

## Wasp Bite in a Referral Hospital in Nepal

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### ABSTRACT

**Background:** Wasp bite is an important occupational hazard in Nepal. Almost 25% of the victims die. This study aimed to identify the demographics, clinical presentation, hospital course and outcome of wasp bite victims in a referral hospital in Nepal.

**Methods:** A retrospective study was conducted in Tribhuvan University Teaching Hospital, Kathmandu. Medical records of patients admitted for wasp bite between January 2008 and December 2012 were reviewed. Demographic, clinical and laboratory data were collected and their effects on outcomes in the form of death, duration of hospitalization, number of dialysis sessions and time to resolution of oliguria were analyzed.

**Results:** All 18 patients came from rural areas, 13 (72%) were farmers, mean age was  $39.6 \pm 16.7$  years (range 7 to 69). Most bites occurred between August and November. Oliguria, vomiting, red urine and jaundice were the main presenting symptoms; oliguria developed within 48 hours of bite in 17 (94 %) cases. Nine patients (50%) required blood transfusion. All developed acute renal failure (ARF) and required dialysis, mean hemodialysis session being  $7.4 \pm 5.3$  (range 1 to 20). Sixteen patients (89 %) received steroid for presumed interstitial nephritis. One patient expired. Mean time to resolution of oliguria was  $15.9 \pm 9.5$  days (range 2 to 35). Mean hospital stay was  $18.7 \pm 13.4$  days (range 1 to 46), those having higher number of bites had longer stay.

**Conclusions:** Wasp bite mostly affects farmers of working age in rural Nepal. Hemolysis and acute renal failure are two important complications. Timely dialysis in established acute renal failure and steroid in suspects of interstitial nephritis improves survival.

**Keywords:** allergic interstitial nephritis; acute renal failure; hemolysis; rhabdomyolysis; wasp bite.

### INTRODUCTION

Medically important insects of the order Hymenoptera comprise- Apoidae (bees), Vespoidae (wasps, hornets and yellow jackets) and Formicidae (fire ants).<sup>1</sup> Wasp or bee stings occur as accidents or occupational exposure, especially in rural areas, in proximity of forests, all over the world.<sup>2-6</sup> Wasp stings are common form of envenomation in the tropics including Nepal and Northern India, especially for farmers in hilly regions.<sup>6-8</sup> Although there are no official records from Nepal, there

are accounts in many villages of casualties from wasp bite. At another tertiary care hospital in Nepal, 11 patients with wasp stings were seen over 21 months.<sup>9</sup>

The clinical manifestations of wasp bite range from local to systemic and benign to life threatening multisystem involvement, each resulting from allergic and/or anaphylactic to toxic reactions.<sup>1,10</sup> Life threatening anaphylaxis begins within 10 minutes to four hours; systemic reactions may develop within 24 hours or

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delayed.<sup>9,11</sup> Death rates of hospitalized patients range from 15-25%.<sup>5,9,12</sup>

Here, we report our study on the presentation, hospital course and outcome of wasp bite victims. We also discuss the pathomechanisms and management of various complications with special focus on renal involvement.

## METHODS

It was a retrospective, descriptive, analytical study. The retrospective design with patient anonymity maintained during data collection exempted us from getting informed consent. The study was approved by Institutional Review Board of Institute of Medicine, Nepal.

Medical records of 18 patients admitted to Tribhuvan University Teaching Hospital (TUTH) between January 2008 and December 2012 (five years) with diagnosis of wasp bite were reviewed. Diagnosis was based on history and physical examination findings. For each case, we collected the demographic, clinical and serial laboratory data. The testing methods used were those traditionally used in the hospital.

The outcome parameters evaluated were death, duration of hospitalization, number of dialysis sessions and time to resolution of oliguria (time for urine output to exceed 500 ml/day).

For statistical analysis, data were expressed as mean ( $\pm$  standard deviation, SD), percentages and ranges wherever appropriate. Since not all clinical data were available, it lead to the number of observations for calculating means to be less than 18 in some variables; when this occurred the corresponding number of observation was used. The correlations of baseline demographic, clinical and laboratory parameters with outcome were also assessed.

