

## Case Report

# Gross Total Hematuria in Pregnancy with Differing Pathologies: Is This Entity on the Increase?

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## ABSTRACT

Gross haematuria in pregnancy, unlike microscopic, is rare and worrisome. We report four consecutive cases seen within four months. The four patients were aged 22, 36, 39 and 42 years respectively. They were all multigravida except the 22-year old who was a primigravida at 31 weeks gestation. Two others were also in the third trimester of pregnancy while one was 4 weeks post-partum. They all presented with gross total haematuria and following evaluation, one of the patients was found to have urinary tract infection (UTI), while the rest had Renal Cell Carcinoma (RCC), squamous metaplasia of the urinary bladder and postpartum preeclampsia with deranged clotting profile respectively. Though rare, four cases of gross hematuria from different causes were seen within four months. In depth evaluation and multidisciplinary approach to management are pertinent for accurate diagnosis

**Keywords:** Gross hematuria, Pregnancy, Different pathologies.

## INTRODUCTION

Microscopic hematuria [three or more red blood cells (RBCs) per high power field on microscopic evaluation of urinary sediment from two of three properly collected urine specimens] is common in pregnancy and hardly associated with adverse foeto-maternal outcome. Gross (visible) hematuria, on the other hand, is rare and often associated with potentially worrisome diagnosis.<sup>1</sup> The commonest cause is urinary tract infection. Other causes include bladder calculi, trauma, obstruction and tumours, renal parenchymal disease, coagulation disorders, drugs, renal vein

thrombosis and emboli, and endometriosis.<sup>2</sup> Existing literature on gross hematuria have been limited to case reports. Pregnancy specific conditions like preeclampsia, placenta percreta, ruptured uterus, can also cause gross hematuria. When no organic cause is found, after complete evaluation, hematuria is classed Idiopathic. The 'Nutcracker phenomenon'<sup>3</sup> also called left renal vein hypertension, described almost fifty years ago by De Schepper, has been used to explain idiopathic hematuria of pregnancy. This results in development of extensive collateral



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venous drainage system involving the gonadal capsular, suprarenal, lumbar, azygous and peri-ureteral veins. The resulting extensive renal varicosities give rise to hematuria when the thin-walled septum separating the veins from the collecting system ruptures. The main presenting symptom is hematuria, with or without left flank pain.<sup>1,4</sup> Occasionally extensive vesical varices (cystovarix) may be responsible. Most authorities believe idiopathic hematuria is due to peculiar changes in the urinary tract resulting from mechanical and hormonal factors related to pregnancy.<sup>5</sup> Such 'pregnancy-induced' hematuria usually begins in late second trimester through the third trimester and resolves after delivery.<sup>6</sup>

We report four cases of total haematuria in pregnancy, seen within 4 months, all presenting similarly but with differing pathologies, could this entity be on the increase?

## CASE HISTORY

### Case Series

- 1) A booked 39-year old G4P3 at 30 weeks gestation, who presented with a two-day history of total haematuria and right loin pain. No history of fever or pain on micturition. She was wasted, pale with fundal height of 36-week size, which was large for date. She had loin fullness with tenderness. Ultrasound scan revealed huge degenerating fibroid (with normal kidneys) coexisting with pregnancy. A clinical diagnosis of fibroid degeneration and urinary tract infection was made. She was admitted for intravenous fluids and antibiotics. Consultant review showed high suspicion of a renal mass rather than a fibroid because the mass was not continuous with the uterus. A repeat scan was requested to be done by a consultant radiologist and the mass was found to be the right kidney. Further history taking revealed that patient was actually diagnosed with renal cancer two years ago by the urologists but declined nephrectomy, a history she was reluctant to divulge. She eventually brought a contrast CT scan done two years prior to pregnancy that revealed a right renal mass with a non-functioning right kidney. A diagnosis of Renal cancer in pregnancy was made. She was counselled on fetal lung maturation, delivery and possible radical nephrectomy followed by targeted therapy however patient still declined treatment. She was discharged to the antenatal clinic. At 36 week visit, she had lost significant weight and had bilateral massive pedal edema. Investigations were requested but she was eventually lost to follow up at 36 weeks.
- 2) A booked 42-year old grand multipara who presented to the Accident and Emergency with total haematuria with occasional clots for the first time at 33 weeks gestation. She had no other symptoms and no family history of such. Her examination findings were essentially normal. Ultrasound showed some debris in the posterior bladder wall. Urine cytology showed squamous metaplasia. Urine culture was negative. She was placed on 10-day empiric antibiotic regimen but hematuria persisted till term and spontaneously resolved before labour. Because she was middle aged, she was scheduled for cystoscopy and biopsy after the puerperium. No bladder mass was seen at cystoscopy. Biopsy still revealed non keratinizing squamous metaplasia (NKSM). A suspicion of idiopathic hematuria was made but venography was not done. Patient is currently on follow up at the urology clinic
- 3) A booked 22-year old primigravida at 31 weeks gestation presented with frequent painful micturition, occasional total haematuria, fever, right sided loin pain and lower abdominal pain. Temperature was 39°C and she had right renal angle tenderness. A clinical diagnosis of acute hemorrhagic cystitis in pregnancy was made. Urine culture revealed *Escherichia coli* and she clinically improved on cefuroxime antibiotic based on sensitivity.
- 4) An unbooked 36-year old para 4 who had home delivery at term and presented three weeks post-partum with a five-day history of headache, dysuria and occasional total haematuria. At presentation, she was diagnosed with severe postpartum preeclampsia and ultrasound revealed a 0.65cm echogenic foci in the urinary bladder, casting posterior acoustic shadows. A working diagnosis of cystitis with bladder calculi was made. She also had deranged clotting profile with anaemia. She was transfused two units of fresh whole blood, had liberal fluid intake and was managed alongside the urologists. Haematuria stopped after transfusion. Repeat USS after the puerperium revealed a normal study

