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Snakebites in Mostar Region, Bosnia and Herzegovina

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ABSTRACT

The aim of this study was to provide an overview of the snakebites in patients hospitalized at the Mostar Clinical Hospital, admitted between 1983 and 2006. A total of 341 patients were recorded, with moderate men predominance (52.8%). Majority of patients were bitten for the first time (99.1%). In 98.8% of patients snakebite occurred to the bare skin, most commonly during June to September period (64.2%). Snakebites were the commonest in agricultural workers (48.1%). Until 2003 all admitted patients were treated according to Russel's scheme (3-anti). As of 2003 new treatment scheme was applied, resulting in the reduction of antidote and supportive treatment use, causing a reduction in the number of clinically apparent allergic reactions. Serum sickness was recorded in only 2 patients, while lethal outcome was recorded in one (0.3%). Overall results indicate that lethality of snakebite is low, and that patients were often administered treatment without medical indication. High number of tourists as well as the presence of the peace keeping troops and other visiting personnel in this region make the snakebites and awareness on snakes not only a local issue, but also more general concern.

Key words: *snakebite, snake, serum, antidote,* Vipera ammodytes*,* Vipera berus*, Bosnia and Herzegovina*

Introduction

Poisonous snakes inhabit all continents, especially areas with tropical and sub-tropical climate[1–5]. Among 3,500 of known snake species, less than 10% are poisonous[5]. Although the exact figures are unavailable, it is estimated that almost half a million of snakebites are registered in the World annually, with 30,000–50,000 lethal outcomes[5]. However, lethal outcomes in the European region are rare[3–5]. Within this region, Bosnia and Herzegovina is characterized by the regular presence of at least two poisonous snake species, hump-nosed viper (*Vipera ammodytes*) and European adder (*Vipera berus*)[6–10]. Additionally, there is a regional variety of European adder (*Vipera berus bosniensis*), which is being considered by some authors as one of the most poisonous snakes in the European region[6,10]. Hump-nosed viper and European adder venom has a necrotizing and hemorrhagic effects, and a moderate neuro-toxic effect[6–12]. Local geographic characteristics and the presence of the favorable climate are the reason why snakebites are common here in Bosnia and Herzegovina[8,9]. Hump-nosed viper is more commonly reported as a source of the snakebite[2,3,9–12], while European adder bites are less common[6–8,10–16]. Although the number of affected individuals is lower in the post-war period compared to the period before the war outbreak, number of exposed individuals is still high, especially in the carst mountainous regions. Finally, there is no uniform and widely accepted treatment scheme for snakebites[2–4,6–8,10–21].

The aim of this paper was to provide basic epidemiological account of snakebites in the region, provide a retrospective overview of the experience gathered during 24 years.

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Materials and Methods

Setting

We investigated the snakebites in the Herzegovina region, in an area with the total population of 448,878, which is gravitating to the Mostar Clinical Hospital[22,23]. Total study follow-up period was 23 years, from January 1,1983 to December 31, 2006. Area under the study was 9,504 km^2, with 47.2 inhabitants *per* 1 km^2 [22,23]. Additionally, ever since 1996 and according to Dayton treaty international peace keeping troops are stationed in Herzegovina region. The region is characterized by the carst regions, lack of surface water and agricultural areas, scarce pastures and patchy woodland areas[24]. Finally, Medjugorje, world known religious location is located in this region.

Measurements

The study was designed as the retrospective cohort[25,26]. Census data from the 1991 and 2000 official census were used[22,23]. Patient follow-up was made from the existing medical and hospital records.

Snakebite reaction in patients was classified according to the Reid and Perssons's scheme[15,27]. Three stages of the clinical presentations were assigned: mild, defined as the patients with only local changes at the bite location; moderate, those with severe local reaction, moderate general symptoms and mild changes in the laboratory findings combined with less than two hours of shock, and finally severe, characterized by the severe local presentation, and severe clinical presentation and laboratory findings and shock that lasted over two hours. Shock was defined as tachypnoea, perspiration, cyanosis, low blood pressure, confusion and loss of conscious[28]. We also recorded every case of disseminated intravascular coagulation[29,30].

Fig 1. Area under study.