## RESULTS

All the 18 patients with wasp bite came from rural areas. Mean age was  $39.6 \pm 16.7$  years (range 7 to 69), 13 (72%) were male and five were female. Thirteen patients (72%) were between 18 and 60 years of age. Thirteen (72%) were farmers, two were students, two were teachers and one was carpenter by occupation. Mean number of bites was  $96.4 \pm 70.1$  (range 35 to 300). Head, neck and upper trunk were the most commonly involved bite areas. The average time between wasp bite and

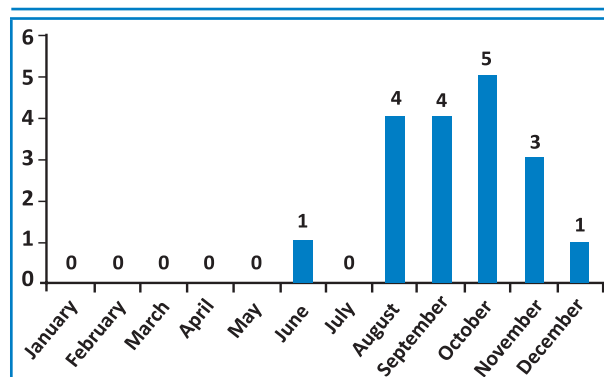
hospital admission was  $5.1 \pm 3.5$  days (range 1 to 12), only four were admitted on the day of bite. All were referred patients; one was referred after four sessions of hemodialysis outside. Sixteen bites (89 %) occurred in August to November (Figure 1).

**Table 1. Available number and values of important muscle enzymes.**

Muscle enzymes	Number of patients with readings available in the first 10 days of bite	Number of readings available in the first 10 days of bite	Number of values available in the first 2 days of bite	Average value of the first two days of bite (U/L)
CPK	15	30	5	36,123.6
LDH	15	24	5	2,926
AST	15	29	4	1,326
ALT	15	28	3	7,70.75

**Table 2. Characteristics of the patient who expired.**

Age	61 years
Day of presentation	first day of bite
Number of bites	>300
Urine output	Anuric
BP at emergency	not recordable
TLC / platelet / cmm	33,600/150,000
CPK, U/L	50,000
AST, U/L	2250
Bilirubin(total/direct) $\mu\text{mol/L}$	150/45
Urea, mmol / creatinine, $\mu\text{mol}$	14.7 / 780
Outcome	expired on day of admission



**Figure 1. Seasonal pattern of Wasp Bite in Nepal (n=18)**

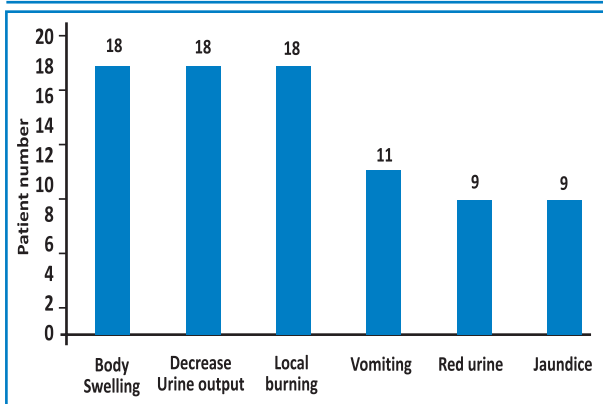


Figure 2. Clinical presentation of wash bite patients (n=18)

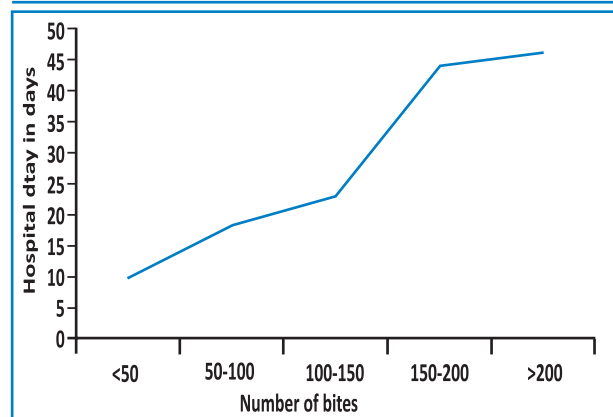


Figure 5. Correlation between of number of bites and length of hospital stay (correlation coefficient=0.97)

