Review article

UDC: 616 001.49(497.11)
doi:10.5633/amm.2020.0413

VENOMOUS SNAKEBITES IN SERBIA THROUGH 125 YEARS: WHAT WE DO (NOT) KNOW IN COMPARISON WITH NEIGHBORING COUNTRIES. A LITERATURE REVIEW

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In Serbia, only three autochthonous species of venomous snakes can be found; the bites of two can be harmful or fatal to humans. All three are protected at the national and/or international levels. The author found only four publications depicting small numbers (164 in total) of venomous snakebites in Serbia between 1893 and 2018. On the other hand, only in 2017, 94 persons were hospitalized due to snakebites. Yet, in a ten-year period, only four deaths were reported. Apparently, no attempts were ever made at systematizing the long-term information of this kind for the entire territory of Serbia. For other ex-Yugoslav countries, the author collected the analyses of around 4,000 cases, for approximately the same period. People often confuse non-venomous species for vipers and fear them all. More importantly, from the available sources, it could be concluded that physicians in Serbia are not always well informed about the species of snakes which inhabit the areas they work in. Therefore, transdisciplinary education of both the general public and medical personnel is necessary in this regard. Also, the collecting of information regarding venomous snakebites should become obligatory and centralized, and their analyses could be published periodically. Although envenomation can be a serious health issue, in Serbia there is no reason for panic regarding venomous snakes.

Acta Medica Medianae 2020;59(4):95-103.

Key words: *venomous snakebites, education, interdisciplinary cooperation*

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Introduction

Worldwide, over 100,000 people die and another 400,000 become permanently physically disabled due to venomous snakebites every year, usually in rural, typically poor parts of Africa, Latin America, and Asia (1). The current global situation with snakebites was recently defined as a crisis, not only humanitarian but also one of the data (1). At the time of this manuscript preparation, no systematized data regarding snakebites existed in Serbia (2).

Of the approximately 600 venomous snake species worldwide, 219 were identified as medically important (1). In Serbia, only three species of venomous snakes occur, *Vipera ammodytes* (nose-horned viper with two subspecies), *V. berus* (European adder, subsp. *bosniensis*), and *V. ursinii* (meadow viper, subsp. *macrops*), and all are strictly protected or protected by national and/or international laws (3). In addition to not being capable of inflicting serious damage to humans, *V. ursinii* in Serbia inhabits only a few small, remote and uninhabited areas (3, 4). Nevertheless, because *V. u*. subsp. *rakosiensis* still inhabits southern parts of the Hungarian portion of the Pannonian Plain (5), the experts did not fully exclude the possibility that the meadow viper could have persisted in some remnants of suitable habitats in northern Vojvodina Province (6). The other two species are fragmentally (adder) or widely distributed (nose-horned viper) in our country and often can be found near villages and arable lands, and even in cities (3, personal field observations).

Like in other species of the genus *Vipera*, the venoms of Serbian vipers are complex mixtures of various components with numerous toxic effects, and are extremely variable (7, 8). Although *Vipera* species have highly sophisticated venom injection apparatus, "there is no reason to fear them too much", because the amount of venom they can produce is not enough to kill an adult, otherwise healthy human (9). However, children and the elderly, especially those with some chronic diseases, are at higher risk of fatal outcomes than average healthy adults; the same stands for pregnant women (10-

13). Nevertheless, severe envenomations are not necessarily more frequent in older patients compared to middle-aged (13).

In certain parts of Europe and the Balkans, snakes were systematically exterminated. In 1909, Radić (14) informed about the state-financed killing of snakes in France: "in three counties, in 1889 and 1890 only, 161,313 venomous snakes were killed, while previously in these areas many deaths due to snakebites occurred". He suggested that our country should follow the example of "more developed" states. In Bosnia and Herzegovina, according to official records, 271,685 venomous snakes were killed in 1907 only; in six-year periods, between 790,000 and 863,000 venomous snakes were exterminated (15, 16). Between 1907 and 1911, 40 people died, of the 780 reported snakebites (15): per single human death around 20,000 snakes were slaughtered.

Due to inadequate general education, laypeople usually cannot distinguish between the species of venomous snakes, and often even between the venomous and non-venomous ones. This can become a problem for the physicians because the bitten individuals are not always capable of correctly describing the snake that hurt them.