Polyvalent antitoxin was used as the antidote, as it reacts to all poisonous snakes in the European region[31].

Until 2003, all admitted patients were treated according to the 3A scheme (antibiotic, antidote and anti tetanus serum)[1,2,6–12,14]. Patients admitted after 2003 were treated according to newer treatment suggestions[5,13,16,17,28,31].

Statistical analysis

For purposes of this study we employed a number of descriptive methods[25,26]. Cumulative incidence was calculated for the entire duration of the study, with 95% confidence intervals. χ^2-statistics was used in the hypothesis testing. All analyses were performed in the SPSS package, with significance set at $p<0.01$.

Results

During 23 years for which the data was included in this study, we recorded a total of 389 cases of snakebites, with equal gender distribution (199 cases or 51.2% men and 190 or 48.8% women, p=0.326; RR 1.11; 95% CI 0.91–1.35). A total of 358 (92.0%) of patients were referred by their GPs, while 31 (8.0%) of them came to the hospital on their own due to the actual bite or just the fear that they had been bitten, within 4 hours from the snakebite occurrence. There was no gender difference in this group either (p=0.215; RR 1.68; 95%; CI 0.82–3.46). All patients were admitted, and in 341 of them (87.7%) clinical examination confirmed snakebite, while in 48 of them (12.3%) we were not able to confirm the snakebite, suggesting that they have arrived or have been referred due to possible snakebite or just the fear that they had been bitten. *Post mortem* snake species determination was made in 8.2% of cases, with hump-nose viper being significantly more common than the adder (93.0% of cases). A total of 147 (43.1%) patients have reported seeing the actual bite without being able to recognize which species it was, while 23% of patients did not manage to see the snake at all. Most patients immediately indicated they had been bitten by hump-nose viper (33.7%).

Medical procedures performed by the GPs were: 6.4% of patients received immobilization of affected region,

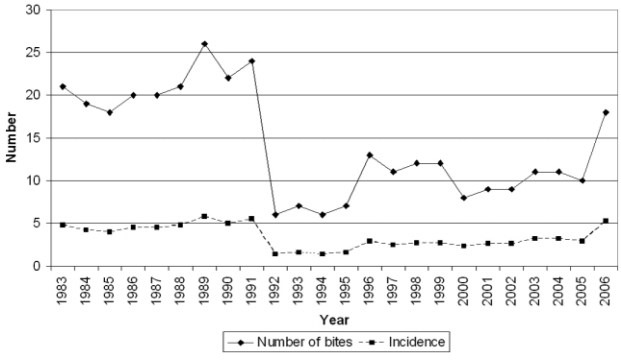

Fig 2. Snakebite frequency in 1983–2006 period, per 10,000, based on the population census data from reference items 22 and 23.

TABLE 1
NUMBER OF REGISTERED SNAKEBITES IN CLINICAL HOSPITAL MOSTAR, IN THE 1983–2005 PERIOD

Age in years	Comfirmed snakebites (%)			RR (95%CI)	p
	Men (*per* 10.000)*	Women (*per* 10.000)*	Total (*per* 10.000)*		
0–20	15 (24.5)*	11 (17.7)*	26 (21.1)*	1.38 (0.64–3.01))	0.531
21–40	31 (40.9)*	17 (24.3)*	48 (32.9)*	1.68 (0.93–3.04)	0.109
41–60	103 (200.9)*	94 (173.7)*	197 (187.0)*	1.16 (0.88–1.53)	0.342
Over 60	31 (104.9)*	39 (87.2)*	70 (94.3)*	1.20 (0.75–1.93)	0.519
Total	180 (82.6)*	161 (69.7)*	341 (76.0)*	1.19 (0.96–1.47)	0.130

18.7% received just antibiotic treatment, and 11.4% received just the antidote, while a total of 36.6% received symptomatic therapy only. Combination of antibiotic and antidote was recorded in just 14.8% of cases. Neither of the patients have received tetanus prophylaxis, while 4.8% of them were referred to the hospital by their GPs without receiving any treatment at all.