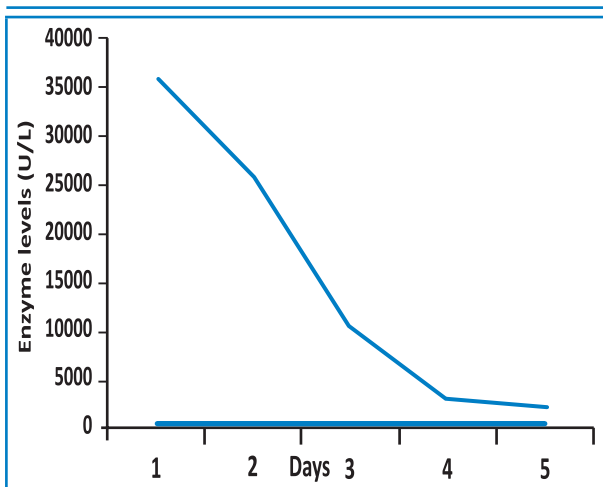


Figure 3. Trend of CPK level from the day of bite

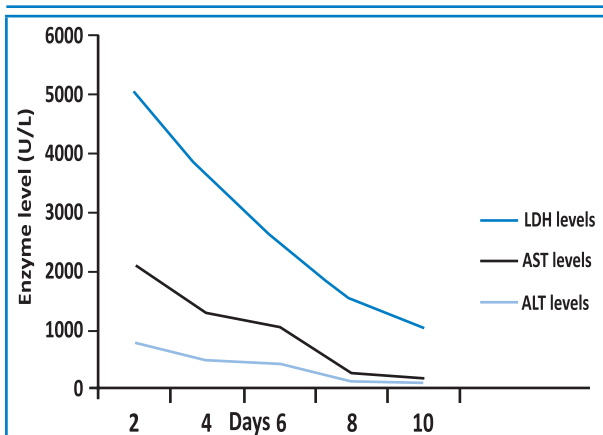


Figure 4. Trend of muscle enzymes from the day of wasp bite

All patients had local burning sensation, decreased urine output and swelling of body at presentation (Figure 2). Urine output decreased on the first day of bite in 12 (67 %) victims while 17 (94 %) had diminished urine output within first 48 hours. One patient presented in shock on the day of bite, while all the rest had normal blood pressure at our hospital. Pallor, icterus and edema were documented in eight (44%), eight (44%) and 15 (83%) patients respectively at presentation.

Six patients (33%) had hemoglobin <10 gm% at presentation; it dropped after admission and reached the lowest on  $14.8 \pm 5.5$  days of admission. Nine patients (50%) eventually received blood transfusion. The mean White Blood Cell (WBC) count was 19,347/cumm at presentation, only four patients had WBC <11,000/cumm while seven had WBC count >20,000/cumm. Only one out of 18 patient had platelet count <100,000/cumm, however. Prothrombin time was deranged in only one patient (18 seconds, control 13 seconds). All the muscle enzymes were significantly elevated in the first two days of bite (Table 1); enzymes tended to settle rapidly in the subsequent days (Figure 3, 4).

All the patients had deranged kidney function at presentation. Average urea and creatinine at admission were 21.1 mmol/L and 637.5  $\mu$ mol/L respectively; creatinine disproportionately increased compared to urea. Mean calcium was 1.8 mmol/L and mean  $PO_4$  was 5.6 mg/dL. Twelve (67%) patients had hyponatremia ( $Na < 135$  mEq/L) while seven (39%) had hyperkalemia ( $K > 5.5$ ) at presentation. All patients had ultrasound available for evaluation; none had findings of obstructive uropathy or chronic kidney disease. One patient did not have urine for evaluation; seven out of 17 patients (41%) had significant hematuria, however there was no comment on dysmorphic cells.

All the patients received hemodialysis (HD). Mean number of HD session was  $7.4 \pm 5.3$  (range 1 to 20), one session HD was for the patient who expired; three patients required >10 dialysis sessions. The most common medicines prescribed were steroids, antibiotics and gastric acid suppressants. Sixteen patients (89%) received steroid and 15 (83%) received antibiotics. The most commonly used antibiotics were ceftriaxone (in 12/18) followed by flucloxacillin (6/18) and cefazolin (5/18). Renal biopsy was done in one patient only; another patient underwent debridement & skin grafting for ulcer in left foot. Mean number of hospital stay was  $18.7 \pm 13.4$  days (range 1 to 46). There was positive correlation between number of wasp bites and duration of hospital stay (Figure 5). The time to resolution of oliguria was  $15.9 \pm 9.5$  days (range 2 to 35). The number of bites did not correlate well with number of dialysis sessions or time to resolution of oliguria (Pearson correlation coefficient 0.61 and 0.77 respectively). Seventeen patients (94%) had clinical and renal function improvement and were discharged home. One patient expired on the day of admission itself; Table 2 shows the characteristics of the patient who expired.

