Clinical study protocol

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Clean Catch Urine Feasibility and Contamination Rate compared to Bladder Catheterization Urine in Pre-Continent Children: Randomized Control Trial

Prospective, randomized controlled trial, pilot, multicentered, non-inferiority, comparing contamination rate between clean catch urine and bladder catheterization.

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1. Research Proposal Cover Page:

Project details	
Date:	15/01/2024
Project title:	Clean Catch Urine Feasibility and Contamination Rate compared to Bladder Catheterization Urine in Pre-Continent Children: Randomized Control Trial
Study design:	Randomized controlled trial. Pilot study
Study clinical site:	Pediatric emergency departments at Royal hospital and An Nahdha hospital, located in Muscat, Sultanate of Oman.
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2. Summary:

Introduction: Urinary tract infections (UTIs) are a common source of infection in children, accounting for a significant proportion of visits every year. Diagnosing UTIs requires obtaining a urine specimen, which can be collected using four methods: invasive techniques, such as suprapubic aspiration and urethral bladder catheterization, and noninvasive techniques, such as sterile bag and clean catch. However, catheterization can be a painful and invasive procedure, particularly in young infants who are less cooperative, and sometimes tends to be rejected by parents.

Given the availability of alternative methods with comparable contamination rates, we aim to investigate the feasibility and contamination rate of clean catch urine compared to bladder catheterization, as well as secondary outcomes such as pain scores, parental satisfaction, and time required to collect urine for each technique.

Methods: To achieve this, we will conduct a randomized control trial in precontinent pediatric patients. A pilot study with 40 samples in each arm will be conducted since there is no prior information about contamination rates in our setting. A well-designed and labeled data collection sheets will be used for data collection, and the data will be entered using EPI-data software. Statistical analysis will be performed using IBM SPSS statistics.

Aim: The main aim of this study is to introduce clean catch urine (bladder massage technique) to our setting, and to compare its feasibility with the bladder catheterization which is the standard practice.

Patient Population: young infants from 0 to 6 months of age

Intervention: There will be two groups:

1. Group A (Experimental group):Urine samples will be collected using the clean catch urine method (bladder massage technique).
2. Group B (Control group): Urine samples will be collected using the standard bladder catheterization method.

Clinical Measurement: All collected urine samples will be labeled and sent to the laboratory. All results will be retrieved from the medical records. Direct measurement will be for the duration of the procedures in both experiment and

control group (stopwatch will be used). Pain score (Neonatal Infant Pain Scale) and parental satisfaction survey will be filled at the time of the procedure.

Outcome: Contamination rate and feasibility of both urine sampling techniques

3. Introduction: literature review and justification of the study.

Urinary tract infection (UTI) is a common source of infection in children. It accounts for 5 to 14 percent of visits by children every year [1]. The overall prevalence is around 7% among different age subgroups of children. Several factors affect the prevalence of UTI including age, gender, and circumcision status [2].

The diagnosis of UTI requires obtaining a urine specimen from the patient. Generally, there are four methods used in collecting urine samples which can be categorized as invasive (such as suprapubic aspiration and urethral bladder catheterization) and noninvasive (such as Sterile bag and clean catch) [3].

The selection of the urine collection technique is mainly determined by whether the patient is toilet-trained or not. In non-toilet-trained patients, urethral bladder catheterization or suprapubic aspiration can be used. The latter is having the least contamination rate in urine culture [3]. Clean-catch urine is commonly used for toilet-trained patients. If the clinical assessment of febrile infants necessitates immediate antimicrobial therapy, urine culture should be obtained either by urethral bladder catheterization or suprapubic aspiration [3, 4].