Incidence of snakebites varied across investigated period, from 6 cases (1.4 *per* 10,000) in 1992 and 1994 to 26 (5.8 *per* 10,000) in 1989 (Figure 2). Average annual incidence was 3.3 *per* 10,000 population. Most bites occurred during summer months, during July-August period (219; 64.2%), with one bite being recorded even in November and December (Figure 3).

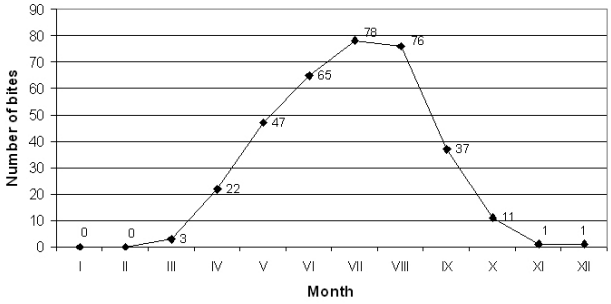

Fig 3. Monthly distribution of snakebites for entire investigated period, 1983–2006.

There was no age related difference in the incidence of snakebites either, although most cases were middle aged (41–60 years of age; Table 1). Age range was 3–93 years. Patients occupation profile indicated that the agricultural workers were the most commonly affected (48.1%), followed by these who were picking mushrooms or other natural products (23.8%), farmers (14.8%), foresters (6.1%) and others 7.2% (including a person who got bitten in the toilet of his holiday home). Most snakebites (99.1%) happened for the first time in the patients life, and it happened on the bare skin (98.8%). The commonest bite location was fists (52.3%), feet (28.2%), shins (15.2%), arms (3.7%), while legs and head were the least common snakebite locations (0.3% each).

A total of 81.2% of patients were received in the mild clinical appearance, while 4.7% had severe clinical presentation, without gender differences (Table 2). Most patients were admitted within 4 hours from the snakebite (82.1%), also without gender difference (Table 3).

The commonest clinical symptoms included intensive fear (92.7%), edema, which was massive in 44.3% of cases, affecting both the limb and torso. Other symptoms included local edema, regional lymphadenitis (40.8%), vesiculae (17.0%), skin necrosis (4.1%) and local infections (1.8%). Systematic symptoms included increased body temperature and gastrointestinal symptoms (21.7%), with marked nausea, diarrhea and vomiting. A total of 5.6% of patients were admitted in shock state, while in 2.1% of them it had lasted for over 2 hours. Lab results showed lekucytosis (31.6%), anemia (7.9%), thrombocytopenia (3.2%) and bleeding, which was recorded in urinary tract (7.6%), gastrointestinal (1.5%) and respiratory system (0.3%). Impaired renal function was recorded in 5.3% of cases (marked by proteinuria, haematuria and

TABLICA 2
ELAPSED TIME FROM THE BITE TO HOSPITALISATION (IN HOURS), BASED ON THE REGISTERED SNAKEBITES IN CLINICAL HOSPITAL MOSTAR IN THE 1983–2005 PERIOD

Elapsed time from bite to hospitalisation (hours)	Number of snakebites (%)			RR (95%CI)	p
	Men (n=180)	Women (n=161)	Total (n=341)		
0–4	147 (81.7)	133 (82.6)	280 (82.1)	0.99 (0.90–1.09)	0.932
5–8	22 (12.2)	21 (13.0)	43 (12.6)	0.94 (0.54–1.64)	0.948
9–12	10 (5.6)	7 (4.3)	17 (5.0)	1.28 (0.50–3.28)	0.793
12 or more	1 (0.6)	–	1 (0.3)	–	–
Subtotal: within first 8 hours	169 (93.9)	154 (95.7)	323 (94.7)	0.98 (0.93–1.03)	0.628

Fig 4. Hump-nose viper bite on the right hand in a 36 year-old female. Oedema, discoloration of skin and ecchymosis of the whole arm and part of the torso.

increased serum creatinine). A total of 8.2% had developed oliguria. Liver function impairment was recorded in 5.0% of cases, with increased bilirubine and liver enzymes, and decrease serum fibrinogen. Neurotoxical symptoms with cranial paresis and paralysis was recorded in 17.9% of cases, most commonly affecting occulomotor nerve with ptosis.

