Evaluating the Predictive Efficacy of Dipstick Urinalysis for Detecting Urinary Tract Infections in Febrile Children Under Five Years of Age at Federal Medical Centre, Owerri, Imo State, Nigeria

[1]Nwigwe U. M., [2]Esezobor C. I., [1]Iregbu F. U. and [3]Ushie S. N.

[1]Federal   University Teaching Hospital Owerri
[2]Lagos University Teaching Hospital Lagos State
[3]Nnamdi Azikiwe University Teaching Hospital Nnewi

ABSTRACT

This study aimed to assess the predictive efficacy of dipstick urinalysis in detecting urinary tract infections (UTI) among febrile children under five years of age at the Federal Medical Centre, Owerri, Imo State, Nigeria. The research involved a hospital-based descriptive cross-sectional study, analyzing the diagnostic performance of nitrite and leucocyte esterase tests on urine dipsticks. The results revealed low sensitivity but high specificity for both tests, suggesting their potential role in excluding UTI. The findings emphasize the importance of combining dipstick urinalysis with urine culture for accurate diagnosis in febrile children.

Keywords: Urinary tract infections, Dipstick urinalysis, Febrile children, Nitrite, Leucocyte esterase, Diagnostic efficacy, Nigeria.

INTRODUCTION

Evaluation of urine specimen for UTI involves quantitative urine culture which is the gold standard for diagnosis, however urinalysis is also important in screening patients whose specimens will be subsequently cultured [1].The components of urinalysis most useful in evaluating for a possible UTI include microscopy, nitrite test and leucocyte esterase test [2]. **Urine Dipstick Tests:** These are a group of tests which involve dipping reagent strips into collected urine.[1] Nitrite and leucocyte esterase tests, parameters tested on dipstick have the advantage of being cheap, easy to perform, interpret and providing immediate results [3-5]. Nitrite test measures the conversion of dietary nitrate to nitrite by nitrate reductase-producing gram negative bacteria and some gram positive organisms [6-8]. A positive nitrite test makes UTI very likely but the test may be falsely negative if the bladder is emptied frequently (reducing the time for the conversion) or if a non-nitrate reductase-producing organism is the cause of the infection [9-12]. Nitrate reducing reagent is sensitive to air and false positive reaction may be obtained if the dipstick container is not tightly covered when stored [13-14]. The leucocyte esterase test is an indirect measure of pyuria and hence may be falsely negative if leucocytes are present in low concentration [15-17]. This test is more sensitive but less specific for UTI than nitrite test ,thus making the combination of nitrite and leucocyte esterase tests highly sensitive and specific for diagnosis of UTI [20-24]. [25], in Tanzania recorded a sensitivity of 68.8% and specificity of 92.4% with nitrite test while the leucocyte esterase had a sensitivity of 76.6% and specificity of 85%. A combination of both gave specificity and sensitivity of 85.9% and 79.6% respectively. Similarly, Amajor[34] in Calabar Nigeria documented sensitivity of 62.5% and 75.0% for nitrite and leucocyte esterase respectively while both had higher specificity both individually and in combination. On the contrary, [26] in the United Kingdom also documented low sensitivity for both leucocyte esterase and nitrite (31.3% and 43.8%) and high specificity of 85.5%

