# ACUTE KIDNEY INJURY AND CYSTITIS ASSOCIATED WITH POST PARTURIENT HAEMOGLOBINURIA IN BOVINES: 6 CASES

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**ABSTRACT**

The present study narrates clinical and diagnostic features of nephrotoxicity and consequent cystitis in special reference to ultrasonographic changes in the urinary tract associated with post parturient haemoglobinuria in one cattle and five buffaloes. A record of history, clinical signs, physical examination, results from haematology and serum biochemistry, urine sediment examination and diagnostic imaging findings were recorded. Haemoglobinuria, stranguria and anaemia were the consistent clinical findings. Urine sediment examination revealed presence of haemoglobin crystals was a prime aid to confirm diagnosis. Ultrasonography of kidneys divulged pyelectasia and renomegaly in most of the cases which is a sign of acute kidney insult induced by haemoglobin crystals and resulting anoxia due to haemolysis. Urinary bladder depicted thickened wall owing to cystitis caused by descending infection.

***Key words***: Nephrotoxicity, cystitis, post parturient haemoglobinuria, phosphorus deficiency

## Introduction

Post parturient hemoglobinuria has been reported as a disease of high yielding dairy animals distinguished by intravascular haemolysis, haemoglobinuria and anaemia (Macwillims *et al*., 1982). The risk of manifestation of disease is high around the revamping phase of late pregnancy and early lactation with peak chances in between 3-4 weeks post-partum and around parturition (Jubb *et al*., 1990; Larsen *et al*., 2001; Macwillims *et al*., 1982). The disease occurrence is described in adult cattle during their 3rd to 6th lactation within 30 days of calving (Blood *et al*., 1989). Skeptic cause of severe hypophosphatemia associated hemolytic anaemia is described to be dietary phosphorus deficiency or feeding of cruciferous plants to the animals along with copper deficiency in some cases (Heuer and Bode, 1998). The biochemical pathway that underlines the process initiates with hypophosphatemia leading to decreased red blood cell glycolysis and ATP synthesis which predisposes them to shift in structure and function and an increased fragility and hemolysis with consequent haemoglobinaemia and haemoglobinuria (Singari *et al*., 1991). Haemoglobin readily decays into heterodimers that are considered to be small enough to extravasate and may enter tissues, such as the kidney, that have less antioxidant capacity than blood which stands as a cause of renal toxicosis (Schaer *et al*., 2013). Laboratory examination of urine reveal dark coffee coloured urine and urine is found 100% haemoglobinuric (Akhtar *et al*., 2008). The ultrasonographic findings reveal changes of acute kidney injury like nephromegaly, pyelectasia and increased renal echogenicity (Laura *et al*., 2018). Treatment involves use of Sodium acid phosphate 60 g dissolved in 300 ml 5 per cent dextrose through i.v. route followed by oral administration of the same dose twice daily for 3 days (Pandey and Mishra, 1987) along with ascorbic acid @ 5g/animal (Benerjee,1998).

## Materials and Methods

### Case selection criteria

The present study was conducted at Guru Angad Dev Veterinary and Animal Sciences University between January 2016 to July 2017 with signs of urinary dysfunction like stranguria, presence of coffee coloured urine, anorexia, loss of milk yield and history of recent parturition.

### Laboratory studies

Complete hemograms including haemoglobin (Hb), total leucocytes count (TLC), packed cell volume (PCV) and platelets were performed by ADVIA haematology system. The blood smears were prepared and evaluated for differential leukocytes count (DLC) after staining by Leishman's stain. Serum evaluation was performed on all the animals on admission/ or later *via* VITROS DT-II Chemistry system for the estimation of parameters like blood urea nitrogen (BUN), creatinine, total protein, albumin, calcium, phosphorus and alanine amino transferase. Microscopic urine examination was done using Leishman's staining.

### Special examination

Special examination included the ultrasonography of the upper and lower urinary tracts. A 5.0 - 10.0 MHz sector transducer connected to a real-time, B-mode ultrasound machine (Sono export) and a 5.0 MHz high frequency linear transducer provided diagnostic quality images per-cutaneously and per-rectally, respectively.