Until 2003, according to Russel scheme, all patients have received antidote, antibiotic (penicillin) and tetanus prophylaxis. Additionally, corticosteroid treatment was applied in 86.3% and antihistamine in 69.5%. A total of 78.7% of patients have received single antidote treatment, while in 21.3% we administered two or more doses. Ever since 2003, treatment scheme has changed, with a total of 50 patients who did not receive antidote in the treatment scheme. After 2003 only 78.0% of patients have received antidote, 66.2% had received antibiotic, while 60.1% had received corticosteroids and antihistamine. Tetanus prophylaxis was administered in 12% of cases, due to high percent of previously administered vaccines due to warfare activities in the years before.

Serum sickness was recorded in 0.6% of patients, 8th–10th day after serum application. We did not record any case of anaphylactic shock nor tetanus.

A total of 17.6% of patients have also received surgical treatment, most commonly bullae incisions (14.1%), necrosis removal (4.7%) and fasciotomy (2.9%), all with complete recovery.

Only one fatal case was recorded, in 85 years old woman who was not referred to the hospital, but was only assisted by the Emergency care, and who after having received treatment went back home. After few hours she lost consciousness, after which she was referred to the hospital, with the total of 8 hours after the snakebite occurred. She had previously been removed one kidney, had hypertension and history of five years of breast cancer without proper treatment. Clinical parameters were showing severe manifestations, including increase levels of serum glucose (14.3 mmol/L), creatinine of 160 mmol/L, prolonged thrombin time (16.9 sec with 53.7%). After receiving proper treatment, the patient became anuric, with signs of epystaxis. She has also received 260 ml of erythrocytes. Third day she developed large hematomas of the arm which started spreading across the torso, marked by more bleeding, develops shock and passes away 40 hours after the snakebite took place due to hemorrhagic shock and multi-organ failure.

Discussion

This study suggests that most of findings from Herzegovina are in line with findings from other countries[3,6,11,12,20,38]. The principal snakebite exposed population group are workers, although the proportion of elderly seems to increase, due to large increase in their number in the population, especially those who are involved in the Asparagus picking[2,3,6,8,12]. Additionally, this seems to be also caused by the young people migration towards larger cities, leaving behind only elderly in the rural and remote areas, or the direct consequence of the 1992–1995 war. One of the suggestions that are derived from the results of this study is that workers should wear protective equipment (primarily gloves), as most snakebites have occurred to bare skin. This is also seen in the finding that during the entire wartime period we did not detect a single snakebite in the military personnel, suggesting that regular wearing of protective clothing may reduce the number of snakebite cases. Monthly profile of snakebites was in line with snake biological cycles, with most bites during summer months.

The least snakebites happened during active warfare periods (1992–1995). The direct consequence of the war

TABLICA 3
CLINICAL PRESENTATION OF SNAKEBITTEN PATIENTS WHO WERE ADMITTED TO CLINICAL HOSPITAL MOSTAR IN 1983–2006 PERIOD

Clinical presentation	Number (%)			RR (95%CI)	p
	Men (n=180)	Women (n=161)	Total (n=341)		
Mild presentation	27 (15.0)	22 (13.7)	49 (14.4)	1.10 (0.65–1.85)	0.844
Moderate presentation	144 (80.0)	131 (81.4)	277 (81.2)	0.98 (0.89–1.09)	0.856
Severe presentation	9 (5.0)	7 (4.3)	16 (4.7)	1.15 (0.44–3.02)	0.978
Lethal outcome	–	1 (0.6)	1 (0.3)	–	–

was the reduction in the overall socioeconomic standard, what has caused increased exposure to various natural sources of food, including picking mushrooms and berries and more often wild animal hunting, all resulting in the increased number of bites in the post-war period.

Similar to previous studies[5,8,11,12], we had also reported substantial amount of snakebite fear, what probably had beneficial effects for the time that lasted from the snakebite to hospital admission, most commonly being well under 4 hours. This also suggests that psychological or even psychiatric treatment should be acknowledge as the integral part of the snakebite treatment[11,14,16]. This is further supported by the finding that a total of 7.7% of patients came to the hospital on their own and 4.4% were referred by their GPs, and in both groups we were unable to confirm snakebites, suggesting that the snakebite fear is very high in this population.

