Urine pH Value and Bacteriology in Purple Urine Bag Syndrome

Yu-Jang Su^{a, b, c} Hsiu-Wu Yang^{a, b} Chen-Wang Chang^{c, d}

^aDepartment of Emergency Medicine, Mackay Memorial Hospital, Taipei, Taiwan; ^bDepartment of Medicine, Mackay Medical College, New Taipei City, Taiwan; ^cMacKay Junior College of Medicine, Nursing and Management, Taipei, Taiwan; ^dDivision of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan

Keywords

Gram-negative bacteria · Gram-positive bacteria · Purple urine bag syndrome · Urinary pH · Urinary tract infection

Abstract

Background: Purple urine bag syndrome (PUBS) is an unusual phenomenon in patients with urinary tract infections. The urine of most of these patients has an alkaline pH. **Objective:** The goal of this study was to identify infectious bacteria and determine urinary pH in patients with PUBS and to evaluate their correlation. **Methods:** PubMed was searched using the term “Purple urine bag syndrome (PUBS)” for studies on this condition published from October 1980 to September 2019. Sixty-seven patients were identified and divided into those with urine cultures positive for Gram-positive bacteria (GPB; $n = 3$), Gram-negative bacteria (GNB; $n = 45$), and mixed Gram-positive and Gram-negative bacteria (MGPNB; $n = 19$). Age, gender, urinary pH, comorbidities (diabetes and uremia), fever, shock, and mortality were compared in the 3 groups. The correlation between urinary pH and type of bacteria in urine cultures was assessed by regression analysis. **Results:** Presentation of fever in PUBS accounted for 66.7, 11.1, and 5.3%, $p < 0.05$, in GPB, GNB, and MGPNB. Regression

analyses showed that *Pseudomonas aeruginosa* was associated with less alkaline urine (regression coefficient -0.936 , $p < 0.05$), whereas *Proteus* spp. was associated with more alkaline urine (regression coefficient 0.489 , $p = 0.04$). GNB were the most predominant pathogens in patients with PUBS. **Conclusion:** In PUBS, urine pH and symptom presentation are different by variable bacteria. Fever is associated with urinary GPB. *Proteus* spp. correlates with more alkaline urine, whereas *Pseudomonas* spp. correlates significantly with less alkaline urine.

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Introduction

Purple urine bag syndrome (PUBS) is an uncommon phenomenon, characterized by urinary catheters with purple-colored tubes and bags. The bacteria responsible for urinary tract infections (UTIs) possess phosphatases and sulfatases, which convert indoxyl sulfate in urine into indirubin (red) and indigo (blue), with their mixture in urine resulting in deep violet-colored urinary catheter tubes and bags [1]. PUBS has been frequently encountered in patients with long-term catheter placement,

Fig. 1. Patients with PUBS enrolled in this study and their division into groups infected with GPB, GNB, and MGPNB. PUBS, purple urine bag syndrome; GPB, Gram-positive bacteria; GNB, Gram-negative bacteria; MGPNB, mixed Gram-positive and -negative bacteria; WBC, white blood cell.

chronic constipation, or alkaline urine, as well as in nursing home residents [2]. PUBS is more common in women than in men [2]. A systematic review from Taiwan in 2018 reported that 93.1% of patients with PUBS have alkaline urinary pH (pH > 7), whereas only 6.9% had urinary pH (pH < 7) [3]. To date, no study has assessed the relationship between the infecting microorganism and urinary pH in patients with PUBS. The present study, therefore, analyzed infectious bacteria and determined urinary pH in patients with PUBS, as well as evaluated their correlation.