## Results and Discussion

Five buffaloes and one cattle were introduced to the large animal clinics with chief complaint of coffee coloured urine and generalized illness after recent parturition mainly between the time elapsing from 22 days to 4 months. Among the six animals, one cattle and two buffaloes were 5-7 years of age. Another two buffaloes were between 7-10 years of age group whilst one was more than 10 years of age. Thus, the parity of all the animals was extending from third to sixth. All the cases were presented during winter season. All the six animals exhibited haemoglobinuria and three manifested severe stranguria. All the animals evinced reduced feed intake while

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one buffalo showed reduced water intake also. Physical examination divulged diarrhoea in cattle while on the contrary buffaloes depicted pipe stem like constipated faeces. There was a marked decline in milk yield in three buffaloes. Pallor of mucus membranes was noted in two buffaloes owing to anemia, while in cattle and three buffaloes it was normal. Pyrexia was noted in cattle only. An increment in heart rate was noted in four buffaloes and cattle. Respiration rate was increased in cattle and one buffalo while the rumen was hypomotile in all the cases. Ancillary diagnostic tests revealed anaemia in all five buffaloes while total leucocytic count was normal in all cases. Absolute neutrophilia was seen in four buffaloes and one cattle while PCV was normal in all cases.

BUN was elevated in five animals while creatinine levels were high in four animals. The blood phosphorus levels were less than normal in all the animals (Table 2).

The urine sediment examination uncloaked presence of waxy casts and hemoglobin crystals (Fig. 1) in the urine of all animals. One buffalo alone showed presence of leukocytes in urine. Two animals unbosomed the presence of urothelial

Table 1: Haematological findings; N=Neutrophils, L=Leukocytes, M=Monocytes, E= Eosinophils

| Clinical Parameter | Hb (g%) (8-15) | TLC (/uL) (4000-12000) | PCV (%) (24-46) | Platelet (100-800) x $10^3$ | N (%) (15-33) | L (%) (45-75) | M (%) (0-8) | E (%) |
|---|---|---|---|---|---|---|---|---|
| Case 1 (Cattle) | 8.2 | 8000 | 32 | 500x$10^3$ | 55 | 51 | 04 | --- |
| Case 2 (Buff) | 5.2 | 8280 | 42 | 427x$10^3$ | 56 | 40 | 04 | ---- |
| Case 3 (Buff) | 7.1 | 7560 | 27.5 | 36x$10^3$ | 66 | 34 | --- | --- |
| Case 4 (Buff) | 5.9 | 9760 | 17.1 | 326x$10^3$ | 80 | 20 | --- | --- |
| Case 5 (Buff) | 5.6 | 8290 | 34 | 205x $10^3$ | 82 | 14 | --- | 4 |
| Case 6 (Buff) | 4.9 | 8670 | 35 | 269x$10^3$ | 32 | 17 | --- | 1 |

Table 2 : Biochemical findings in blood serum analysis

| Clinical Parameter | Phosphorus (mg/dl) (4.3-7.1) | BUN (mg/dl) (8.8-25.9) | Creatinine (mg/dl) (0.6-1.8) |
|---|---|---|---|
| Case 1 (Cattle) | 3.6 | 26 | 2.3 |
| Case 2 (Buff) | 1.8 | 12 | 1.3 |
| Case 3 (Buff) | 3.0 | 40 | 4.2 |
| Case 4 (Buff) | 2.2 | 96 | 14 |
| Case 5 (Buff) | 1.9 | 27 | 0.9 |
| Case 6 (Buff) | 4.1 | 39 | 2.5 |

cells with equal distribution among cattle and buffalo.

Per-rectal examination perceived a sense thickened urinary bladder in three buffaloes and renomegaly in four animals (Fig. 2 and 3). The ultrasonographic findings unveiled and affirmed an overall increase in the size of kidneys with increased echogenecity with evidence of pyelectesia which are indicators of acute kidney injury caused by haemoglobin crystals in all the animals. Three buffaloes depicted an increase in the thickness of urinary bladder wall confirming descending cystitis. Based on clinical and diagnostic examination the cases were diagnosed to be suffering from post-parturient haemoglobinuria. The treatment was initiated with sodium acid phosphate (SODAPHOS, ZYDUS AH) 60 g dissolved in 300 ml 5 per cent dextrose through intravenous route followed by oral administration of the same dose twice daily for 3 days along with ascorbic acid (REDOXON) @ 5 g/animal. Following treatment two buffaloes died whereas other animals survived.