The aim

What the author presented here is, apparently, the first attempt at collecting the long-term data on venomous snakebites for entire Serbia. The purpose of this article is to inspire other competent researchers to thoroughly search for and adequately analyze and publicize the information regarding this long-neglected health issue and to devise and implement proper educational programs for laypeople and professionals regarding venomous snakes.

Materials and methods

The author searched through the available scientific publications for all kinds of analyses of venomous snakebites in Serbia and other countries of ex-Yugoslavia published until the end of 2018. She wrote to the editors of national medicinal journals and librarians in respective institutions. To obtain concrete data regarding the numbers of fatalities due to snakebites (code T63.0: 44), the author contacted the Statistical Office of the Republic of Serbia (request No. 19956 of December 14, 2018). For the numbers of persons hospitalized due to snakebite envenoming, she communicated with the Institute of Public Health "Milan Jovanović Batut", Center for Informatics and Biostatistics.
Only the "one-sample t-test between percents" was used (www.quirks.com/tools/calculator).

Results

The author found only four papers concerning actual cases of venomous snakebites in Serbia (17–20). Two additional ones were theoretical reviews of venomous snakebites, their effects and treatment (21, 22), and yet another publication described the reactions of a single person to the bite of a non-venomous snake, but this is questionable, because "two punctiform wounds" were reported (23). The retrieved publications cover the period between 1893 and 2007, with a total of 164 cases. Of these, 155 were analyzed in a single paper, from the hospital in Western Serbia (18). For the neighboring ex-Yugoslav countries, on the other hand, a lot of well-systematized information exists, with approximately 4,000 of in-depth analyzed cases found. In all studies, bites of *Vipera ammodytes* prevailed. In Serbia no fatalities were presented, while in other countries 48 deaths were recorded, 40 of these between 1907 and 1911. Regarding the reactions to snake venoms, i.e., clinical pictures in the hospitalized persons, the majority was classified as minor to moderate (Table 1).

The highest numbers of snakebites in Western Serbia were recorded between June and August (127 of 155, 81.9%) although variations in months with most bites were registered among years (18). Other bites in Serbia were recorded between April and July (17, 19, 20). A comparison of data available for Serbia with some of the information from Bosnia and Herzegovina and Croatia (12, 13, 18, 19, 29, 39) showed slight variations in months with maximum numbers of snakebites.

In the only overview available for Serbia (18), among the bitten individuals, "children and pupils" prevailed (45%), followed by "housewives" (29%) and farmers (13.5%). The youngest patient was a 15-month young child, and the oldest had 64 years. Most people were bitten on feet and hands, less on legs and other parts of the body (18, 19).

In many among the analyzed cases, the snakes bit unwary people – farmers working in fields or walking through rough terrain, people picking plants/berries/mushrooms – who did not see the animals and provoked them incidentally (12, 13, 18, 25, 27, 39). Nevertheless, in some cases, the snakes defended from intentional attempts at their capturing and unprofessional handling (19).

According to the Statistical Office of Serbia, there were four cases of death related to snakebites between 2008 and 2017: women fatalities were recorded in 2008, 2013 and 2017 and a man died in 2011.

During 2017, 94 persons were hospitalized in Serbia with the ICD (International Statistical Classification of Diseases and Related Health Problems) code T63.0: Toxic effect of snake venom. One-sample t-test between percents showed that more male (58, 61.7%) than female patients (36, 38.3%) were treated in hospitals: $t_{93,\ 0.05} = 2.334$, $p = 0.022$. According to the national Statistical Office, in 2017, the assessed number of inhabitants of Serbia was 7,020,858, therefore the morbidity and mortality rates due to snakebites (per 100,000 inhabitants) in the given year were 1.34 and 0.01, respectively.

Table 1. Overview of the available data regarding venomous snakebites in most ex-Yugoslav countries. Surveyed periods (and probably some data) in certain areas/hospitals partly overlap.