## DISCUSSION

Gross hematuria in pregnancy, though concerning, remains a rare entity. Data on gross hematuria have been limited to case reports. This rare entity was seen four times in four months between September 2018 to January 2019 necessitating a review of the Obstetrics and labour ward registers in the preceeding year which showed no case of gross hematuria as a presenting complaint. This has generated the question whether this entity is on the increase or simply a mere coincidence.

In this series, a review of the four cases revealed that they all had different underlying pathologies, ranging from renal cell carcinoma in pregnancy, a likely idiopathic hematuria, *Escherichia coli* urinary tract infection and coagulopathy. All pathologies are known causes of hematuria in pregnancy and some have been reported by previous researchers.<sup>1,7,8</sup>

In the first case, the diagnosis was initially missed both clinically and radiologically in which the huge renal mass was mistaken for a degenerating huge fibroid. This is not surprising as having a renal cancer in pregnancy is uncommon hence the low index of suspicion. Another reason the diagnosis was missed was because the patient was reluctant to volunteer the history of her previous diagnosis of renal cancer made two years before pregnancy. Management of renal cell carcinoma in pregnancy is quite challenging due to lack of standard treatment guidelines.<sup>9</sup> Surgery is the mainstay of treatment and adjuvant chemotherapy no longer has a role.<sup>9</sup> The relatively slow doubling time of RCC (300-500 days) and fetal lung maturation are the main factors that determine timing of surgery. The index patient was immediately counseled on surgery because she has already had a two year delay and was already in the third trimester. Patient declined surgery and other treatments despite health care financing is by the National Health Insurance Scheme. She solely believed in divine intervention for her treatment. She would have benefitted from targeted therapies such as mTOR inhibitors (eg everolimus), anti-angiogenic agents (eg bevacizumab), multikinase inhibitors (eg sunitinib) and immunologic agents (eg high dose interleukin-2) following surgery. All these drugs are categories C or D in pregnancy hence the need to give following delivery.<sup>10</sup>

Squamous metaplasia of the bladder is defined as the transformation of the normal urothelium into stratified squamous epithelium and

can either be keratinizing or not.<sup>11</sup> The keratinizing squamous metaplasia is said to be a premalignant condition usually as a result of chronic mucosal irritation from recurrent urinary tract infection, prolonged catheterization, lithiasis et cetera. Urinary tract infection is the most common etiopathogenesis.<sup>12</sup>

On the other hand, non keratinizing squamous metaplasia, also called vaginal metaplasia and mostly found in females, is usually not associated with chronic irritation and has a characteristic lack of cellular atypia.<sup>11</sup> This was the type of metaplasia found in our patient. NKSM is considered to be an anatomic variant, present in 85% of women of reproductive age and 75% of postmenopausal women at the trigone area and caused by hormonal influx. It usually has no clinical significance<sup>12</sup> and is considered a normal histologic finding, unlike its keratinizing counterpart. Non keratinizing squamous metaplasia may cause irritative lower urinary tract symptoms (pseudomembranous trigonitis) but is not known to cause gross hematuria unlike its keratinizing counterpart. This is why a likely idiopathic hematuria was entertained in the patient.

The nutcracker phenomenon, or left renal vein hypertension is a rare vascular abnormality caused by the idiopathic decrease in the angle between the superior mesenteric artery and the aorta with consequent compression of the left renal vein. A high index of suspicion is required as it could co-exist with other conditions. The patient had no family history of hematuria so a familial presentation was ruled out. In the case of our patient, her hematuria resolved spontaneously before delivery which is usually not the case<sup>1</sup>

For the third case, *Escherichia coli*, the commonest cause of UTI in pregnancy was responsible for her hematuria. This is causative organism in up to 90% of UTI in pregnancy. *Escherichia coli* arises from fecal contamination of the periurethral area causing an ascending infection and is a documented cause of gross hematuria.

All cases are alive and well and had no adverse pregnancy outcome except Case 1, who was lost to follow up prior to delivery.

## CONCLUSION

In conclusion, gross total haematuria can signify different pathologies in the pregnant patient.

In this case series, diverse causes such as bacterial urinary tract infection, squamous metaplasia, renal cancer and bladder calculi/coagulopathy accounted for the patients' similar presentation.

In depth evaluation and multidisciplinary (obstetrician, urogynaecologist, urologist, radiologist, neonatologist et cetera) management are pertinent for accurate diagnosis and treatment for the preservation of feto-maternal health.

Gross total hematuria is a rare entity in obstetrics. Four cases (from renal cancer, idiopathic, urinary tract infection, and coagulopathy) were seen within four months in our unit. Could this entity be on the increase?

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