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Comparison of snakebite cases in children and adults

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Abstract. – OBJECTIVE: There are very few studies that compare the snakebite cases in children and adults. The present study aimed to compare the demographic characteristics, clinical presentations, laboratory findings, and developed complications in pediatric and adult patients due to snakebites.

PATIENTS AND METHODS: This study included the patients admitted to the hospital and monitored due to snakebite between July 1999 and December 2012. The condition of each patient who had been bitten was admitted to the hospital was monitored from the time of admission to the end of their hospital stay. The fact that a snakebite occurred was recorded if the subjects saw the snake or if the appearance of the puncture sites was convincingly a snakebite.

RESULTS: The present work included 290 patients, of whom 123 were children and 167 were adults. The most common location of the bites was the lower extremity with 78.9% (n=97) and 63.5% (n=106) in pediatric and adult patients, respectively. All of the pediatric patients received prophylactic treatment with antibiotics, whereas 62 (37.1%) adult patients received antimicrobial treatments due to the soft tissue infection. The most common complication developed was pulmonary edema in children at a rate of 33.3% (n=41) and compartment syndrome in adult patients at a rate of 3% (n=5).

CONCLUSIONS: Patients admitted to the hospital due to snakebite should be monitored for at least 12 hours, even if there is no sign of clinical envenomation. Antivenom treatment should be administered to the patients requiring clinical staging. Patients should be kept under close monitoring to prevent the development of serious complications such as cellulitis, pulmonary edema, compartment syndrome, and disseminated intravascular coagulation.

Key Words:
Snakebite, Antivenom, Clinical features, Compartment syndrome.

Introduction

Snakebites are an emergency medical condition requiring very rapid treatment procedures. Injury and death due to snakebite, which are important health issues in the tropical regions in particular, are seen in almost every place around the world. There are three million snakebite cases and 150,000 deaths due to snakebites every year worldwide[1,2]. The majority of envenomations occur during the summertime when snake and human activities increase. The mortality due to snakebite approached 25% in previous years; however, mortality decreased to under 0.5% through easy access to antivenom and the development of emergency interventions[3]. In Turkey, snakebite cases are frequently seen, especially in the Southeastern Anatolia region, due to its climatic and geographical characteristics. The most common kind of snake causing bites is the Viperidae[3]. Viperidae venom has necrotizing and hemorrhagic effects, and a moderate neurotoxic effect[4,5]. Snakebites have similar clinical presentation in adults and children; however, the clinical course is more severe and more complications develop in children. There are very few studies that compare snakebite cases in children and adults. The present study aimed to demonstrate the demographic characteristics, clinical presentations, laboratory findings, and developed complications in pediatric and adult patients due to snakebite.

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Patients and Methods

This study included patients admitted to Dicle University Medical Faculty Hospital Infectious Diseases and Pediatrics clinics and followed-up due to snakebite between July 1999 and December 2012. The condition of each snakebite patient admitted to the hospital was monitored from the time of admission to the end of their hospital stay. The incidence of a snakebite was recorded if the subjects have seen the snake or if the appearance of the puncture sites was convincingly from a snakebite. The included cases were further confirmed based on clinical symptoms of local swelling and hemotoxicity. The patients who had suspected snakebites, who did not see the snake, and did not have bite marks of a snake, were excluded from the study. Patient follow-up was conducted by the patient follow-up cards completed at the admission and the hospital records. A data collection sheet was used to extract relevant information pertaining to patient characteristics, clinical presentations (local and systemic), laboratory investigations, treatment regimens, and complications. Specific treatment approaches, treatment of the symptoms and complications were evaluated. The protocols of this study were approved by the Batman State Hospital Ethics Committee.

Statistical Analysis

Standard descriptive and analytical statistical methods for univariate and bivariate analysis, such as mean, standard deviation (SD), chi-square, Mann-Whitney Tests were used. Cumulative incidence was calculated for the entire duration of the study, with 95% confidence intervals. For all analyses, SPSS v18.0 was used (SPSS Inc., Chicago, IL, USA). p values of 0.05 (two-sided, where applicable) were considered statistically significant.