Previous observational studies showed approximately a 1 percent contamination rate using the suprapubic aspiration technique [5,6,7,8,9]. In a prospective study done on premature infants it was found that the suprapubic aspiration technique resulted in increased pain and a higher probability of procedural failure compared to urethral bladder catheterization [10]. According to American academy of pediatrics (AAP), for non-toilet trained children, it's advisable to gather a urine sample through methods like ureteral catheterization or suprapubic bladder aspiration, especially when a sample obtained using a perineal bag shows positive results on a dipstick test [11]. The latest guideline from AAP recommends urine culture to be obtained via either SPA or bladder catheterization in pediatric patients aged between 8 to 60 days old, due to false positive results that can occur in the other urine collection techniques [12].
Urethral bladder catheterization carries a 6 to 12 percent of contamination rate. In regard clean catch urine method 16 to 63 percent of the contamination rate [2].

As outlined in the guideline in National Institute for Health and Care Excellence (NICE) guideline, to use clean catch urine wherever possible in pediatric patients below 16 years old. And to reserve bladder catheterization and suprapubic aspiration when noninvasive methods are not possible or practical [13].

Herreros et al. demonstrated a safe and noninvasive technique to collect midstream clean-catch urine in infants. It was based on bladder stimulation and paravertebral lumbar massage [14]. This technique yielded accurate and low contamination rates for infants below 90 days old. Moreover, the success rate was 86.3 percent, while the contamination rate was 5 percent. Nilgun et al. emphasized the safety and efficacy of the same stimulation technique in a neonatal intensive care unit setting. The median time to collect urine was 64 seconds. The success rate is 90 percent. However, Labrosse et al. showed a lower success rate reaching 61 percent, possibly due to patients with a low oral intake that were not excluded from the study [6,15].

In the effort to reduce bladder catheterization in children, different techniques were introduced in the previous literature to improve the clean catch urine success rate as well as the contamination rate [6,14,15,16]. Bladder and lumbar paravertebral massage maneuvers as described by Herreros et al are a safe, time-saving technique that needs to be studied further.

In our setting, the recommendations from international guidelines are being followed. For non-toilet trained children suspected to have UTI, initial urine specimen for urine dipstick is collected by sterile bag or bladder catheterization. If the result of the urine dipstick came positive, then urine culture is obtained via bladder catheterization, if the initial specimen collected by the sterile bag. In addition, we lack the statistics of urine culture contamination in our laboratories.

The main aim of this study is to introduce clean catch urine (bladder massage technique) to our setting, and to compare its feasibility with the bladder catheterization which is the standard practice.

4. Objectives and hypothesis of the study:

Primary outcome:
To compare the contamination rates between the two method and parent satisfaction.
Secondary outcome:
To compare procedure duration in both methods. And pain score (using neonatal infant pain scale)

Study hypothesis

- The contamination rate of clean catch urine sampling is similar to the bladder catheterization.
- Less painful as it is less invasive.

5. Feasibility of the study

It is a multicentered study which enrolls pediatric patients who need urine collection according to the mentioned inclusion criteria. Notably, urinary tract infection (UTI) is a very common presentation in this age group, and it should be considered in almost all pediatric patients with fever with no clear source of infection. All the previously mentioned points can assure that the targeted sample size can be achieved within the designated timeline.

6. Research Design and Methods

Study design:

This pilot study will be conducted as randomized controlled trial.

Characteristics of study area and target population:
Study will be conducted in a tertiary hospital, pediatric emergency, and pediatric ward. Target population are pediatric patients aged between 0 to 6 months.

Primary and secondary endpoints:
Primary endpoints: Urine culture contamination rate and parental satisfaction
Secondary endpoints: Pain score (utilizing Neonatal Infant Pain Scale) and duration of the procedures.

Selection and withdrawal of subjects:
All infants younger than 6 months of age, who require urine sample as part fever work-up in emergency department.
Any subject may be withdrawn from the study at any time for any reason and without penalty or prejudice.

Sampling and sample size:
A pilot study with 40 samples in each arm will be conducted since there is no prior information about contamination rates in our local setting.

7. Randomization

The study will utilize computerized block randomization technique to assign participants into experimental and control groups, with each block being randomized to ensure unbiased allocation. The randomization will occur in the emergency triage.