Region/Municipality	Period	Duration (years)	Total number of cases reported	Clinical signs and symptoms severity: numbers/percentages	Reference(s)
Serbia					
Srem District , Fruška Gora Mt.	1893, 1897	12 years of practice	2 confirmed	moderate	17
Western Serbia, Užice	1960–1968	9	155	many mild and moderate several serious no fatalities	18
Banat province, Vršačke Planine Mts.	1978–1996	18	6	no effect 1 systemic intoxication 5 neurointoxication 3 fatalities 0	19
Southeastern Serbia, Leskovac	2007		single case report	serious (alcohol consumption and walking)	20
Sum for Serbia	***1893–2007***	***114***	***164***	***No fatalities***	***4***
OTHER EX-YUGOSLAV COUNTRIES					
Slovenia					
national Poison Control Centre	1999–2008	10	39	Not provided	24
central part	not specified		single case report	grade 2b (of max 3)	25
Ljubljana	2015	1	3	moderate 2 serious 1	26
Croatia					
Rakovica Municipality	1966–1975	10	24	mild 2 moderate 16 serious 6 fatalities 0	27
Rakovica Municipality	1979	1	single case report	toxic shock: direct bite to blood vessel	28
Split Area	1968–1979	12	397	moderate dominate mild 9 severe present fatalities 0	29
Split	1980–1995	16	391	no complications 78.2% local and general complications 21.8% fatalities 2 (soldiers)	30
Split	1982–2002	21	542	minor 15.1% mild 40.5% moderate 26% severe 18% fatalities 0.4% (2 persons)	13
Zadar	1999–2009	11	93	mild 60.2% intermediate 29% severe 10.8%	31
Zagreb	2000–2012	13	54	4 serious cases no fatalities	32
Split Area	1979–2013	35	160 children < 18 yrs	minor 9.4% mild 35% moderate 30.6% severe 24.4% fatalities 0.6% (1 case, 45-day-old infant)	34, 33
Split Area	2018		2	moderate (woman of 84) severe (boy of 9)	35
Bosnia and Herzegovina					
entire country	1907–1911	5	780 officially reported	40 deaths	15

Trebinje	1971–1980	10	130	mild and moderate effects one fatality: bitten directly on the varicose node	36
Mostar	1972–1983	12	189	provided percents of local and general symptoms, no grades; no fatalities	37
Mostar	1997–2002	6	71	mild 5.6% moderate 90.1% severe 4.2% fatalities 0	38
Mostar	1983–2006	24	341 confirmed	mild 49 (14.4%) moderate 277 (81.2%) severe 16 (4.7%) fatalities 1 (0.3%) 85-yr old woman, rich medical history	12
Konjic Municipality	2010–2014	5	30	mild 63.34% moderate 20% severe 6.66% fatalities 0	39
Montenegro					
entire country	1971–1980	10	971		40
Sum for other ex-Yugoslav countries	***1907–2015***	***108***	***4,219***	***48 fatalities***	***20***

Discussion

Although envenomation resulting from venomous snakebites can be a serious health issue and the author did not intend to underestimate it in any way, in Serbia and the surrounding countries there is no reason for the usual panic regarding venomous snakes: on the population level, stings by hymenopterans and ticks and bites by dogs are more numerous and sometimes more dangerous (22, 27).

To the best of the author's knowledge, the information regarding venomous snakebites in Serbia is being collected, but at the time of the preparation of this manuscript the data were not available (2, 41), i.e., the central register still does not exist. Similar is the case in other parts of the world, including those inhabited by numerous species of highly venomous snakes (1, 42). Being non-infectious, snakebites are not a condition which the physicians are obliged to report to the national public health authority – despite the appeals from several decades ago that they should be better monitored (18, 29).

The highest numbers of venomous snakebites occurred in summer; nevertheless, there were few cases of bites in winter months, when the snakes were disturbed in their hiding places (12, 29). Variations in annual numbers of snakebites were probably related to weather conditions (18, 29).

Incidence/morbidity of snakebites and fatalities resulting from envenomation in Serbia are negligible compared to the neighboring countries and, especially, to strongly affected continents: from 41, i.e., 2.1 (at the beginning of the XX century) in Bosnia and Herzegovina (15), through 2.64/0.027 in Hungary (43) and 5.2, i.e., 1.8% in Croatia (13), up to 653, i.e., 54 in Africa, and Asia and Oceania (42). For comparison, in two towns in Serbia, the incidences of dog bites per 100,000 population were 148.5 and 284.3 (22).

Patients of all ages were treated in hospitals – from babies to persons older than 80 (12, 18, 27, 33, 34). Relatively high numbers of children and women bitten by venomous snakes in previous decades were related to the everyday activities of these two groups: compared to modern generations, they were spending much more time outdoors, keeping livestock, collecting wood or picking berries (29). Later on, an increase was recorded in the numbers of snakebites in elderly people (due to general demographic trends), in tourists and those active in outdoor sports (12, 13, 27).