and 94.2% for leucocyte esterase and nitrite respectively. Furthermore a combination of both showed low sensitivity of 25.0% and high specificity of 97.8%. Also, [27] in Tanzania documented low sensitivity for nitrite and leucocyte esterase individually and in combination (of 21.7% and 8.8% respectively individually and 28.6% in combination), though the specificity was high for nitrite and leucocyte esterase (97.8% and 99.1% respectively). Some Nigerian authors have also documented similar findings in their studies [28-32]. **Urine Microscopy**: Urine microscopy is important to ascertain whether there are white blood cells in the urine which is a sensitive indicator of inflammation associated with infection [33-35]. Pyuria is 73% sensitive and 81% specific for the diagnosis of UTI. Leucocyturia is defined as more than five white blood cells per high power field in centrifuged urine and greater than 10 white blood cells per high power field in uncentrifuged urine [36-40] However, the absence of pyuria does not exclude a UTI especially in infants less than two months of age [41-45]. Urine microscopy apart from detecting white blood cells also demonstrates the presence of red blood cells, casts, bacteria and yeast cells [46-48]. A gram stain of unspun urine helps in the identification of the nature of the bacteria hence guides the clinician to initiate antibiotic therapy [49-53]. A gram stain of unspun urine has a sensitivity and specificity of approximately 90-93% [54-57] in Tanzania documented a high specificity of 86.5% and positive predictive value 68.4% for urine microscopy in the diagnosis of UTI. The high sensitivity and specificity recorded may be attributed to the use of uncentrifuged urine and the cut off for pyuria of > 10WBC/hpf unlike the previous studies where pyuria was regarded as 5 WBC/hpf. **Urine Culture**: This is the gold standard for microbiological diagnosis of UTI [54]. A growth of greater than or equal to 100,000CFU/ml is considered culture positive for midstream urine specimen, 50,000CFU/ml for transurethral catheterization and for any number of colonies for SPA specimen [55-60].

Aim and Objectives

The aim of this research was to evaluate the predictive efficacy of dipstick urinalysis for detecting urinary tract infections in febrile children under five years of age at federal medical centre, Owerri, Imo state, Nigeria.

RESEARCH QUESTION

What is the predictive value of dipstick urinalysis in the diagnosis of UTI among febrile under-five children?

Specific Objective

To determine the predictive value of dipstick urinalysis in the diagnosis of UTI in febrile under-five children.

METHODOLOGY

Study Area

The study was carried out at the Paediatric Outpatient Clinics and Emergency Paediatric Unit of the Federal Medical Centre Owerri, Imo state. The State is one of the five states of South-Eastern Nigeria and it is made up of 27 local government areas. Owerri is the capital of Imo State and it is made up of three local government areas namely: Owerri Municipal, Owerri North and Owerri West. The estimated population of Owerri is about 400,000. The projected population for 2020 is about 872,604. The Federal Medical Centre is a tertiary health facility located centrally in Owerri. It has two outreach centres located at Umunama-Mbaise and Izombe-Oguta and serves as a referral centre for hospitals from all over the state and the neighbouring states of Rivers and Anambra. The Paediatric Outpatient Clinics run from Mondays through Fridays between 8am and 4pm. An average of 70 patients are seen daily with an annual average of 13,000 patients. It is the first point of care for all sick children visiting the hospital except for emergencies and children who come to the hospital during the weekend who are managed in the emergency paediatric unit. Sick children presenting after 4pm are also seen at the emergency unit. The emergency paediatric unit runs a 24-hour service and an average of 300 patients seen monthly with an average of 4000 patients seen per annum.

Study Design

This was a hospital-based descriptive cross-sectional study.

Ethical Considerations

Ethical clearance and permission to carry out the study was obtained from the Research and Ethics Committee of the Federal Medical Centre Owerri. Also, parents and care givers of eligible children provided a written informed consent. The study was conducted in a manner that ensured that participation in the study did not result in undue delay of commencement of standard treatment or management. In addition, the results of children with positive urine culture were passed on to the team responsible for the care of the child as soon as it became available.

Study Population

The study population consisted of all febrile (axillary temperature > 37.5°C) children between the ages of 0 and 59 months attending the Paediatric Outpatient Clinics and Emergency Paediatric Unit that met the inclusion criteria.

Inclusion Criteria

1. Children between the ages of 0 and 59 months presenting with fever (axillary temperature > 37.5°C).
2. Children whose parents or caregivers provided written informed consent.

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Exclusion Criteria

1. Very ill children requiring immediate resuscitation and commencement of antibiotics which would have delayed by participation in the study.
2. Children who received systemic (oral or parenteral) antibiotics within the previous 72 hours.

Sample Size Calculation

The minimum sample size was estimated using the Cochran formula for prevalence studies.[115]

Sample size, $n = \dfrac{Z^2 pq}{d^2}$

Where n= sample size

    Z= Standard normal deviation at 95% confidence level= 1.96
    P= Prevalence of UTI in febrile under 5 children in Enugu[9] = 11%
    Q= (1-p)
    d =level of precision= 0.05

$$n = \dfrac{Z^2 pq}{d^2}$$

= [(1.96)² × 0.11 × 0.89]/ (0.05)²
Therefore, the minimum calculated sample size=152

A further 10% (16) was added to the minimum sample calculated to factor in risk of attrition.
Therefore 170 children were recruited for the study.