Materials and Methods

In order to study urine pH value and bacteriology in PUBS, we retrieved the data in a systemic review manner. PubMed was searched using the term “purple urine bag syndrome” or “PUBS” for studies published between October 1980 and September 2019. The 118 identified articles included 186 patients with PUBS. Eighteen studies involving 119 patients were excluded, including 14 studies that did not describe patients’ sex and 4 that did not report patient age. An additional 37 studies did not report patient white blood cell counts, shock, fever, or etiology. Urinary pH was not reported for 48 patients, and urine culture data were not reported for 16 patients; these patients were also excluded. This study finally enrolled 67 patients with PUBS, including 3 with urinary cultures positive for Gram-positive bacteria (GPB) alone, 45 positive for Gram-negative bacteria (GNB) alone, and 19 patients positive for mixed Gram-positive and Gram-negative bacteria (MGPNB) (Fig. 1).

The demographic and clinical characteristics of the 67 included patients were recorded, including age, sex, fever, shock, white blood cell count, urinary pH, indwelling urinary catheter status, constipation, nursing home residence, history of diabetes, history of uremia, results of urine and blood cultures, and survival. Age, gender, urinary pH, and rates of comorbidities (diabetes and ure-

mia), fever, shock, and death were compared in the GPB, GNB, and MGPNB groups. Ethical approval was not required because this article was based on a review of the literature in the PubMed database.

Results

Culture of urine from the 67 patients yielded 24 positive for GPB (*Enterococcus faecalis*, *Streptococcus agalactiae*, *Staphylococcus aureus*, and *Corynebacterium* spp.) and 75 positive for GNB, including *Escherichia coli*, *Proteus* spp., *Morganella morganii*, *Klebsiella* spp., *Providencia* species, *Pseudomonas aeruginosa*, and *Citrobacter* spp. Bacterial species did not strongly correlate with urinary pH in patients with PUBS. Mean urinary pH was highest in urine positive for *Proteus* spp. (8.45 ± 0.5) and lowest in patients positive for *P. aeruginosa* (7.56 ± 1.15) (Table 1). The 6 most frequently observed bacterial species in these patients with PUBS were *E. coli*, *E. faecalis*, *Klebsiella* spp., *P. aeruginosa*, *M. morganii*, and *Proteus* spp.

GNB were more prevalent in women than in men. Presentation of fever in PUBS accounted for 66.7, 11.1, and 5.3%, $p < 0.05$, in GPB, GNB, and MGPNB, respectively. The mortality rate was higher in the MGPNB (10.5%) than in the GPB (0%) and GNB (4.4%) groups (Table 2).

Urinary pH of PUBS, with urine culture revealing *P. aeruginosa*, was more acidic with statistical significance. Correlation analysis showed that age, gender, comorbidities, fever, shock, and infection with *E. coli*, *E. faecalis*, *Klebsiella* spp., and *M. morganii* did not correlate strongly with urinary pH. Regression analyses showed that *P.*

Table 1. Bacteria present in 99 urine cultures of 67 patients with PUBS

	Pathogen	N	% in the 99 urine cultures	Urine pH
Gram positive, G (+)	<i>Enterococcus faecalis</i>	13	13.1	8.27±0.73
G (+)	<i>Enterococcus</i> spp.	4	4.0	7.75±1.06
G (+)	<i>Streptococcus agalactiae</i>	3	3.0	7.50±0.50
G (+)	<i>Staphylococcus aureus</i>	2	2.0	7.50±1.32
G (+)	<i>Corynebacterium</i> spp.	2	2.0	6.75±0.35
Gram negative, G (-)	<i>Escherichia coli</i>	25	25.3	8.08±0.92
G (-)	<i>Klebsiella pneumoniae</i>	14	14.1	7.96±0.54
G (-)	<i>Proteus mirabilis</i>	10	10.1	8.45±0.5
G (-)	<i>Pseudomonas aeruginosa</i>	8	8.1	7.56±1.15
G (-)	<i>Morganella morganii</i>	7	7.1	8.0±1.08
G (-)	<i>Providencia</i> species	7	7.1	8.5±0.75
G (-)	<i>Citrobacter</i> spp.	4	4.1	8.1±0.75

Urine pH is presented as mean ± SD. PUBS, purple urine bag syndrome; SD, standard deviation.