In the published overviews, the time elapsed from bites to admission in hospitals varied from app. half an hour to several days. The reasons for some of the delays were the self-administered first aid or attempts at applying some traditional cures; importantly, fear was indicated as a significant reason for early visits to general practitioners and subsequent admission to hospitals (12, 17, 19, 38).

Most reactions to venomous snakebites developed into mild to moderate clinical pictures; some of the serious complications occurred because the snakes hit blood vessels (Table 1). The rare fatal outcomes of envenomation were recorded in small children and patients with a history of chronic diseases (12, 34). Serum sickness and anaphylactic shock are also very rare; some cases of anaphylactic shock (in Hungary) resulted from repeated (up to 13, intentional!) snakebites (12, 32, 43). The author reminds that systemic, anaphylactic reaction can quickly develop after the sting of a single bee, wasp

or hornet (22) – the animals that people are much more likely to meet compared to snakes.

In neighboring countries, numerous studies were also performed on the composition, effects and mechanisms of toxicity of venoms of the Balkan *Vipera* species, including the efficacy of various antivenoms (7, 25, 26, 44). For Serbia, the author found only two (45, 46).

During a single year, 94 people were hospitalized in Serbia due to snakebites. This amounts to 57% of the number of all cases described in available scientific publications during the previous 125 years. Annual numbers of snakebites are surely higher: the data regarding the numbers of people who were bitten and treated in (primary) medical facilities are not readily obtainable: one would have to contact individual local medical facilities throughout Serbia and ask for the data. Also, bitten persons sometimes do not seek medical help at all.

Vipers are not aggressive and try to bite only in self-defense, i.e., when they are cornered or handled (47, personal field experience); often they remain motionless, possibly napping, seemingly "hoping" they will stay unnoticed, but that can be dangerous because people do not see them (14, 47).

The media contribute much to the general attitudes towards snakes: most often, the reports of snake occurrences (even regarding non-venomous species) and rare bites in Serbia are unrealistic and dramatized. Unfortunately, thanks to various foreign TV shows, people are usually still better acquainted with exotic species than with local herpetofauna (14, 48). Acknowledging their power, the media could be used in reversing the picture regarding snakes and nature in general.

Traditional treatments of venomous snakebites were known and described even in Serbia 120 years ago (17). In many other parts of the world people still use local traditional remedies/treatments and do not (or are not in the position to) seek the help of official medicine hence still many cases of snakebites remain unreported and the official medical statistics usually underestimate their numbers (1, 15, 16, 27, 41, 49).

Authors have repeatedly concluded that farmers (the most affected category) often work barefoot; in the reviews of bites, many were inflicted on bare skin. In short, as the best prevention of the bites of venomous snakes, simple changes in everyday routine and proper education of both laypeople and medical personnel were suggested, for over a century now (14, 15, 18, 22, 29, 50). Despite the deeply rooted fear, people do react well to appropriate education regarding snakes (51).

In contrast to legitimate bites to local people by autochthonous snakes, many bites are inflicted by exotic, "pet" snakes. In Hungary, for example, 97 snakebites were recorded in 36 years, by 19 exotic (61 of all bites, 62.9%) and two native snake species: bites by the exotics "resulted in severe or life-threatening envenomations" (43). Sometimes, this results from the unavailability of antivenoms. In 2018, a man in Serbia was bitten by his "pet" rattlesnake (52).

Numerous authors emphasized that not all physicians are trained well enough for treating snakebites; also, the inexistence of information regarding this health issue was accentuated numerous times: these can have serious consequences, including the inappropriate treatment of envenomation (14, 18, 12, 39, 43, 53). In previous times some wrong advice (e.g. the sucking of the wound) was available in the literature, even in professional and medical papers (14, 18). This did change recently (22), but apparently still has not reached the wider audience (also 43).

The classification of cases according to their severity varies and changes with new scientific insights, as does the treatment of patients (12, 18, 54). Therefore, continuous education of medical personnel and standardization of procedures is needed in this area, based on the most recent scientific findings (41).

