

## Emphysematous Cystitis – A rare clinical entity & its outcome from conservative management.

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**Abstract:** *Background*-Emphysematous cystitis is one of the uncommon disease which characterized by the presence of gas in the bladder wall and or lumen. The gas found in the bladder consists of nitrogen, hydrogen, oxygen, and carbon dioxide but exact mechanisms for underlying gas formation are not clear. It is one of the rare form of complicated urinary tract infection. The primary risk factors are diabetes mellitus, urinary tract obstruction, neurogenic bladder, and female sex. It can be considered in cases of urinary tract infections especially in diabetic patients with unusual presentations. Its clinical manifestations usually ranging from asymptomatic to severe sepsis. Imaging studies like conventional plain abdominal radiography and computed tomography are necessary to detect it. Urine routine microscopy with culture and sensitivity gives clue of severity of infections. Cystoscopy is done to know pattern and changes in mucosa of urinary bladder in Emphysematous cystitis **Objective**-Our study aims to create awareness and evaluation of outcome from conservative management of a rare clinical entity emphysematous cystitis which is one of the unique complication of urinary tract infection. **Method**- In this study patients of persistent and unresolved urinary tract infections were admitted and evaluated ,and among them emphysematous cystitis was diagnosed by a computed tomography scan. They were retrospectively reviewed for their age , sex, comorbidities, clinical features , microorganisms identified on urine culture and sensitivity, presenting white blood cell count, treatment, and outcomes from conservative management. **Results**- Escherichia coli and Klebsiella pneumoniae are usual microorganisms detected from urine cultures. Management of emphysematous cystitis depends on the severity of the disease. Conservative treatment successful in most cases which consists of combination of antibiotics, bladder drainage and diabetic control. Patients who does not respond to medical management or those with severe necrotizing infections may require surgical treatment. Early treatment intervention can achieve a favourable prognosis.

**Key words**:- Emphysematous cystitis, Diabetes mellitus, UTI, CT scan, Antibiotics

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### I. Introduction

Emphysematous cystitis (EC) is a rare but severe clinical problem. It was first discovered on autopsy in the late 1800s by Eisenlohr<sup>[1]</sup> which was later defined as “cystitis emphysematosa” by Bailey in 1961. It is the presence of air within the bladder wall and/or the bladder lumen. The gas found in the bladder consists of nitrogen, hydrogen, oxygen, and carbon dioxide but exact mechanisms of underlying gas formation are not clear. Air within the urinary tract can be found due to instrumentation, fistula to a hollow viscus , tissue infarction with necrosis, or infection by gas-forming organisms<sup>[2]</sup>. The common risk factors associated with emphysematous cystitis are diabetes mellitus , urinary tract obstruction, neurogenic bladder, and female sex. Elevated tissue glucose levels in diabetic patients may provide a more favourable microenvironment for gas-forming microbes. In diabetic patients an elevated tissue and urinary glucose level is a source for gas forming bacteria which is contributed by associated impaired renal perfusion, diabetic nephropathy, bladder neuropathy, and impaired leukocyte function. In non-diabetic patients higher levels of urinary albumin, lactose, or tissue proteins can cause formation of hydrogen and carbon dioxide gas. Escherichia coli and Klebsiella pneumoniae are often isolated from urine cultures. Due to its life-threatening nature, it requires prompt evaluation and management. Presenting complains of this rare entity are fever, dysuria, irritative voiding symptoms like frequency , urgency with abdominal discomfort and pneumaturia. As there is no typical clinical signs, diagnosis can be made by imaging studies . This disease having non-specific clinical symptoms which has little or no

diagnostic clues for emphysematous cystitis. It usually diagnosed radiologically by conventional radiography as increased radiolucency in the bladder wall. Recently, uprise in reported cases occurs due to a wider use of radiological imaging. Early diagnosis and treatment is necessary to prevent progression to its complications. The severity of the disease determines the surgical treatment method, i.e., surgical debridement, partial cystectomy, total cystectomy or even nephrectomy in combined EC/EP cases. Differential diagnosis of emphysematous cystitis are vaginal fistula, colovesical fistula mainly due to diverticular disease, Crohn's disease, carcinoma of the colon or bladder, instrumentation and after trauma. All these may have unresolved urinary tract infection and requires radiological imaging for diagnosis. In this study all patients of unresolved UTI retrospectively analysed to get its clinical information, treatment and outcomes of treatment.