## DISCUSSION

Hymenoptera (except Africanized bees and yellow jackets that attack with minimal or no provocation) are social creatures that typically sting following provocation to protect themselves and their colony.<sup>1,3-5,13</sup> In temperate climates, stings may occur during any warm month, but their numbers peak in August.<sup>13</sup> In the present study, 16 bites (89%) occurred between August and November (Figure 1). The exact species could not be identified in our study; any stinging insect of the order Hymenoptera is identified by a common person as a 'wasp'.<sup>14</sup> All the victims in our study came from rural areas, most of them were farmers and 13 (72%) belonged to active working age group (18 to 60 years). Relatively higher incidence of wasp bites has been reported from Nepal in the past as well,<sup>6,8,9</sup> proving the point that wasp bite is an important occupational and environmental hazard in Nepal.

The toxic compounds in the wasp venom include enzymes like phospholipase  $A_2$  and hyaluronidase; active peptides like melittin, amines like histamine and serotonin; and others like mastoparan, kinins, apamine, acetylcholine and antigen 5.<sup>1,5,6</sup> Phospholipase  $A_2$  initiates inflammation, hyaluronidase causes spread of venom, melittin has hemolytic, vasoactive, contractile and cellular antimembrane properties, histamine increases vascular permeability and apamine is a neurotoxin.<sup>1,5</sup>

The local reactions following wasp bite include pain and swelling, while systemic allergic reactions may be mild, moderate (angioedema, asthma, abdominal pain) or severe (laryngeal edema, hypotension, loss of consciousness).<sup>10,13,15</sup> Systemic complications due to toxic effects of the venom include renal, cardiac (myocarditis, myocardial infarction, arrhythmias), hepatic (centrilobular necrosis, portal triaditis and pericholangitis), neurological (acute encephalopathy, Guillain-barre syndrome, stroke), vasculitis and hematological complications (hemolysis, disseminated intravascular coagulation, thrombocytopenia).<sup>2,11,12,16-20</sup> We observed that local burning sensation and ARF were present in 100% of victims. Though all the markers of hemolysis were not available, nine patients (50%) had jaundice and red urine at presentation (Figure 2) and the same number (50%) eventually required blood transfusion suggesting that hemolysis was present in nearly 50%. Neutrophilic leucocytosis present in 78% of our patients during admission is in agreement with other studies,<sup>5</sup> but thrombocytopenia was less commonly observed. Hymenoptera sting is said to result in triad of rhabdomyolysis, ARF and toxic hepatitis.<sup>3,16,21,22</sup> Though rise in AST, ALT was seen in our patients, they accompanied parallel rise in CPK suggesting muscle to be the origin of those enzymes; hemolysis lead to hyperbilirubinemia and only one patient had elevated PT. Though cases of fatal liver failure consequent to wasp stings have been reported,<sup>2,20,23</sup> we suggest that hepatic injury in general may not be common in wasp bite. We did not encounter cardiac and neurological complications.

Renal involvement in wasp bite takes different forms- ARF, nephrotic syndrome and renal tubular acidosis.<sup>5,24,25</sup> Renal failure or death may occur in the range of 20-200 wasp stings.<sup>21</sup> Mean number of bites in our patients was  $96.4 \pm 70.1$  (range 35 to 300). Since 17 patients (94 %) had oliguria within the first 48 hours of bite, it can be suggested that wasp bite victim be managed and observed for initial 48 hours before being discharged home safely. The mechanisms of ARF include acute tubular necrosis (ATN), acute allergic interstitial nephritis, acute cortical necrosis and thrombotic microangiopathy.<sup>6,14,22,26</sup> ATN results from shock (anaphylactic or hypovolemic), pigment nephropathy (severe rhabdomyolysis or hemolysis) or due to direct tubular toxicity of the venom.<sup>12,14,22,27</sup> ARF occurs in 33-50% of patients with rhabdomyolysis, the main mechanisms of renal injury are hypovolemia, renal vasoconstriction, intraluminal cast formation and direct myoglobin toxicity. Myoglobin

is freely filtered by the glomeruli; in presence of high concentration, dehydration and acidic urine (pH<5.6), myoglobin is first transformed to ferrihematin and precipitates in the proximal tubule to form obstructive casts. Myoglobin can also release free iron which catalyses free radical production and further enhances ischaemic tubular damage.<sup>7,28</sup>