The incidence of post parturient hemoglobinuria in the total cattle population has been described to be very low (Madson and Nielson, 1939) which was evident in the present study where only one cattle was seen to be afflicted and a major chunk was shared by buffaloes. The disease encompasses adult dairy animals during third to sixth lactation (Blood *et al.,* 1989), which corroborated with high incidence of diseases in animals more than 5 years of age. All the cases were presented during winter months. The results were in accordance with the previous studies *viz.* Soren *et al*. (2014) and Akhtar *et al*. (2006) who reported higher incidence of nutritional hemoglobinuria in winter (87.50%) as compare to summer (12.50%). Buffaloes suffer from mineral imbalance at peak levels of production due to stress which is further intensified by pregnancy and late stage of gestation and finally coincides with ingestion of cruciferous plants in winter season resulting in development of disease (Heuer and Bode, 1998). Present study showed alignment of disease towards post parturient phase in comparison to advance pregnancy, similar observations were made by previous workers, who suggested that disease mostly occurs in post-partum period (Dalir Naghadeh *et al*., 2006). Clinical signs like hemoglobinuria and stranguria were the indicators of urinary dysfunctioning and other signs like straining/ constipation and pale mucous membranes were also evident. The clinical signs evinced in

Fig.1: Haemoglobin crystals in urine sediment of a buffalo

Fig.2: Pyelectasia in kidney of a buffalo

Fig.3: Thickened urinary bladder wall in a buffalo

the present study were in agreement with Bhikane and Kawitkar (2004) and Radostits *et al*. (2007). Khan and Akhtar (2007) reported that color of urine in PPH affected buffaloes varied from red (28%), dark red (20%) to coffee colored (52%) depending upon the severity and duration of illness. Pallor of mucus membranes progress with anaemia, tachycardia, rapid and shallow breathing, depression, decreased milk production (Nagpal *et al*., 1968), faeces may be constipated with foetid, firm, black and dry consistency (Raz *et al*., 1988), may be diarrheic (Heuer and Bode, 1998), normal in consistency along with frequent urination has been described. There may be inappetence or normal appetite, which progressively decreases (Akhtar *et al*., 2006). There may be significant rise in the rectal temperature (Cheema *et al*., 1980) in some cases as was seen in one case. The acute and chronic nephrotoxicity of heme proteins and heme is well recognized (Nath and Murali, 2009). Heme proteins can cause acute kidney injury through 3 main mechanisms: decreased renal perfusion, direct cytotoxicity, and intratubular casts formed from the interaction of heme proteins with Tamm-Horsfall protein. Cytotoxic effects of large amounts of heme result from its lipophilic, oxidant, proinflammatory, and apoptotic effects. This can also be cited as a reason for renomegaly and concurrent cystitis in the present study. Microscopic examination of urine of PPH affected buffaloes shows few epithelial cells (Jubb *et al*., 1990). These urinary disturbances in PPH affected buffaloes can be attributed to damage to kidneys resulting from anaemic hypoxia due to extensive hemolysis (Digraskar *et al*., 1991). PPH affected buffaloes are showed to have lower erythrocyte count, haemoglobin, haematocrit and higher erythrocyte sedimentation rate similar to Durrani *et al*. (2014), which can be attributed to intravascular haemolysis (Mahmood *et al*., 2013).The ultrasonographic findings were in accordance as explained by Laura *et al*. (2018) depicting changes of acute kidney injury like nephromegaly, pyelectasia and increased renal echogenicity (Laura *et al*., 2018). Therapeutic efficacy of sodium acid phosphate and ascorbic acid in haemoglobinuric buffaloes has been previously recorded by Chakarbarti (1994) and Bhikane and Kawitkar (2000) and four cases revived with the same treatment in the present study.

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