## **II. Materials and Methods**

We retrospectively studied cases of EC admitted to our department during the period 2017-2019. Total 6 cases were analysed. Patients of urinary tract infections which were not cured completely by conventional primary antimicrobials therapy admitted for evaluation. All patients were diabetic. They having complain of intermittent attack of dysuria, hematuria, abdominal pain, urinary urgency and frequency. They have doubts regarding complain of pneumaturia. All patients started empirical treatment for urinary tract infections including adequate hydration and antibiotics according to urine culture and sensitivity. Routine haemogram and urine tests were done. Laboratory testing revealed the raised serum white blood count, blood urea, serum creatinine, blood glucose, HbA1C. Urine routine microscopy with culture and sensitivity gives clue of severity of infections. So in this study the urine analysis showed red blood cells, significant pus cells and bacteria. Initial imaging studies included abdominal radiography which revealed suspicion of gas in the bladder. For confirmation Computed tomography of the abdomen and pelvis was done which showed diffuse bladder dilation with urine and gas. It also revealed gas within the bladder wall. Diagnostic cystoscopy was done to know the mucosal pattern of urinary bladder which was altered by presence of gas in its lumen and wall. It also diagnosed and exclude bladder outlet obstruction. All cases were reviewed for patient age and sex, comorbidities, clinical features, microorganisms identified on urine culture, presenting white blood cell count, treatment, and outcomes. Diabetic control was done by guidance of endocrinologist with insulin therapy. All patient's clinical conditions improved. They became asymptomatic and then per urethral catheter was removed. A repeat urine culture and sensitivity become sterile. Laboratory parameters becomes normal. They were discharged on oral antimicrobials. At follow-up after discharge, the patient's urine analysis and culture were with in normal range. Repeat Ultrasonography of abdomen and pelvis showed resolve of bladder wall thickening and no intraluminal gas.

## **III. Results**

We reviewed 6 cases of Emphysematous cystitis admitted to our department. The mean age of the patients at presentation was 72yr years. Most cases were females (5:1). All patients had type-1 DM with uncontrolled blood sugar. Four female patient had also urethral stenosis. Blood sugar of diabetic patients were controlled by consultation of endocrinologists with injection insulin. Patients with urethral stenosis were managed by Urethral dilatation and 16F PUC placement. Laboratory testing showed abnormal leukocyte count and renal functional parameters [Table 1]. Total white blood cells with its neutrophil differentiation raised. Blood urea and serum creatinine values are above the normal range which is showed in table 1. Other blood markers of bacterial infections like erythrocyte sedimentation rate, C-reactive proteins and other acute phase proteins are above the normal range. All cases were discovered during routine USG imaging of lower urinary tract for UTI which was not cured with a full course of Oral antibiotics as per Urine C/S report. Confirm diagnosis was done by using NCCT KUB following suspicious features in Ultrasonography as shown in figure 1 & 2. NCCT confirmed the presence of intraluminal gas, diffuse thickening of the bladder wall and gas in the bladder lumen. The organism isolated from urinary culture was Escherichia coli in 4 cases followed by Klebsiella pneumonia in 2 cases. All patients had leukocytosis with raised Neutrophils and raised Urinary Pus cell. Renal function test was also deranged (Table 1). Diagnostic cystoscopy was done to know any urethral and bladder pathology. Mucosal blebs and multiple thin walled vesicles which looks like bunch of grapes noted and mild to moderate degree of trabeculation and multiples small diverticulae seen.



Figure1

Figure2

**Figure1 & Figure 2** showing EC in NCCT KUB Axial & coronal view respectively

**Table 1 showing demographics & Patient characteristics**

	Age (yrs)	Sex	TLC	B Ur/ S cr	Comorbidity	Microorganism in urine c/s	Radiological imaging	Treatment	Antibiotics	Hospital stay day
Patient 1	61	F	12000	124/3.1	DM BOO	E Coli	USG NCCT KUB	Conservative	Meropenem	10
Patient 2	65	F	11400	67/1.7	DM BOO	E Coli	USG NCCT KUB	Conservative	Meropenem +Polymixin	12
Patient 3	56	F	16000	90/3	DM BOO	Klebsiella	USG NCCT KUB	Conservative	Meropenem	10
Patient 4	78	M	18200	162/5.6	DM	E Coli	USG NCCT KUB	Conservative	Meropenem	16
Patient 5	82	F	16800	68/1.8	DM BOO	Klebsiella	USG NCCT KUB	Conservative	Meropenem+ Teicoplanin	12
Patient 6	90	F	11600	78/1.9	DM	E Coli	USG NCCT KUB	Conservative	Meropenem	10