Sampling Technique

Eligible children were recruited consecutively.

Study Procedure

Each recruited subject had a detailed history and physical examination. The findings were documented in the data entry form. The variables entered into the form included demographic data (research number, age, and gender), history of fever, presence of symptoms suggestive of urinary tract infections and treatment received prior to enrolment in the study. Other information recorded in the form included the temperature reading, the presence of bladder mass, ballotable kidneys, uncircumcised penile shaft, neural tube defects and the presence of other focus of infections.

Temperature

Body temperature was measured by using mercury in glass clinical thermometer. This was placed in contact with the skin on the subjects' axilla for four minutes after which reading was recorded. A subject was considered febrile when the temperature was above 37.5°C.

Specimen Collection

After recruitment into the study, the investigator labelled the sample bottles appropriately and midstream urine was collected by the researcher or the caregivers under supervision. This was done by voiding the initial part of the urine stream into the toilet or another container and at approximately the middle of the urine flow the specimen bottle was positioned to capture urine. However, in children not yet toilet trained, spot urethral catheterization was carried out under aseptic conditions. In collecting the sample by urethral catheter, the researcher or the assistant wore sterile gloves then the child was placed in supine position and the labia or penis was cleaned with antiseptic swab. In females, the labia was parted to expose the urethral opening, the catheter was lubricated with sterile anaesthetic gel (KY jelly) before insertion into the urethral opening upward until urine begins to flow out. For the male child, the penis was lifted and the foreskin retracted in the uncircumcised. The urethral opening was cleaned with antiseptic swabs in a circular motion from the urethral opening to the base of the penis and a sterile lubricant was applied to the catheter before insertion. The penis was held with slight upward tension and perpendicular to the child's body and the catheter was inserted. The size of the catheter to be used was French gauge (Fr) 6 for children under one year of age while French gauge (Fr) 8 was used in subjects older than one year. Urine specimen was collected into two sterile wide necked leak proof universal bottles. One sample was used for dipstick urinalysis and the other for microscopy, culture and sensitivity in the laboratory. Specimens for culture were sent to the laboratory within 15-20 minutes of collection. In cases where a delay was anticipated before processing, specimens were stored in the refrigerator for no longer than six hours.

Specimen Processing

A macroscopic examination was done for every urine sample to record the colour and nature (to assess whether the urine was clear or turbid). Urinalysis was also carried out qualitatively using chemstrip-10 dipsticks (Roche

Diagnostics Montreal, Quebec Canada) to detect the presence of protein, blood, nitrite and leucocyte esterase. The strip was dipped for no longer than one second into the specimen and excess urine was removed by drawing the edge of the strip along the rim of the container, the test strip was turned on its side and placed on a piece of absorbent paper to prevent mixing of chemicals. A timer was set for two minutes. After one minute, the strip was held close to the colour blocks printed on the reagent vial and read for protein, blood and nitrite while the leucocyte esterase was read at two minutes. Each test pad was carefully matched to its reference. All results were read and recorded between one and two minutes. Results were subsequently recorded in the questionnaire.

Urine Microscopy

Urine microscopy was carried out at the laboratory by the microbiologist with active participation of the investigator using a wet preparation. This was done using about 5 ml of well mixed urine which was aseptically transferred to a labelled conical tube and centrifuged at 2000 revolutions per minute (rpm) for five minutes. The supernatant was decanted into a second container. A drop of the well mixed sediment was transferred to a slide and covered with a cover glass. The preparation was viewed under a light microscope using 40x objective. Presence of pyuria (>5WBC/HPF) was regarded as significant and suggestive of UTI.