Results

The present study included 123 pediatric and 167 adult patients. The overwhelming majority (99%) of bites occurred between April and November. The peak incidence in snakebite cases was reported in June. Most of these snakebites occurred during the daytime (6:00 am to 6:00 pm). Of the pediatric patients, 44 (35.8%) were girls, 79 (64.2%) were boys; the mean age was 10 ± 3.2 years, and the mean hospital stay was 6.7 ± 4.6 days. Of the adult patients, 76 (45.5%) were female, 91 (54.5%) were male; the mean age was 34.5 ± 17.2 years and the mean hospital stay was 6.3 ± 3.7 days. The most common location of the bites was the lower extremity with 78.9% (n=97) and 63.5% (n=106) in pediatric and adult patients, respectively. The most common findings from the physical examination of the patients were edema, ecchymosis, and vesicular lesions. An overview of symptoms and clinical signs of the remaining 290 patients is given in Table I. The most frequently determined was the moderate presentation with 56.9% (n=70) and 63.5% (n=106) in pediatric and adult patients, respectively (Table II). Leukocytosis was most frequently seen from the laboratory findings of the patients (Table III). Thrombocytopenia was found in 73 (43.1%) of the adult patients. The most common observation was the hemoglobin drop in the day 5 laboratory values of the patients (Table IV). The pediatric patients received one dose of snake venom antiserum, whereas 67 (40.1%) of the adult patients received

Table I. An overview of symptoms and clinical signs in patients.

	Adults n (%)	Children n (%)	Total n (%)	RR (95% CI)	p
Edema	143 (85.6)	120 (97.6)	263 (90.7)	6.71 (1.97-22.84)	0.001
Ecchymosis	42 (25.3)	93 (75.6)	135 (46.7)	9.15 (5.33-15.71)	< 0.001
Vesicle	31 (18.6)	30 (24.4)	61 (21)	1.42 (0.80-2.50)	0.229
Necrosis	16 (9.6)	36 (29.3)	52 (17.9)	3.91 (2.05-7.45)	< 0.001
Hypotension	19 (11.4)	27 (22)	46 (15.9)	2.19 (1.15-4.16)	0.015
Tachycardia	23 (13.8)	30 (24.4)	53 (18.3)	2.02 (1.11-3.69)	0.021
Dyspnea	4 (2.4)	27 (22)	31 (10.7)	11.46 (3.89-33.75)	< 0.001
Sweating	5 (3)	27 (22)	32 (11)	9.11 (3.40-24.45)	< 0.001
ECG-changes	1 (0.6)	8 (6.5)	9 (3.1)	11.55 (1.43-93.59)	0.005
Plaster -splints	51 (30.5)	38 (30.9)	89 (30.7)	1.02 (0.61-1.68)	0.948
Complications	13 (7.8)	41 (33.3)	54 (18.6)	5.92 (3.00-11.68)	< 0.001

Table II. Clinical presentation of snakebitten patients.

Clinical presentation	Number (%)				
	Adults (n: 167)	Children (n: 123)	Total (n: 290)	RR (95% CI)	p
Mild presentation	6 (3.6)	10 (8.1)	16 (5.5)	0.32 (0.11-0.92)	0.034
Moderate presentation	131 (78.4)	70 (56.9)	201 (69.3)	0.87 (0.28-2.66)	0.805
Severe presentation	29 (17.4)	42 (34.1)	71 (24.5)	0.60 (0.03-11.47)	0.734
Lethal outcome	1 (0.6)	1 (0.8)	2 (0.7)	–	–

one dose, 63 (37.7%) received two doses, 36 (21.6%) received three doses, and one patient received four doses of snake venom antiserum. Two patients developed an allergic reaction to the antivenom treatment. All of the pediatric patients received prophylactic treatment with antibiotics, whereas 62 (37.1%) adult patients received antimicrobial treatments due to the soft tissue infection. The most common complication developed was pulmonary edema in the children at a rate of 33.3% (n=41) and compartment syndrome in adult patients with a rate of 3% (n=5). Additionally, disseminated intravascular coagulation (2.4%), anaphylaxis (1.2%), pulmonary edema (1.2%), and cellulitis (0.6%) were seen in the adults. Five patients who developed compartment syndrome underwent fasciotomy and were discharged without any complications. A plaster splint was applied to 89 (30.7%) of the patients for preventing the development of compartment syndrome upon the disseminated edema after the snakebite. Two fatalities (0.7%) were reported in the study groups.

