Purple urine bag syndrome- a rare clinical entity in chronic urinary catheterization: a case series and literature review

Abstract
Purple urine-bag syndrome (PUBS) is a rare phenomenon in which the urine bags turn purple following prolonged urinary catheterization in chronic debilitated states. We present a case series and review of literature of this rare phenomenon.

Objectives: To identify the potential causative factors and outcomes for PUBS in chronic catheterized patients.

Patients and Methods: An observational case series study of patients with PUBS was conducted from January 2011 to June 2013. The demographic data, co-morbidities, indications, duration of chronic catheterization, Debility score (Bartel index), types, material and color of urinary catheters were assessed. Blood chemistries, urine analysis, urine cultures and required imaging were done in all the affected patients. Outcomes of treatment and follow-up of minimum 1 year was done in all patients.

Results: Total of 14 patients of PUBS with chronic urinary catheterization were enrolled in the study with mean (SD) age of 52.8 (14.3) years. All the cases had catheter associated urinary tract infection, alkaline urine and seven different bacterial species isolated in urine culture. Constipation was noted in 9 (64.3%) patients. Other features noted were encrusted retained catheter, vesical calculus, neurogenic bladder, stricture urethra and renal failure. After treatment, purple discoloration of urine subsided in 12 patients. Two patients had persistent PUBS.

Conclusion: PUBS is a rare entity where the causative factors were constipation, chronic catheterization, urinary tract infection, alkaline urine and chronic debilitated patients in our study cohort. Surgical correction of the underlying disease and treatment of symptomatic UTI can reduce the likelihood of this problem.

Keywords: neurogenic bladder, purple urine bag syndrome, tryptophan, urinary catheter, urinary tract infection

Abbreviations: CISC, clean intermittent self-catheterization; PUBS, purple urine bag syndrome; PVC, poly vinyl chloride; UTI, urinary tract infection

Introduction
Purple urine bag syndrome (PUBS) is a rare visually striking entity discovered by Golding in 1857, where urine bags and tubings turn purple. The purple discoloration is due to tryptophan from food which is metabolized into indole by bacteria colonizing the large bowel. The indole is absorbed into the portal circulation and detoxification in liver results in indoxyl sulphate as a by-product. In urine, indoxyl sulphate is converted by enzymes produced by bacteria resulting in indigo (blue), indirubin (red) pigment and mixture of both (purple) staining the urine in the presence of an alkaline environment and bacteria which precipitate and react to the synthetic components of the urine bag. This condition is seen in women, chronic debilitated patients with chronic catheterization and urinary tract infection. We present a case series of PUBS to identify risk factors and outcomes in chronic catheterized patients.

Objectives
To identify the potential risk factors and outcomes for Purple urine bag syndrome in chronic urinary catheterized patients.

Materials and methods
An observational case series study of 14 patients with purple urine bag syndrome was conducted from January 2011 to June 2013 in the department of urology after informal consent and institute ethical committee approval. We recorded the demographic data, co-morbidities (like coronary heart disease, Cerebro-vascular accidents, chronic kidney disease, Diabetes mellitus type 2 and hypertension), indications and duration of chronic catheterization, consciousness and functional assessment done by Bartel index, types, material and color of urine catheters, bowel habits, usage of laxatives and enema dependence. Blood chemistries (urea, creatinine, sodium, potassium and chloride), urine analysis and urine cultures were done in all the affected patients. Imaging of the abdomen with Ultrasonography, computerized tomography and retrograde urethrogram was done when indicated in our patients. Treatment outcomes were analyzed...
in our patients with a minimum follow-up period of 1 year. Data was analyzed with values reported in mean and standard deviation with category in numbers and percentage.