All patients were treated with medical management, including Injectables antibiotics as per urine C/S report with dose modification when required, bladder drainage with 16 French foley’s catheter, and adequate glycaemic control with urethral dilatation. None of the patients received any form of surgical treatment. One cases of EC was associated with EPN, improved with conservative management. Mean hospital stay 11.7 days. All cases were discharged with profound improvement clinically and radiologically. At follow-up after discharge, the patient’s urine analysis and culture were in normal range. Repeat Ultrasonography of abdomen and pelvis showed resolve of bladder wall thickening and no intraluminal gas. The gas which was present in urinary bladder was reabsorbed after control of the infection. The development of complications like emphysematous ureteritis, nephritis, or adrenalitis which have poor prognosis did not develop in any patients in this study due to early and proper start of treatment.

#### IV. Discussion

EC is an infection of the bladder associated with gas production<sup>[2]</sup>. The gas found in the bladder consists of nitrogen, hydrogen, oxygen, and carbon dioxide but exact mechanisms underlying gas formation are not clear. It is one of the rare form of complicated urinary tract infection. Emphysematous conditions are usually diagnosed radiologically, and in modern era its incidence of reporting increases with greater use of abdomino-pelvic imaging. However, radiological imaging is not performed routinely in patients with classical UTIs, many number of emphysematous infections are underreported. It is mostly found in females and reported female to male ratio is 2:1<sup>[3]</sup>. In this study also mostly females affected. EC, a complicated UTIs can be predisposed by recurrent urinary tract infections, indwelling urethral catheter, neurogenic bladder, immunosuppression, & DM<sup>[4]</sup>. In diabetic patients an elevated tissue and urinary glucose level is a source for gas forming bacteria which is contributed by associated impaired renal perfusion, diabetic nephropathy, bladder neuropathy, and impaired leukocyte function. In non-diabetic patients higher levels of urinary albumin, lactose, or tissue proteins can cause formation of hydrogen and carbon dioxide gas. Urinary tract obstruction, and resulted urinary stasis can also result in this infectious condition. Presenting complains of this rare entity are irritative voiding symptoms, abdominal discomfort and pneumaturia<sup>[3]</sup>. The clinical features of emphysematous cystitis are similar to those of uncomplicated cystitis and patients may have nonspecific complaints or even asymptomatic. Pneumaturia is an infrequent presentation. Therefore, a high index of suspicion is required for diagnosis especially in patients who has risk factors. Clinical presentation does not correlate with the severity of inflammation<sup>[1]</sup> Bailey showed pneumaturia in these cases<sup>[4]</sup>. Many patients are not able to recognize pneumaturia, while some others are not willing to acknowledge the condition. The exact mechanism of

pneumaturia is not clear and very poorly understood. Impaired gas transport which occurs due to pathology of local inflammation & obstructive processes which can increase intracellular pressure while simultaneously decreasing circulation can also aggravate the risk of pneumaturia. So pneumaturia is highly suggestive, but rarely reported by patients in their clinical history. EC is a possibly life-threatening disease because of rapid progression to bladder necrosis, EP, urosepsis, and death. EC should be kept in mind in diabetic patients with abdominal pain<sup>[5]</sup>. Laboratory testing may reveal about the raised serum white blood count, blood urea, serum creatinine, blood glucose, HbA1C. The urine analysis may show red blood cells, significant pus cells and bacteria. Usually patients have an elevated serum level marker of bacterial infection like procalcitonin, acute-phase reactants such as erythrocyte sedimentation rate, C-reactive protein. Measuring procalcitonin may help physicians make the diagnosis earlier, differentiate infectious from sterile causes of severe systemic inflammation, assess the severity of systemic inflammation caused by bacterial infections, and decide whether to start or discontinue antibiotic therapy. To avoid its complications early evaluation and treatment is necessary. EC is mostly diagnosed radiologically. Most accurate examination is the computed tomography scan of the abdomen/pelvis<sup>[6]</sup>. An abdominal X-ray has a very low specificity however found that simple radiograph of the abdomen is diagnostic in only 13%.<sup>[6]</sup> Plain x-ray of the kidney, ureters and bladder (KUB) one of the initial diagnostic modality in all patients which may exclude stones, may show air fluid levels in the bladder or a typical “cobblestone” or “beaded necklace” appearance but presence of bowel gas can create difficulty in interpreting feature. Cystoscopy alone is less sufficient to diagnose EC but it can exclude presence of bladder outlet obstruction and urinary bladder fistula. Histology of urinary bladder showed multiple variably sized gas-filled cavities interspersed in mucosa and muscularis propria. Flattened cells with occasional foreign body type giant cells line these cavities. Cystography can show irregular thickening of the bladder wall, & submucosal blebs of air in the emphysematous cystitis.