8. Study flow

Patient will be assessed in triage and cases to be included in the study as per the inclusion criteria, after that patients will be randomized using computerized block randomization technique into two groups. Then, patients will be assigned to a bed, pulse oximetry to be applied, data collection sheet to be filled, confirm that infant had good feeding/ didn't pass urine over last 20 minutes and proper cleaning to be done. The next step will be, collecting urine sample according to randomization group. Group A patients (control group), urine to be collected by standardized catheterization technique while group B by standard CCU technique. Meanwhile, time of each procedure to be documented. Regarding group B , after collecting urine by CCU , we recommend to collect another sample by catheterization to guide the management and antibiotic choice. (Appendix: Study flow chart)

9. Study procedures

Clean catch urine (bladder massage technique) provided in the appendix.

10. Variable definitions and measurements

Data collection tools and methods: (provided in the appendix)
Data quality:
In each site there will be a focal point doctor, responsible for the site. Before conducting the study, we will do training sessions about the study and we will prepare a video teaching the physicians/ nurses the steps of urine collection of by clean catch technique. Individual meetings to be conducted with the focal point for each site to clarify their inquiry. We will use a research assistant for data collection to facilitate the process and to help monitoring the flow of the study protocol.

Data analysis: We will use Statistical Package for the Social Sciences (SPSS) applications version 25 for our analysis.

11. Ethical considerations

Already we have the ethical approval from the ministry of health of Oman (proposal ID: MoH/CSR/23/26368), all recommended changes were adjusted before starting the study. If any risk on patient safety noticed during our study, we will make sure to stop the study protocol. We are not anticipating any harm to patient as the technique our study introducing is less invasive and more comfortable to patients. For the patient group with CCU collection, we are recommending another sample of urine to be collected to guide the antibiotics choice as CCU contamination rate and accuracy will be studied by this paper.

12. Conflict of interest

No conflict of interest

13. Incentives

No incentives of any kind will be given to the participants.

14. Results Dissemination

The study results will be disseminated through various channels to ensure wider reach and maximum impact. This includes local and international publication of the

study in peer-reviewed journals, as well as presentation of findings at relevant conferences and symposiums. Additionally, we plan to share the study outcomes with relevant stakeholders such as healthcare professionals, policymakers to ensure that the findings are effectively translated into practice and policy.

15. Management and monitoring of the research activities

Each focal point will be responsible for that hospital work flow. As each focal point will be in direct contact with the workers at the specific site. Daily monitor to be done to check the new enrolled cases. The other researchers to follow the whole workflow weakly by contact the assigned focal point.

16. Limitations and difficulties of the study:

1. Constrained timeframe for research due to residency program obligations
2. Ensuring an adequate sample size

17. Rationale for subject selection and recruitment.

This is a randomized control study, aiming to study the feasibility and contamination rate of urine collected by clean catch technique comparing to catheterization technique. The population enrolled in this study, pediatric patients, that will benefit of introducing clean catch technique. This is a population who cannot give urine sample for laboratory testing without catheterization which is a painful procedure. The clean catch technique will be of much help for this age group as it is painless and less invasive technique. Therefore, it seems highly beneficial to study the contamination rate of CCU collection in order to introduce it in local guidelines to replace the current use of catheterization.

18. Statistical analysis:

For data entry purposes Microsoft Excel software will be used and for the data analysis IBM SPSS statistics will be used. Normally distributed continuous data will be analyzed using student T test, if abnormal MANN-WHITNEY test will be used. For categorical comparisons CHI-square test will be applied. P-value of less than 0.05% will be considered as statistical significance.

19. Criteria for terminating the study.

A subject who is included in the study, and failed urine collection by CCU , will be removed from study and counted as CCU collection failure. After that to be managed by in-charged doctor as per the treating doctor plan.
The full study to be terminated once required sample size reached, and all data is obtained and documented on the data collection sheet and transferred to Microsoft Excel software.