**Results**

Among the 14 patients with long term urinary catheterization who had PUBS, 9 were males and 5 were females with a mean age of 52.8±14.3 years. It was interesting to note that in most of our patients, the purple pigments adhered to the urine bags and colored it, with urine being clear (Figure 1). The demographic data of the affected patients with PUBS varied accordingly (Table 1). The Barthel’s score in PUBS-affected patients was less than 20 in 5 (35.7%) and more than 20 in 9 (64.3%) patients respectively. In PUBS affected patients, constipation was noted in 9 (64.3%) with enema dependence in 7 (50%) patients respectively. Blood chemistries were normal in all patients except in 2 patients who had chronic kidney disease. Urine analysis in the PUBS patients showed alkaline urine (6.7±0.67), bacteriuria (35.7%) and pyuria noted in all patients. Seven bacterial species (*Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus vulgaris*, *Klebsiella pneumoniae*, *Providencia rettgeri*, *Morganella morganii* and *staphylococcus saprophyticus*) and fungal species (*Candida albicans*) were isolated from the urine samples of our PUBS-affected patients.

| Table 1 Demographic data of patients with PUBS |
|-----------------------------------------------|
| Demographics | PUBS (n-14) | Percentage |
| Age (years) | 52.8±14.3 |  
| Catheterization Duration (mn) | 11.5±8.3 | 64.30% |
| Male | 9 | 35.70% |
| Female | 5 | 64.30% |
| Barthel Index Score | |  
| <20 | 5 | 35.70% |
| ≥20 | 9 | 64.30% |
| Indication for Catheterization | |  
| Anterior Urethral Stricture | 3 | 21.50% |
| Posterior Urethral Stenosis | 5 | 35.70% |
| Neurogenic Bladder | 6 | 42.80% |
| Type of Catheter | |  
| Periurethral | 5 | 35.70% |
| Suprapubic | 9 | 64.30% |
| Material of catheter | |  
| Silicone | 4 | 28.50% |
| Latex | 10 | 71.50% |
| Urolithiasis | 4 | 28.50% |
| Constipation | 9 | 64.30% |
| Enema Dependent | 7 | 50.00% |
| Chronic Kidney Disease | 2 | 14.30% |
| Hypertension | 7 | 50.00% |
| Diabetes Mellitus | 5 | 35.70% |
| Cerebro-Vascular Accident | 6 | 42.80% |
| Coronary Artery Disease | 3 | 21.50% |

**Note:** Values are in mean ± standard deviation and category numbers with percentage. mn- months.
Table 2 Outcomes of Treatment in patients with PUBS

| Indication                      | Intervention          | Catheter support | Urine culture at 1 year | PUBS recurrence |
|---------------------------------|-----------------------|------------------|-------------------------|-----------------|
| Anterior Urethral Stricture (n=3) |                       |                  |                         |                 |
| Patient 1                       | Substitution Urethroplasty | Yes (6 months)  | Normal                  | No              |
| Patient 2                       | Perineal Urethroplasty  | Yes (3 months)   | Normal                  | No              |
| Patients 3                      | Perineal Urethroplasty  | Yes (3 months)   | Normal                  | No              |
| Posterior Urethral stenosis (n=5) |                       |                  |                         |                 |
| Patient 4                       | Perineal Urethroplasty  | No               | Normal                  | No              |
| Patient 5                       | Perineal Urethroplasty  | No               | Normal                  | No              |
| Patient 6                       | Perineal Urethroplasty  | No               | Normal                  | No              |
| Patient 7                       | Catheterizable Stoma   | CISC             | Asymptomatic Bacteriuria| No              |
| Patient 8                       | Perineal Urethroplasty  | No               | Normal                  | No              |
| Neurogenic Bladder (n=6)        |                       |                  |                         |                 |
| Patient 9                       | Catheterizable Stoma   | CISC             | Asymptomatic Bacteriuria| No              |
| Patient 10                      | No                    | CISC             | Asymptomatic Bacteriuria| No              |
| Patient 11                      | No                    | CISC failed      | Positive                | Yes             |
| Patient 12                      | Catheterizable Stoma   | CISC             | Asymptomatic Bacteriuria| No              |
| Patient 13                      | No                    | CISC failed      | Positive                | Yes             |
| Patient 14                      | No                    | CISC             | Asymptomatic Bacteriuria| No              |

Figure 1 Others include formic acid poisoning, acute diarrhoeal diseases, Rhabdomyolysis, drugs, acute pyelonephritis, cardiac failure, rapidly progressive glomerulonephritis, acute interstitial nephritis, malaria, transfusion reaction, myocarditis etc.