Urine Culture

 A sterile calibrated wire loop that takes 0.001 ml of urine was used to inoculate a loopful of urine on blood agar and Cysteine Lactose Electrolyte Deficient (CLED) agar. Then the plate was incubated aerobically at 35^0C- 37^0C for18 - 24 hours, after which those with significant growth (colony count $\geq 10^5$ CFU/ml for MSU or $\geq$ 50,000 CFU/ml for catheter specimen) were identified by standard bacteriological methods, colonial morphology and *Microbact*® 12 A[116]. Urinary tract infection was defined as the presence of compatible clinical features and significant bacteriuria taking into consideration the mode of urine collection[8]. Urinary tract infection was defined as a growth of at least 50,000CFU/ml of a single organism in catheter specimen urine and at least 100,000 CFU/ml in midstream urine samples. The results of subjects with confirmed UTI was communicated to the managing team for treatment according to standard protocol and the subsequently referred to Nephrology clinic for follow-up.

Antimicrobial Susceptibility Testing

Antimicrobial susceptibility testing was also done on the isolates from urine samples with significant bacteriuria. This was determined using Kirby Bauer discs diffusion method[114]. In this method, four colonies were inoculated into 5ml sterile normal saline compared with 0.5 McFarland standard (with approximate cell density of $1x10^8$ CFU/ml) to ensure equal turbidity and a sterile swab stick dipped into the suspension. The swab was streaked on the entire agar surface of Mueller Hinton agar and a known concentration antibiotics disks which have been equilibrated with the room temperature were placed gently equidistant to each other with five disks per 90mm petri dish. The plates were incubated aerobically at 35-37°C for 24 hours after which the diameter of the zones of inhibition were measured to the nearest millimetre using transparent calibrated ruler and compared to the Clinical and Laboratory Standards Institute (CLSI) 2014 interpretative chart[113]. The susceptibility test was carried out using these antibiotics co-trimoxazole (25/23 □g), nitrofurantoin (30 □g), ciprofloxacin (5 □g), co-amoxiclav (20/10 □g), gentamycin (10 □g), cefixime (30 □g) and cefuroxime (30 □g) the other antibiotics tested were levofloxacin (5 □g), amikacin (30 □g) and ceftriaxone (30 □g). The antibiotic susceptibility testing and all other procedures were quality controlled using ATCC 25923 *Staphylococcus aureus* and ATCC 25922 *Escherichia coli.*

Data Analysis

Data was coded and entered into a computer. It was analysed using IBM Statistical Package for Social Sciences (SPSS) version 20.0. Frequency tables, charts and figures were used to summarize variables as appropriately required. Mean and standard deviation were used to summarize quantitative variables that were normally distributed. Chi square (□²) and where necessary Fisher's exact test and likelihood ratio were used to test for association between categorical variables. A p-value of < 0.05 was considered statistically significant. Security of data was ensured as information on the data entry form was made anonymous by excluding names and phone numbers. The proforma were also kept safe and made available only to the researcher, supervisors and research assistants.

RESULTS

Demographic characteristics of study subjects

One hundred and seventy children aged 0-59 months were recruited for this study. One hundred and fourteen (67.1%) of the 170 subjects were males while 56 (32.9%) were females with a male-female ratio of 2:1. Fifty (29.4%) of the subjects were aged 0-11 months. The mean age was 24.0±16.1 months. (Table 1)

Table 1: Demographic characteristics of study subjects

Variables	Frequency n (%)
Gender	
Male	114 (67.1)
Female	56 (32.9)
Age Groups (months)	
0 − 11	50 (29.4)
12 − 23	39 (22.9)
24 − 35	37 (21.9)
36 − 47	22 (12.9)
48 − 59	22 (12.9)

Presenting complaints of febrile under-five children

Cough (103; 60.6%) and catarrh (93; 57.6%), were the most common symptoms at presentation to the hospital among the study participants. A small proportion of the children had symptoms suggestive of urinary tract infection; Twenty-three (13.5%), 4 (2.4%), and 4 (2.4%) had frequent urination, foul smelling urine and painful urination respectively. Most symptoms were non-specific. (Table 2)

Table 2: Presenting complaints of febrile under-five children

Symptoms	Frequency n (%)
Fever	170 (100)
Cough	103 (60.6)
Catarrh	93 (57.6)
Vomiting	46 (27.1)
Abdominal pain	30 (17.6)
Frequent urination	23 (13.5)
Diarrhoea	14 (8.2)
Convulsions	5 (2.9)
Foul smelling urine	4 (2.4)
Painful urination	4 (2.4)
Jaundice	1 (0.6)