Table 2. General data of 67 PUBS cases in age, gender, urine pH, comorbidity with diabetes mellitus, uremia, presence of fever, shock, and mortality

	Gram (+) (n = 3)	Gram (-) (n = 45)	Mixed G (+) and G (-) (n = 19)	Total (n = 67)
Age, years	69.7±22.2	76.1±11.3	75.9±13.5	75.7±12.5
Gender (M/F)	2/1	17/28	10/9	29/38
Urine pH	8.17±1.04	8.09±0.87	7.95±0.91	8.06±0.91
Diabetes mellitus, n (%)	0	11 (24.4)	2 (10.5)	13 (19.4)
Uremia, n (%)	0	11 (24.4)	3 (15.8)	14 (20.9)
Fever, n (%)	2 (66.7)	5 (11.1)	1 (5.3)	8 (11.9)
Shock, n (%)	1 (33.3)	2 (4.4)	2 (10.5)	5 (7.5)
Mortality, n (%)	0	2 (4.4)	2 (10.5)	4 (3.2)

Data are presented as mean ± SD for numerical variable and count (%) for categorical variables. PUBS, purple urine bag syndrome.

aeruginosa made urine less alkaline (regression coefficient, -0.936, $p < 0.05$), whereas *Proteus* spp. made urine more alkaline (regression coefficient, 0.489, $p < 0.05$; Table 3).

Discussion

PUBS was thought to be associated with catheter-associated urinary tract infections (CAUTIs) and alkaline urine [2, 4]. About 6.9% of patients with PUBS presented with acidic urine [3]. Interestingly, we found that *Proteus* spp. was strongly correlated with alkaline urine, whereas *Pseudomonas* spp. was significantly associated

with less alkaline urine. *P. aeruginosa* facilitates the acidification of the local microenvironment. In mice, this acidic environment in the host inflammatory response to *P. aeruginosa* infection is likely related to an increase in IL-1 β [5], resulting in less alkaline urine in patients with PUBS.

About 7% of patients with PUBS in our study were negative for urine culture results. This inability to culture bacteria may have been due to concurrent antimicrobial treatment, a partial course of treatment, the status of the indwelling catheter, and malignancy, all of which are independent risk factors for bacteremia that cannot be cultured from urine [6]. The ratio of GPB:GNB cultured from patients with PUBS was about 1:3.125.

Table 3. Multivariate regression model of the relationship of factors with urinary pH in patients with PUBS

	Coefficient	95% CI	p value
Age	0.003	−0.016 to 0.024	0.740
Gender (M/F)	−0.299	−0.8 to 0.203	0.240
DM	−0.222	−0.941 to 0.497	0.550
Uremia	0.016	−0.643 to 0.679	0.960
Fever	−0.304	−1.065 to 0.456	0.430
Septic shock	0.641	−0.314 to 1.596	0.190
<i>Escherichia coli</i>	−0.338	−0.87 to 0.195	0.210
<i>Enterococcus faecalis</i>	0.157	−0.446 to 0.76	0.610
<i>Klebsiella pneumoniae</i>	−0.179	−0.799 to 0.442	0.570
<i>Pseudomonas aeruginosa</i>	−0.936	−1.764 to −0.108	0.030*
<i>Morganella morganii</i>	−0.522	−1.333 to 0.289	0.210
<i>Proteus mirabilis</i>	0.489	0.149 to 1.127	0.040*

PUBS, purple urine bag syndrome; CI, confidence interval; M, male; F, female. * $p < 0.05$.

Most patients with CAUTI are asymptomatic and do not have associated fever [7]. Of elderly patients with PUBS, 8.2% presented with fever, less than the general population with PUBS [1]. In our study, only 11.9% (8 of 67) patients with PUBS presented with fever. Fever was more frequent in patients with urinary cultures positive for GPB than those positive for GNB and MGPNB.