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Discussion

PUBS has been shown to be associated with many other factors such as elderly debilitated patients, predominantly females, constipation, chronic catheterization, urinary tract infection and type of catheters.2,3,5,6 In our study, we have identified that patients who had chronic urinary catheterization with urinary tract infection were predominantly with most of the affected being males. Apart from the above factors, when diet rich in tryptophan is consumed there is an increase prevalence of PUBS in this population. The pathogenesis being that tryptophan is converted into indole by the intestinal bacteria resulting in increased absorption into the portal circulation and converted to indican by the liver. The indican is excreted into the urine to form indirubin and indigo in an alkaline urine pH with bacteriuria.7 The predominant tryptophan rich diet pattern in our study population was noted in only a few patients. Constipation has been considered as one of the most common symptom in PUBS affected individuals. Since there is decreased gut motility and prolonged transit time, there is more tryptophan being metabolized to indole and increased absorption as reported by Su et al.1 In our study, we observed that PUBS-affected patients had constipation (64%) and 50% of the patients were enema dependent. Recurrent Urinary tract infection (UTI), bacteriuria and multiple bacteria isolated and reported in the culture are the main factors associated in PUBS. The most common isolated bacteria associated with PUBS were Escherichia coli, Proteus species, Klebsiella pneumoniae, Pseudomonas aeruginosa, Enterobacter species, Enterococcus species, Faecal streptococci, Morganella morgani, Citrobacter species and Providencia species.

Most of these bacteria produce sulphatase and urease which in alkaline urine can convert urinary indoxyl sulphate into indoxyl in the purple discoloration.7,9 Seven different species of bacteria and fungus were isolated from the cultures in our study. All the subjects had pyuria and alkaline urine and only 35% having bacteriuria which would explain the causal relationship of UTI and PUBS. However, the presence of these bacteria in the urine with alkaline pH may not always be associated with PUBS as reported in literature.7 Most PUBS-affected patients were old and immobile who are more prone to reduced gut motility, chronic urinary catheterization and UTI.10,11

We have categorized our subjects based on the Bartel’s scoring index as measure for disability and daily activities, where 35% had a score less than 20.12,13 The scoring index would give the objective assessment of subject’s performance, degree of independence from any help, physical or verbal and the need for supervision over the preceding longer duration of disability. All the subjects in our study, had purple discoloration adhered to the tubes and urinary bags only. There have been many reports regarding the purple discoloration of the tubes and urine bags such as contaminants and indinubin leading to oxidation of the pigments in urine.8,14 Another most frequent association with occurrence of PUBS is with polyvinylchloride (PVC) containing urine bags as compared to non-PVC urine bags.8

Treatment of PUBS is directed towards control of UTI and the correction of underlying urological disease. According to the literature, most of the patients who presented with PUBS were, largely, asymptomatic.8 PUBS is not a disease, nor does it represent any grave prognosis to the patient. Lin et al.,7 advocated that it is unnecessary to treat PUBS-affected patient’s aggressively. In order to prevent the discoloration of urine-bag and catheters, they need to be changed more regularly in catheterized patients or intermittent catheterization should be considered. Correction of the underlying disease and treatment of symptomatic UTI can reduce the likelihood of this problem. All the patients in our study presented with PUBS had underlying urological disease which was surgically treated and managed with appropriate medications. However, two patients had recurrence of PUBS due poor compliance. From our clinical experience, administration of appropriate antibiotics based on the sensitivity of the urine culture in symptomatic subjects would be appropriate. Treatment with oral ciprofloxacin can be considered empirically, due to the typically high resistance rate to first-line antibiotics. Prophylactic antibiotics to prevent UTI should not be recommended to treat these patients with PUBS.

Conclusion

PUBS are a rare clinical entity with the causative factors including constipation, chronic catheterization, urinary tract infection, alkaline urine and chronic debilitated patients in our study cohort. Surgical correction of the underlying disease and treatment of symptomatic UTI can reduce the likelihood of this problem. Prevention of the discoloration of urine-bag and catheters can be done by regular change of catheters or intermittent catheterization should be considered. Asymptomatic PUBS is unnecessary to be treated by antibiotics.

Acknowledgements

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Conflict of interest

Author declares that there is no conflict of interest.

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