20. Quality control and quality assurance.

To ensure quality control of the data, we will take several steps.
First, we will design and well-labeled data collection sheets to ensure that all relevant information is captured accurately and consistently. These sheets will be tailored to the specific needs of our study and will include clear instructions and guidelines for data collection.
Second, we will train our research team on the standardized procedures for data collection, including how to complete the data collection sheets accurately and consistently. We will also conduct periodic spot checks and quality control checks to ensure that the data collected is accurate and complete.
Third, we will use Microsoft Excel software to manage the data entry process. This software allows for easy data entry, validation, which will reduce the risk of errors during data management.
Finally, we will conduct a thorough review of the data after it has been collected and entered into the system. This will include checking for inconsistencies, missing data, and outliers, and addressing any issues that are identified. By taking these steps, we will ensure that the data collected is of the highest quality and is suitable for analysis

21. Data handling and record keeping.

Subject information obtained because of this study is considered confidential and disclosure to third parties is prohibited. Medical information may be assessed only after approval from the subject to the investigator. The investigator will not disclose any confidential information regarding subjects during performance of study duties without justifiable reasons. The investigator affirms the subject's right to protection against invasion of privacy. All data collection sheets are collected in a locked and secured box in the emergency department and no access is allowed except for investigators. Any electronic file containing patient data will be protected by a complicated password. No data will be shared though any social platforms including WhatsApp. Data can be shared between investigators only by password protected Google Drive account. After termination of the study and

finishing data analysis, data will be stored for a period of 3 year and will be discarded safely and securely.

22. Anticipated results

We anticipate that our intervention will show a comparable methodology to the standard urinary catheterization in terms of contamination rate, but is less invasive and more feasible, with higher patient and parent satisfaction rates. This conclusion has the potential to improve patient care and management, as it offers a more patient-centered approach to catheterization. Our study may influence policy-making by demonstrating the potential benefits of the intervention and advocating for its wider adoption in clinical practice.

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24. Appendix

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Data collection sheet

Data Collection Sheet

Patient demographics

- Serial number:
- MRN:
- Name of the hospital: • RH …… , • ANH……
- Age (in months):
- Gender: • Male • female
- Weight (Kg):

Current illness:

- Urinary Tract infection is one of the differential diagnosis
- • Yes • No
- Urine collection by:
- • Clean Catch • Catheterization

Duration of procedure (in minutes): ……..

Pain Score (Neonatal infant pain Scale):

……..

Pain Assessment		Score
Facial Expression		
0 - Relaxed Muscles	Restful face, neutral expression	
1 - Grimace	Tight facial muscles; furrowed brow, chin, jaw (negative facial expression – nose, mouth brow)	
Cry		
0 - No cry	Quiet, not crying	
1 - Whimper	Mild moaning, intermittent	
2 - Vigorous cry	Loud scream; rising, shrill, continuous (Note: Silent cry may be scored if baby is intubated as evidenced by obvious mouth and facial movement	
Breathing Pattern		
0 - Relaxed	Usual pattern for this infant	
1- Change in breathing	Indrawing, irregular, faster than usual; gagging, breath holding	
Arms		
0 - Relaxed/Restrained	No Muscular rigidity; occasional random movements of arms	
1 - Flexed/Extended	Tense, straight arms; rigid and/or rapid extension, flexion	
Legs		
0 - Relaxed/Restrained	No Muscular rigidity; occasional random movements of legs	
1 - Flexed/Extended	Tense, straight legs; rigid and/or rapid extension, flexion	
State of Arousal		
0 - Sleeping/Awake	Quiet, peaceful, sleeping or alert, random leg movements	
1 - Fussy	Alert, restless and thrashing	

Specify time antibiotics giving (before/after clean catch or before/after catheterization?)

……..

