospital with complained swelling and pain on his penis since a night before. Before that, he pulled his penile foreskin backward. Then the foreskin made constriction band of tissue on the middle of his penile body. He went to nearby clinic and then referred to Namira Islamic hospital, East Lombok, and diagnosed as paraphimosis. We performed emergency surgery later.

Results: We found constriction band of tissue on his middle part of his penile body. Distal part of constriction ring became swelling, and skin color became dark purple. Then we performed dorsal slit procedure continued with circumcision. After procedure, penis color became normal.

Discussion: Paraphimosis most often happens in boys and older man. It is still can happen on partial circumcised man, because there is foreskin extent, which could become risk factor of paraphimosis. Treatment of paraphimosis is dorsal slit procedure with or without circumcision.

Keywords: paraphimosis, dorsal slit procedure, circumcision

Introduction

Paraphimosis is a true urologic emergency that occurs in uncircumcised males when the foreskin becomes trapped behind the corona of the glans penis, leading to strangulation of the glans as well as painful vascular compromise, distal venous engorgement, edema, and even glans penis necrosis.[1,2]

Etiology Paraphimosis commonly occurs iatrogenically, when the foreskin is retracted for cleaning, placement of a urinary catheter, a procedure such as a cystoscopy, or for penile examination.1 Failure to return the retracted foreskin over the glans promptly after the initial retraction can lead to paraphimosis. Other less common causes include penile coital trauma and self-inflicted injuries[3]

Paraphimosis occurs most frequently from preputial edema caused by genital trauma, such as preputial laceration, penile hematoma, or castration. Paraphimosis may be a manifestation of disease characterized by extensive edema, such as dourine and purpura hemorrhagica or it may be caused by damage to penile innervation. The last has been associated with spinal disease, trauma, and infectious diseases, such as equine herpes-virus 1 and rabies. Paralysis associated with priapism, debilitation, or exhaustion has been reported too[3,4]

Epidemiology of paraphimosis in males who do not circumcision or incomplete

circumcision, can occurs at any age, most commonly in adolescents. Paraphimosis occurs in 0.7% of boys uncircumcised. Approximately 1-5% of men will experience paraphimosis before the age of 16 year.[5]

Pathophysiology of paraphimosis is when a constricting band of the foreskin allowed to remain retracted behind the glans penis for a prolonged period, it can lead to impairment of distal venous and lymphatic drainage as well as decreased arterial blood flow to the glans. Arterial blood flow can become affected over the course of hours to days. This change can ultimately lead to marked ischemia and potential necrosis of the glans.[1,7]

When evaluating a patient with paraphimosis, doctor must explore history of any recent penile catheterizations, instrumentation, cleaning, or other procedures. The patient should be asked about his routine cleaning of the penis too. It is also important to ask if the patient is circumcised or uncircumcised. It is still possible to develop paraphimosis in a patient who has previously been circumcised.[7]

Symptoms of paraphimosis include erythema, pain, and swelling of foreskin and glans penis due to the constricting ring of the foreskin. Sometimes patients describes as "penile swelling" and may be relatively painless. Diagnosis is made clinically by direct visualization on physical examination, as well as the inability to easily reduce the retracted foreskin manually.[7]

Treatment of the mild uncomplicated paraphimosis may be reduced manually, usually without sedation or analgesia. Local anesthesia needed in more difficult or complicated cases.[5]

Manual reduction of the paraphimosis is possible with or without compression methods, using osmotic agents and puncture-aspiration techniques. Manual pressure may reduce edema. A gloved hand is circled around the distal penis to apply circumferential pressure and disperse the edema. Ice packs are also useful in reducing swelling of the penis and prepuce. Penis is first wrapped in plastic, with ice packs applied intermittently until the swelling subsides.[5]

If conservative treatment failed to make paraphimosis back to normal, an emergency dorsal slit procedure should be performed. This procedure should be performed with the use of a local or general anesthetic.[5]

Circumcision is strongly recommended in all patients who have had a significant paraphimosis due to the very great risk of a recurrence.10

Failure to remove the constricting band of paraphimosis will result in necrosis of the glans.[11]

Method

A case circumcised 60 years old man, complained swelling and pain on his penis since a night before admitted to Namira Islamic Hospital, East Lombok. On physical examination, we found there was constriction band of tissue at the middle of his penile body. The glans penis and distal part of penile body became swelling. We diagnosed this patient as paraphimosis. Then we performed emergency surgery, which were dorsal slit incision and circumcision procedure. There was no problem intra operative and post-operatively. Patient discharged on the 2nd day after surgery.

Results

The night before, this patient complained couldn't urinate and pulled his penile foreskin inward. Then the distal foreskin trapped in the middle of penile body and made constricting band of tissue that clamped his penis. Distal part of the band on his penile body

and glans penis became swelling. He felt pain on his penis too. Then he went to clinic nearby, and was inserted with catheter, then referred Namira Islamic Hospital, East Lombok.

On physical examination, 16 hours after symptom started, general condition was good and patient looked pain. The vital sign was normal, so the general status of his body too. On penis examination, we found constricting band of tissue on middle of penile body. There was edema on glans penis and distal part of penile body. There was pain on palpation too.

On 21 hours after symptom started, we found the color of distal part of constriction band became dark purple. Laboratory examination was normal.