Discussion

Snakebites, which are an important health issue especially in tropical regions, are also an important public health issue in our region. The kind of snake seen in Turkey's Southeastern Anatolia Region is *Vipera lebetina*[6]. The venom has a complex structure with a combination of many toxics and proteins. The venom has hematotoxic, neurotoxic, myotoxic and nephrotoxic effects. The most commonly seen effect is hematotoxic and may lead to hemolysis, ecchymosis, petechial hemorrhage, epistaxis, hematemesis, melena, and coagulopathy. The patient can develop local or systemic symptoms depending on the severity of the venom toxin[7,8]. Pain, increased temperature, edema, ecchymosis, hemorrhage, lymphangitis, and tissue necrosis, as well as systemic findings such as fever, nausea, vomiting, circulatory collapse, jaundice, convulsion, and coma may develop at the location of the bite. The observed edema and ecchymosis result from a venom-induced capillary leak,

Table III. Laboratory findings of patients.

	Adults	Children	p
WBC (K/uL)	15.20 ± 4.94	15.10 ± 7.23	0.899
Hemoglobin (g/dL)	13.47 ± 2.27	13.36 ± 1.76	0.664
Platelet (K/uL)	178.11 ± 92.45	284.96 ± 91.29	0.000
Eosinophils (%)	2.79 ± 3.16	1.24 ± 2.36	0.000
PTZ (sn)	15.01 ± 2.90	13.71± 2.97	0.001
Urea (mg/dL)	35.92 ± 14.63	28.59 ±10.43	0.000
Creatinine (mg/dL)	0.80 ± 0.32	0.56 ± 0.18	0.000
AST (U/L)	31.38 ± 28.36	36.58 ± 25.53	0.130
ALT (U/L)	28.91 ± 22.52	19.04 ± 9.65	0.000
Total Protein(g/dL)	6.36 ± 0.86	6.69 ± 1.00	0.009
Albumin (g/dL)	3.56 ± 0.67	3.74 ± 0.56	0.025
LDH (U/L)	296.59 ± 157.13	395.93 ± 348.67	0.002
CK (U/L)	336.68 ± 682.18	348.51 ± 416.98	0.877
Calcium (mg/dL)	8.52 ± 0.83	9.21 ± 0.84	0.000

WBC: white blood cell, PTZ: Prothrombin time, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase LDH: Lactate dehydrogenase, CK: Creatine kinase.

Table IV. Comparison of laboratory findings according to 1.day and the 5.day.

	1.day	5.day	p
WBC (K/uL)	16.03 ± 6.16	8.55 ± 4.10	**< 0.001**
Hemoglobin (g/dL)	13.76 ± 2.14	11.07 ± 2.39	**< 0.001**
Platelet (K/uL)	196.96 ± 105.49	200.80 ± 100.43	0.664
AST (U/L)	31.13 ± 26.01	35.92 ± 30.23	0.118
ALT (U/L)	25.14 ± 15.82	33.14 ± 31.38	0.010

WBC: white blood cell, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase.

which causes extravasation of plasma and erythrocytes[9-12]. In the present study, the most common findings were edema and ecchymosis in both children and adults.

Baseline laboratory tests should include a complete blood count with platelet count, electrolytes, blood urea nitrogen, fibrinogen levels, and prothrombin time. Laboratory investigations for snakebite may reveal leukocytosis, anemia, mild thrombocytopenia, increased sedimentation rate, and elevated serum bilirubin[13,15]. Recurrence or persistent coagulopathy may be seen within two weeks after the envenomation in almost half of the cases. T, ST, and QT changes on ECG, and leukocyturia and erythrocyturia in urine may be observed. Some venoms that undergo rhabdomyolysis due to the phospholipase A2 content may result in myoglobinuria, hyperphosphatemia, hyperpotassemia, and hypocalcaemia, elevated serum aspartate aminotransferase, and creatine phosphokinase levels[1,6]. In the present work, the most common laboratory finding was leukocytosis and low hemoglobin in the pediatric cases. In the adults, thrombocytopenia, prolonged prothrombin time and eosinophilia were observed more frequently compared to the pediatric cases ($p < 0.05$). Leukocytosis recovered on day 5 of the follow-up; however, there was a reduction in thrombocyte count and hemoglobin amount in some cases. Since the toxic effect of the venom may appear in the later period, especially in cases with moderate and severe clinical presentation, it is considered more appropriate to monitor these cases for a longer period of time.