***For the Doctor/nurse*: Do you agree collecting urine using CCU(bladder massage) is easier than bladder catheterization? (Yes or No) ……..**

***Parent satisfaction*: are you satisfied with the used technique (Yes or No) ……..**

Physician name: …….. **Signature: ……..**

Written informed consent:

Informed consent form

Research title

Clean Catch Urine Feasibility and Contamination Rate compared to Bladder Catheterization Urine in Pre-Continent Children: Randomized Control Trial

Research Idea

Our study aims to test an alternative way to urine collection by catheterization. primary outcomes are to compare the contamination rates between the two method and parent satisfaction. The secondary outcomes, include procedure duration, pain score (using neonatal infant pain scale)

Methodology

The patient will be randomly distributed into two groups: group one, urine will be collected through catheterization, group two urine will be collected by Clean Catch urine collection.

Contact information

If you have any questions, you may ask now or later, even after the study has started. If you wish to ask questions later, you may contact any of the following:

-Dr.Sulayyem Al Hasrousi , contact number +968 97383155, E-Mail: alharsoosi@gmail.com.
- Dr. Dr. Muna Al Ka'abi, contact number +968 91797366, E-Mail: r2126@resident.omsb.org

- I am the parent of ……..
- I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it.
- Any questions that I asked, they have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.

Authorized to consent name:
Relationship to the patient:
Signature date:
Researcher/Doctor:

Clean catch urine technique

Clean catch urine (bladder massage technique)

- Two people (trained nurses and/or physicians) were needed to perform the procedure, and a third to measure the time taken. This technique involves a combination of fluid intake and non-invasive bladder stimulation maneuvers .
- To provide breast-feeding or formula intake appropriate to the age and weight of the newborn. In babies fed infant formula, 10 ml was provided on the first day of life, increasing to 10ml per day during the first week. From the second week onwards, 25 ml/kg were administered before the onset of stimulation .
- Twenty-five minutes after feeding, the infant's genitals were cleaned thoroughly with warm water and soap and dried with sterile gauze .
- A sterile collector was placed near the baby to avoid losing urine samples.
- Hold the baby under their armpits with their legs dangling. One examiner then starts bladder stimulation which consists of a gentle tapping in the suprapubic area at a frequency of 100 taps or blows per minute for 30 seconds .
- Stimulation of the lumbar paravertebral zone in the lower back with a light circular massage for 30 s. Both stimulation maneuvers are repeated until micturition starts, and a midstream urine sample can be caught in a sterile collector.
- Success is defined as the collection of a sample within 5 min of starting the stimulation maneuvers.

Definitions for UTI, contamination, and insignificant growth

	Urine culture results		
Definition	**Urinalysis result**	**Organism(s) Cultured**	**Colony Threshold[a]**
No growth	Negative	No growth	No growth
UTI	Positive[b]	1 Uropathogen[c]	≥100,000 CFU/mL
	Positive	1 Uropathogen	10,000–100,000 CFU/mL[d]
Contaminated	Negative	1 Non-uropathogen	≥100,000 CFU/mL
	Negative	≥2 Organisms (≥1 non-uropathogen)	Any colony count
	Negative	Mixed bacterial flora[e]	≥100,000 CFU/mL
Insignificant Growth	Positive or negative	1 Non-uropathogen	≤10,000 CFU/mL
	Negative	1 Non-uropathogen	≤100,000 CFU/mL

[a]Urine culture colony counts had the same thresholds regardless of the method used to obtain the urine specimen (ie, urethral catheterization or bladder massage).
[b]Urinalysis indicative for UTI-labeled positive: positive leukocyte esterase test and/or nitrite test, in addition to evidence of pyuria with >10 white blood cells per microliter. Urinalysis results that do not meet criteria for positive are considered negative.
[c]The identified organism is considered a uropathogen based on clinical judgment of the provider caring for the patient.
[d]For this range, providers must consider the patient's clinical presentation and whether the urinalysis supports the diagnosis of a UTI.
[e]Nomenclature indicating growth of 3 or more organisms.

Study flow chart