Clinical presentation was most commonly moderate, without any gender differences. Symptoms were the consequence of dual nature of snake toxins – more pronounced haematotoxicity and less often expressed neurotoxicity[6–9,11–14,16,19,20]. All patients have reported local pain, and most of them had hematoma (Figure 4). Favorable clinical outcome is seen in only one fatal case during the entire period, which was aggravated by the presence of previous disease in the medical history.

The results of this study show that the treatment scheme applied by GPs was not unified, what is also seen in the hospital treatment algorithms. Prior to 2003, treatment scheme included local snakebite actions (poison suction, cryotherapy, incision)[1,6–12,14,18–20], which has not been shown to have substantial improvement. As of 2003, treatment scheme has been changed[5,13,16,17]. This includes administration of antidote, which has been reduced due to possibility of serious adverse effects[8,11–13,16,20,31]. Although skin tests have no confirmed value in predicting serum sickness[6,13,16], we nevertheless performed them it in every case. ELISA antigen testing in order to asses the severity of clinical presentation has been recommended perilously[34]. Although we acknowledge possible benefits of this treatment, financial and organizational difficulties were the reason why this was not done. Antidote was then administered most commonly intramuscular, and in severe clinical manifestations we sometimes also applied it intravenously[31]. In line with previous studies, usefulness of antidote was the highest if applied up to 4 hours after the bite[13,16,31], when single dose can be sufficient in moderate clinical manifestations.

As of 2003, antibiotic treatment was applied only in cases that local infection was present, with marked skin necrosis or abscesses, thus reducing routine antibiotic application[5,13,16,17,21]. Penicillin was most commonly administered, or other antibiotics based on the antibiogramme (most commonly cephalosporines). Despite suggestions that anti-tetanus vaccination is not suggested as there are no known post-bite cases of tetanus[5,8,11–13,16], we performed this in those who had not received it related to 1992–1995 war[35], what was the general suggesting that we tried to follow in every treatment case. Besides these, we also tried to deliver appropriate symptoms therapy, reduce fear, pain, maintain good liquid intake, and prevent development of shock. After 2003, treatment costs have gone down too, due to reduced number of allergic reactions.

Despite not being highly lethal, we still believe that snakebites in Herzegovina region do not receive appropriate attention among medical professionals, leading to inappropriate immediate treatment and low amount of information on this, including insufficient education of health personnel. This situation could be substantially improved by the development and application of guidelines. Additionally, WHO suggestions indicate that snakebite information should be collected, and that especially tourists and temporary migrants (including foreign soldiers) should be informed about the risks snakebites in certain areas. This information should also be delivered to religion tourists, who present the major number of people visiting Medjugorje every year.

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UGRIZI ZMIJA NA MOSTARSKOM PODRUČJU, BOSNA I HERECEGOVINA

S A Ž E T A K

Cilj ovog istraživanja bio je prikazati pojavnost zmijskih ugriza među pacijentima koji su bili hospitalizirani u Kliničkoj bolnici Mostar, u razdoblju 1983.–2006. godine. Ukupno je tijekom tog razdoblja zabilježen 341 pacijent, s nešto većim brojem muškaraca (52,8%). Većini pacijenata to je bio prvi ugriz (99,1%). Također, kod većine pacijenata ugriz se dogodio na golu kožu, najviše tijekom ljetnih mjeseci. Ugrizi su bili najčešći kod poljoprivrednika (48,1%). Do 2003. godine pacijetni su liječeni Russelovom shemom liječenja, a od 2003. godine korišten je novi oblik liječenja koji je bio obilježen manjom količinom korištenja zmijskog protuotrova i smanjenjem broja alergijskih reakcija. Serumska bolest zabilježena je samo kod dva pacijenta, a smrtni ishod samo kod jednog (0,3%). Sveukupni rezultati govore u prilog malom mortalitetu i da je pacijentima često primjenjeno liječenje bez stvarne indikacije. Veliki broj turista i vojnog osoblja u ovom području je razlog zbog kojeg pojavnost zmijskih ugriza nije samo lokalni nego i mnogo širi problem.