Association between urinalysis findings and urinary tract infection among study subjects

Nitrite was found more often in children with UTI than those without (18.8% vs. 0.7%). Similarly, this was also seen among children with leucocyte esterase (12.5% vs. 2.2%). (Table 3)

Table 3: Association between urinalysis findings and UTI among study subjects

Dipstick urinalysis	UTI		Statistical tool	P-value
	Absent n=138 (81.2%)	Present n=32 (18.8%)		
Nitrite				
No	137 (99.3)	26 (81.2)	Fisher's	
Yes	1 (0.7)	6 (18.8)	Exact	<0.001
Leucocyte esterase				
No	135 (97.8)	28 (87.5)	Fisher's	0.020
Yes	3 (2.2)	4 (12.5)	Exact	

Association between urine microscopy findings and urinary tract infection among study subjects

Among participants with UTI, 3.1% had >5 WBC/HPF while none of the participants without UTI had >5 WBC/HPF. Out of those with UTI, 9.4% had RBCs and this was significantly associated with UTI (p=0.022) while only 1.4% of those without UTI had RBCs (Table 4).

Table 4: Association between urine microscopy findings and urinary tract infection among study subjects.

Variables	UTI n (%)		$\square^2$	p-value
	Absent, n =138	Present n =32		
WBC/hpf				
<5	138(100.0)	31 (96.9)	Fisher's Exact	0.15
>5	0 (0.0)	1 (3.1)		
RBC				
No	136 (98.6)	29 (90.6)	Fisher's Exact	
Yes	2 (1.4)	3 (9.4)		0.022
Cast				
No	135 (97.8)	31 (96.9)	Fisher's Exact	
Yes	3 (2.2)	1 (3.1)		0.57

Diagnostic value of Urinalysis in urinary tract infection among study subjects

 Nitrite and leucocyte esterase had low sensitivity of 18.8% and 12.5% respectively and high specificity of 99.3%, and 97.8% respectively. A combination of nitrite and leucocyte esterase had a low sensitivity of 6.3% and a high specificity of 100.0% as well as high positive and negative predictive values of up to 100%. (Table 5).

Table 5: Diagnostic value of urinalysis in urinary tract infection among study subjects

Urinalysis findings	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Nitrite	18.8	99.3	85.7	84.1
Leucocyte Esterase	12.5	97.8	57.1	82.8
Nitrite and Leucocyte Esterase	6.3	100.0	100.0	82.1

PPV Positive Predictive Value
NPV Negative Predictive Value

DISCUSSION

Dipstick urinalysis in this study showed that both nitrite and leucocyte esterase individually and in combination, had low sensitivity and high specificity for the diagnosis of UTI [59-64]. The low sensitivity of leucocyte esterase test could have been due to the low concentration of pyuria in majority of the study participants; similarly the low sensitivity of the nitrite observed in this study may have been due to the use of random urine specimen for analysis as long bladder incubation period is required for conversion of dietary nitrates to nitrites. This is similar to the report by Festo *et al* [29] in Tanzania as well as some Nigerian researchers[11,33,110] Contrarily, Hay *et al* [27] in the UK, Frederick *et al* [30] in Tanzania and Amajor *et al* [34] in Calabar Nigeria documented high sensitivity and specificity for both nitrite and leucocyte esterase. This supposes that the use of dipstick urinalysis (nitrite and leucocyte esterase) for screening of UTI in febrile under-five children could lead to missed cases of UTI due to the large number of false negatives, however it could be valuable in the exclusion of UTI due to the high specificity and negative predictive value. Therefore these tests should be used in combination with urine culture which remains the gold standard in the diagnosis of UTI in febrile under-five children.

CONCLUSION

In conclusion, nitrite and leucocyte esterase tests on dipstick urinalysis demonstrated high specificity and negative predictive value but low sensitivity in detecting UTIs among febrile children under five years of age. While these tests may aid in excluding UTIs, their limited sensitivity highlights the necessity of employing urine culture as the

gold standard for precise diagnosis in this population. This study contributes valuable insights to the diagnostic approach for febrile children, emphasizing the need for a comprehensive evaluation combining dipstick urinalysis and urine culture for enhanced diagnostic accuracy.

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