Snakebites are mostly seen in the lower extremities. Snakebites seen in the head and the body cause 2-3 times greater threat to life compared those in the extremities[2,6]. In the present study, the most common location of bites was the feet in both children and adults, followed by the hands. The clinical presentations (symptoms, signs, and laboratory findings) were generally mild in nature. The severity of the reaction to snakebites depends on the nature, location, depth, number of bites, the amount of venom injected, the species and size of the snake involved, the age and size of the victim, and the victim's sensitivity to the venom. After a snakebite, complications such as disseminated intravascular coagulation (DIC), acute renal failure, pulmonary edema, compartment syndrome, cellulitis, and death may occur[7,9,16]. In the present study, 33% of the children developed pulmonary edema and this rate is higher compared to the general literature data. This is because pulmonary edema is seen mostly in moderate and severe cases, and most of these cases' admittance to the hospital are delayed. These patients should be closely monitored in the intensive care unit (ICU), in particular. Cellulitis was frequent in the adult patients; however, the development of compartment syndrome and DIC was rare. Compartment syndrome is a rare complication resulting in ischemic contracture and extremity amputation if untreated. Compartment syndrome is characterized by the loss of function due to ischemia, which occurs in nerve and muscle tissues because of the increased perfusion pressure within the closed muscle fasciae in the extremities[2,6]. The local findings observed as a result of snakebite occur within 30 to 60 minutes; however, compartment syndrome may be seen during the first week[10,11]. Therefore, the administration of medical treatments such as elevation and mannitol therapy should be held off until the clinical findings are completely settled, and fasciotomy should be performed when clinically suspected. In the current study, fasciotomy was performed in all cases developing compartment syndrome.

Soft tissue infection is a major complication of snakebites with local envenomation. The proteolytic properties of snake venom cause exten-

sive tissue destruction and devitalization, which predisposes the wound to bacterial infection from the snake's indigenous oral flora[7,17]. Prophylactic antibiotic treatment should be abandoned because the risk of wound infection after viper envenomation is low. Although bacteria are a major cause of wound infection in snakebite patients, the role of prophylactic antibiotics to prevent their formation is debatable. Furthermore, the venom effects of swelling and blistering are commonly mistaken for bacterial infection[7,16-18]. In the present study, all of the pediatric patients were receiving prophylactic antibiotic treatment. Thirty-seven point one percent of the adult patients were receiving antibiotics due to cellulitis or local wound infection. In particular in patients with fever in the presence of necrosis or abscess, increased white blood cell (WBC) count and C-reactive protein (CRP) should be evaluated for antibiotics and those with an eligible clinical presentation should be started on antibiotics. Randomized controlled trials are required to determine the efficacy of prophylactic antibiotic treatment. It seems that a more selective use of antibiotics should be encouraged[11].

In particular, prior to 2003, the use of heparin, steroids, and antibiotics were more frequent in snakebite cases. These patients were routinely vaccinated against tetanus. Despite suggestions that anti-tetanus vaccination is not suggested as there are no known post-bite cases of tetanus (9). The tetanus toxoid should be administered to patients who have not received it within five years or in patients whose immunization history is in question[15]. Currently, the mainstay of the treatment consists of antivenom, elevation, pain, and bleeding management. The use of heparin and steroids may be recommended in severe complications developed such as DIC and anaphylaxis. The administration and dose of antivenom should be determined based on the disease severity and localization. The dose of venom delivered is a function of the size of the snake, the location of the bite, and the size of the patient. Because of children's smaller relative size, they receive a higher dose of venom[11,19]. Campbell et al[7] monitored 114 pediatric patients with snakebites and used antivenom only in 7 (6%), and found no mortality in the patients. The clinical course of the patients and the complications were found to be similar to the present study; however, the pediatric cases in the present study were receiving antivenom. The researchers, however, still recommend administering antivenom to the patients admitted due to snakebites and believe that multi-center, randomized controlled trials are required on non-administration of antivenom.

Conclusions

Snakebites are a life-threatening condition, which require emergency intervention. All patients should be monitored in a controlled manner for at least 24-48 hours. Pediatric patients in particular should be monitored and treated at hospitals equipped with ICU. Snakebites are significantly more likely to result in severe envenomation requiring antivenom administration. Patients should be closely monitored to prevent the development of serious complications such as cellulitis, compartment syndrome, and DIC.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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