The most common GPB in these patients with PUBS were *E. faecalis*, whereas the most common GNB in these patients were *E. coli*. These results are compatible with the results in double-J carriers, in which *E. coli* and *Enterococcus* were the most common microorganisms [8]. Many infants with enterococcal UTIs had underlying structural abnormalities such as hydronephrosis or vesicoureteral reflux [9].

E. coli has been reported to be the most common pathogen isolated in patients with CAUTIs, with rates ranging from 52.3 to 66.9% [10–12]. *E. coli* and *Klebsiella pneumoniae* were the most identified microorganisms in elderly patients with UTI [13, 14].

M. morganii is a member of the subfamily Proteaeae in the Enterobacteriaceae family. This organism is considered as an unusual opportunistic pathogen that causes postoperative wounds and UTIs. *M. morganii* has been reported to cause sepsis, abscesses, PUBS, chorioamnionitis, and cellulitis. *M. morganii* is not considered an overlooked opportunistic pathogen because of its increased degrees of resistance and virulence [15].

Proteus mirabilis is frequently involved in patients with CAUTIs caused by >1 microorganism. *P. mirabilis* is often accompanied by urolithiasis, the development of bladder

or kidney calculi due to the alkalization of urine from urease-catalyzed urea hydrolysis [16]. Urine cultures from patients with PUBS positive for *P. mirabilis* had higher pH than urine cultures positive for other microorganisms.

PUBS is often asymptomatic, benign, and harmless because CAUTI is associated with a low complication rate, and only 6% of patients with CAUTI have blood cultures positive for the same organism within 2 days [4, 17, 18]. The mortality rate in elderly patients with UTI has been reported to range from 5 to 9.3% [11, 14]. Medical advances have reduced the mortality rate in patients with PUBS, from 6.8% in 1980–2016 to 4.3% in 2011–2016 [3]. Of our 67 patients with PUBS, 4 (3.2%) died, a rate comparable to the 2–4% in patients with CAUTI-related bacteremia, 3 times higher as in patients with nonbacteriuric CAUTI [19].

Although PUBS has previously been considered a benign process in most patients with indwelling catheters, early examination and antibiotic administration are probably required if there are obvious symptoms of UTI, especially in patients infected with both GPB and GNB [3]. Although PUBS was thought to be a CAUTI with alkaline urine, 6.9% of patients with PUBS present with acidic urine. This condition may be prevented by avoiding unnecessary catheterization, by decreasing the duration of catheterization, and by improving catheter care [20]. In asymptomatic PUBS, there is no need of aggressive antibiotic treatment besides hydration [21].

Limitations

Although this is a novel study analyzing bacteriology and urinary pH in patients with PUBS, there are several limitations. First, the data were from a PubMed search, which may have resulted in an underestimation of the number of patients worldwide. Second, the number of patients enrolled in this study was relatively small, with only 3 patients having urine cultures positive for GPB. This may have led to bias or confounding in statistical analysis. Third, the data were assessed retrospectively and confined to the normal distribution.

Conclusion

In PUBS, the urine pH and symptom presentation are bacteria based. GNB are predominant pathogens in patients with PUBS. Fever was associated with GPB infection with *Proteus* spp. being strongly correlated with alkaline urine and *Pseudomonas* spp. with less alkaline urine. The most common GPB in patients with PUBS were *E. faecalis*, and the most common GNB were *E. coli*.

The mortality rate in patients with PUBS was 3.2%. Although PUBS has been considered a benign process in most patients with indwelling catheters, early examination and antibiotic treatment are required if there are symptoms of UTI.

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Statement of Ethics

This study was based on PubMed search, with all included articles having received ethical approval prior to publication. Informed consent was not required because this study was a review of previously published studies.

Conflict of Interest Statement

None of the authors has any conflicts of interest to declare.

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Author Contributions

Dr. Su Y.J. wrote the draft, revised, designed, and corresponded this project. Dr. Yang H.W. collected data. Dr. Chang C.W. proceeded data static analysis. Yang H.W. and Chang C.W. discussed together with Su Y.J.

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