Since kidney biopsy was not performed in the majority of our patients (17, 94%), the definitive cause of renal failure could not be ascertained. Because of late presentation, muscle enzyme values of the initial days of bite were available in only some patients. Still, since all the CPK values done within the first six days of bite were significantly elevated (>5 times normal) and 50% of our patients eventually received blood transfusion, there was disproportionate rise in serum creatinine compared to urea, there was hypocalcemia and hyperphosphatemia; we infer that pigment nephropathy resulting from rhabdomyolysis and hemolysis was the main cause of ARF in our patients. However, average time for urine output to cross 500 ml/day was 15.9±9.5 days and 41% (7/17) had significant hematuria suggesting that interstitial nephritis could be the cause or accompanying event of ARF in at least some of our patients.<sup>26</sup> We observed that the elevated muscle enzymes (CPK, AST, ALT, LDH) tended to settle rapidly and by the end of one week they almost normalized (Figure 3, 4).

In a study of ARF due to multiple bee stings by G. Mejía-Vélez, hypotension was present in 60.9% cases and 14% patients had improved without hemodialysis.<sup>5</sup> In a study by Paudel et al, only nine out of 11 patients developed ARF.<sup>9</sup> Our observation was different because all our patients were referred after the onset of oliguria and some after reports of deranged kidney function. All of our patients required dialysis. Mean number of HD session was 7.4±5.3 (range 1 to 20) in our study compared to other study showing average session of HD 4.7±3.3.<sup>5</sup> This delayed recovery alludes to coexisting interstitial nephritis.

The main prognostic factors in wasp bite seem to be age of the victim, number of bites and time since bite to reach the hospital.<sup>5,8,10</sup> Early deaths are mostly because of severe anaphylaxis and cardiac events while fatalities later are the effects of renal failure.<sup>18</sup> We had patient survival with renal function improvement in 94%, this outcome is better than previously reported figures.<sup>5,8</sup> We observed that patients with higher number of bites had

longer hospital stay (Pearson correlation coefficient 0.97) (Figure 5). Because of the size of the study population and small number of events, we could not identify the factors associated with death in wasp bites. However, the one patient who expired had bad prognostic markers (Table 2) as stated in other reports.<sup>2,5</sup> Unlike the finding of Paudel et al,<sup>9</sup> we could not correlate time since wasp bite to hospital admission with different outcome measures because the time between bite and first health care contact was not documented.

Early diagnosis and management are crucial in wasp bite. They include removal of the stings and use of adrenaline, chlorpheniramine maleate and hydrocortisone for severe reactions.<sup>2</sup> We had no record of whether and how the stings were removed. The main stay of initial management of rhabdomyolysis consists of rapid expansion of intravascular volume by using normal saline solution to maintain urine output at more than 200-300 ml/hour followed by alkalinization of urine with sodium bicarbonate and mannitol to flush the blocked tubules; such measures could potentially prevent development of ARF.<sup>7,21,29,30</sup> We do not know whether such therapies were administered to our patients.

Subsequent management in wasp bite depends on organ dysfunction that develops. Early renal biopsy is justified in selected cases diagnose allergic interstitial nephritis and institute steroid therapy.<sup>26</sup> Though biopsy was done in only one patient in our cohort, 89% received steroid to address the possibility that interstitial nephritis could have caused delayed recovery of their ARF. Most of our patients received antibiotics though the source of infection was not evident. This reflected the uncertainty in the treating team's part to rule out coexisting infection in patients with leucocytosis. Paudel et al reported sepsis in 9% of wasp bite patients,<sup>9</sup> but overall prevalence of antibiotic use has not been looked into by other workers. G. Mejía-Vélez reported leucocytosis in 89% of their cases.<sup>5</sup> This teaches us that leucocytosis is common in wasp bite and does not necessarily indicate infection; judicious use of antibiotics is warranted.

The main limitations of the study are retrospective design and small study population consisting of referred patients only; hence the inferences/conclusions drawn may not be applicable to other set ups. However, study of this size is one of the largest mentioned in wasp bite literature and contributes to our understanding of various aspects of wasp bites.

## CONCLUSIONS

Wasp bite is an important occupational hazard to farmers of working age group in rural Nepal, most exposures happening between August and November. Hemolysis and ARF are two most important systemic complications. ARF usually results from ATN secondary to pigment nephropathy and allergic interstitial nephritis. Optimal dialytic therapy in established ARF and steroid in cases with delayed renal recovery plus haematuria could improve survival. Antibiotics should be used only if infection is likely. In-hospital observation and monitoring for initial 48 hours of bite is suggested to see if the patients develop ARF.

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