The management of EC usually includes of broad spectrum antibiotics, bladder drainage, control of blood glucose level, and treatment of any underlying comorbid disorders<sup>[7]</sup>. The gas is reabsorbed once infection is treated. In severe cases, infection can spread to renal parenchyma causing EPN. Prostatic abscess can also occur which is reported in literature. Some time bladder rupture can occur as a sequel of emphysematous cystitis and in that conditions patients may present with haematuria, anuria, suprapubic pain and fever. Rupture can be either intraperitoneal or extraperitoneal depending on the site of disruption. Intraperitoneal rupture is usually associated with an acute abdomen. Cystography can identify the type and extend of rupture. Intraperitoneal rupture require surgical intervention. In the series of Grupper et al.<sup>[8]</sup> a mortality rate of 9.4% was found. Hyperbaric oxygen therapy is also an effective treatment option for EC<sup>[9]</sup>. Surgical treatment can be needed in severe cases, when conservative treatment failed. EC can be successfully treated with conservative management if diagnosed early. A delay in diagnosis may cause bladder rupture, septicaemia, peritonitis and death. *Escherichia coli* and *Klebsiella pneumoniae* are often isolated from urine cultures<sup>[7]</sup>. Other organisms reported in EC include *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Candida albicans*, and *Candida tropicalis*, *Aspergillus fumigatus*, *Staphylococcus aureus*, Group D *Streptococcus*, *Enterococcus faecalis*, *Enterobacter aerogenes*, and *Clostridium perfringens* and *Cl. welchii*. Both aerobic and anaerobic cultures are necessary for identification of the etiological agents of emphysematous cystitis. Although this disease is rare, but it requires careful attention, especially in diabetic patients<sup>[10]</sup>. In this study prognosis was favourable after treatment with antibiotic therapy, antidiabetic treatment and bladder drainage by indwelling catheter<sup>[11]</sup>. Surgical interventions were not required in this study but Surgical options depends on the severity of the disease which determines the surgical treatment method, i.e., surgical debridement, partial cystectomy, total cystectomy or even nephrectomy in combined EC/EP cases. The development of complications like emphysematous ureteritis, nephritis, or adrenalitis who have poor prognosis did not develop in any patients in this study due to early and proper start of treatment. Knowledge of this rare entity can help in early diagnosis and appropriate management. This study requires more time to follow up and to know long term complications and sequelae of emphysematous cystitis.

## V. Conclusion

Emphysematous cystitis is an uncommon infectious condition of the bladder caused by gas producing microorganisms. Because of its possible insidious clinical presentation physicians should be aware of this clinical entity, especially in high risk patients. A high degree of suspicion should be required in diabetics and at-risk patients for complicated UTIs that do not respond to standard therapy. Knowledge of this rare entity can help in early diagnosis and appropriate management. Early detection and treatment of EC is important, to avoid the potential morbidity and mortality associated with this infection.

**Abbreviation:-** EC- Emphysematous cystitis, UTI-Urinary tract infection, CT scan-Computerized tomography scan, DM-Diabetes mellitus, PUC-Perurethral catheter, USG-Ultrasonography, Urine c/s-Urine culture and sensitivity, NCCT KUB-Non-contrast computerized tomography kidney ureter bladder, F-Female, M-Male,

TLC-Total leukocyte count, B ur-Blood urea, S cr-Serum creatinine, BOO-Bladder outlet obstruction , EPN-Emphysematous pyelonephritis

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