Then we performed dorsal slit procedure under spinal anesthesia. Intra operative we performed longitudinal incision on constriction band at dorsal, left and right part. We tried to pull the foreskin forward, but the edema of penile gland and distal part of the foreskin made it difficult. So we aspirated edema fluid and venous blood from the distal foreskin and glans penis using 10 cc syringe. There was black venous blood flew out of glans penis. After the edema of penile gland and distal foreskin relieved, we can pull the distal foreskin back to normal position. It appeared that the patient was partially circumcised. Then we performed longitudinal incision on constriction band, at 3, 9, and 12 o'clock, continued by circumcision to avoid the recurrence.

After surgery, the color of penile gland became reddish and distal part of penile body became brown, same color skin as proximal part. Patient then was cared in hospital for 3 days and had given intravenous ceftriaxone injection 1 gr daily and ketorolac injection 2 times daily. He was discharged from hospital with indwelling catheter in good condition.

Discussion

Paraphimosis can occur on partially circumcised patient1,3, because there is still rest of foreskin that covered part of gland penis. Sometimes it covered more than half of gland penis. That is not uncommon occurred in Indonesia, especially on elder patient in rural area, caused they were circumcised not by doctor or nurse but traditional physician. They cut foreskin shortly, reversed backward, just to make penile gland open. So there was still foreskin left that sometimes could become risk factor of paraphimosis.

In this case, patient age was 60 years old and lived in rural area. His penis was partially circumcised, and the preputial skin covered one third of his penile gland. When he pulled the foreskin backward and didn't return it to normal position, then paraphimosis occurred, because this rest of foreskin made constriction band of tissue at his penile body.

Prevalence of paraphimosis in uncircumcised children, four months to 12 years old, with foreskin problems, is 0.2%. It is less common than other penile disorders such as balanitis (5.9%), irritation (3.6%), penile adhesions (1.5%), or phimosis (2.6%)[5]

In adults, paraphimosis is most commonly found in adolescents. It will occur in about 1% of all adult males over 16 years of age.5 In other report said that paraphimosis occurred more often in boys and older men, but actual number wasn't shown up.4 So it's not surprisingly in this case, paraphimosis occurred in 60 years old man. Sandip EJ and Sujata SJ reported 52 % of paraphimosis case in their research were 21 – 60 years old and 2 % more than 61 years old.[8]

Paraphimosis is almost always an iatrogenically or inadvertently induced

condition; however, case reports have described paraphimosis occurred at sexual intercourse case, as well as penile piercings, and masturbation leading to paraphimosis.1,8 Predisposing events on boys are retraction by self and by mother.8 In most cases, the foreskin reduces on its own and therefore precludes paraphimosis; however, if the slightest resistance to retraction of the prepuce is present, leaving it in this state predisposes it to paraphimosis. As edema accumulates, the condition worsens.[1]

If a constricting band of the foreskin is allowed to remain retracted behind the glans penis for a prolonged period, it can lead to impairment of distal venous and lymphatic drainage as well as decreased arterial blood flow to the glans. Arterial blood flow can become affected over the course of hours to days. This change can ultimately lead to marked ischemia and potential necrosis of the glans.5

In this case paraphimosis occurred when patient pulled his penile foreskin backward, then the foreskin trapped at the middle of his penile body, because he didn't return it to normal condition. He did that after suddenly he couldn't urinated and expected could urinated again if he pulled his penile foreskin. Then he felt pain and swelling on his penis, especially at distal part of penile body and glans penis.

This condition as same as the majority of paraphimosis cases. In other research reported that on paraphimosis physical examination found that the glans penis is enlarged and congested with a collar of edematous foreskin. A constricting band of tissue is noted directly behind the head of the penis. The remainder of the penile shaft is unremarkable.1

Treatment of paraphimosis is to control pain first, by providing adequate analgesia and local anesthesia using a dorsal penile nerve block and circumferential penile ring block with lidocaine, bupivicaine, or a combination of the two.1

In this case, patient felt very pain, especially when we touched or palpated his penis. We gave intra venous ketorolac injection to reduce the pain and inflammation. We also gave 1 gr ceftriaxone injection to prevent infection.

Actually, once pain control is adequate, manual reduction by attempting to circumferentially compress the foreskin and holding for 2-10 minutes to "squeeze" the edematous fluid along the penile shaft may be attempted.1,5 We didn't perform manual reduction in this case because the edema was big and he felt pain when we touched his penis. So we directly performed emergency surgery under spinal anesthesia. Intra operatively we attempted to perform manual reduction, but the foreskin edema made it difficult. So, we aspirated the foreskin but only minimal fluid came out there. Then when continued aspirating glans penis, with 10 cc syringe. Black venous blood flew out of glans penis. After the edema reduced, then we performed dorsal slit incision and circumcision. Then the glans penis color became reddish which means that the blood flow in penis became normal.

If paraphimosis is left untreated for too long, the distal portion of the penis can become ischemic and even necrotic. Partial amputation of the distal penis has been reported.1

After patient discharged from hospital, he checked again in urology clinic at day 7th. The color of his glans penis and penile body was normal and the wound was good. No complain of pain anymore. Patient still used urethral catheter, and we plan to perform urology ultrasound to find the cause of urinary retention.

Paraphimosis does not recur after a proper circumcision. Outcome after a dorsal slit procedure or a circumcision is excellent. Sometimes, patients with a favorable outcome from dorsal slit procedures decline circumcision.1

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