Laypeople often confuse non-venomous species (including *Natrix tessellata*) for vipers and sometimes report the bites erroneously (e.g. adder bites from the regions this species was never recorded in). However, some mistakes are possible: according to the most recent analysis, the ranges of the three *Vipera* species in Serbia do overlap in several places: *V. ammodytes* and *V. berus* were found in sympatry in 22 localities, *V. berus* and *V. ursinii* in two, and *V. ammodytes* and *V. ursinii* in one (3). The three Serbian vipers look alike and usually clearly differ from non-venomous snakes (the exception is *Coronella austriaca* which can resemble adders) hence given due caution mistakes in recognition are highly improbable. Only the melanistic *V. berus* can puzzle inexperienced persons thus presenting a potential threat. Nevertheless, there is no reason whatsoever to intentionally touch/catch/torture any snake: by simply avoiding them, people can be safe. Constant caution is surely necessary while walking, picking fruits/flowers, climbing rocks, hiking, etc., in the areas inhabited by venomous snakes. Fortunately, the viper anti-venom available in Serbia (produced from the *V. ammodytes* venom) is effective in the treatment of both *V. ammodytes* and *V. berus* bites (18, 21, 55).

People use(d) to kill and bring to medical facilities the snakes that bit them, and this was even recommended, not only in Serbia (12, 13, 19, 27, 29, 50). The killing of snakes has to be permanently precluded: all ten snake species in Serbia are (strictly) protected by law, with fines prescribed for their killing and disturbing (56, 57). Populations of *V. ammodytes* declined seriously due to their multidecennial collecting for the venom extraction (58).

Sometimes, mostly in older references, the species lists provided in the available medical publications were incorrect (16, 27, 29, 23, 39). Apparently, the authors made no attempts at communicating with experts in herpetology and faunistics/taxonomy. This can raise a concern: high variability of snake venoms and their effects are long-known facts (8, 18). Several recent publications describe the variability of Vipera sp. venoms at various life stages/seasons and levels (between species, subspecies, populations, among individuals within a

single population, and during a lifetime of an individual) – with consequent concerns regarding the production of antivenins. The effectiveness of available antivenins could be unsatisfying/suboptimal in certain cases (7, 8, 25, 26, 59). In Europe, it is still hard to find comparable studies of Vipera sp. antivenoms and their effects, "and none is licensed with the European Medicines Agency" (60).

Conclusion

In 1909, Radić (14) wrote about field-based education regarding wildlife in North America and recommended that our teachers and priests should be better educated so they could instruct their pupils and flocks. He observed that we are all more interested in the exotic, "overseas" plants and animals – actually completely useless information – convinced that we already know all that should be known about our nature. Instead, he suggested, we should first learn about the species we can see in our country. Recent studies support such an attitude (48, 51).

Medical doctors should attempt to collect, analyze and publicize precise information regarding venomous snakebites, from single hospitals to the national level. Also, they should be constantly educated about the new approaches in the treatment of this health issue.

As noted already by Milićević (18), people from rural areas are well aware of the changes and fluctuations of wildlife in their surroundings (including the numbers of snakes observed in successive years). They should also be consulted in future assessments of both distribution and population sizes and dynamics of snakes in Serbia.

In short, the exchange of information among several disciplines and transdisciplinary education of both the general public and medical personnel is necessary in this regard. Simple brochures and posters could be produced and distributed to health facilities, schools, farmers, etc., with descriptions and distributional details of the three Serbian viper species. This should be accompanied by lectures (and fieldwork: 48, 51) held together by biologists and physicians. Also, collecting and mapping (1, 61, 62) of information regarding venomous snakebites should become obligatory and centralized, and their analyses should be published periodically. Such an approach would benefit all: the incidence of snakebites would be lowered, the treatment of bitten persons improved, the distribution maps of species filled in, and fewer snakes would be intentionally killed.

Acknowledgements

The author's esteemed colleagues from Croatia, Bosnia and Herzegovina, and Montenegro sent her invaluable old publications regarding snakes and snakebites in their countries through history. Several papers she got from the librarians of the Military Medical Academy (Belgrade) and the editor of the Medical Review (Novi Sad). The book by Đorđe Radić was provided by Mirjana Savić, a historian. Professor Zoran Radovanović instructed the author regarding the ICD codes and national sources of information regarding health issues. Rastko Ajtić, a PhD herpetologist in the Institute for Nature Conservation of Serbia, helped with the vipers' distribution. The work of Sonja Nikolić is financed by the Ministry of Education, Sciences and Technological Development of the Republic of Serbia. The present research received no specific funding. The author declares no conflict of interests. Two anonymous reviewers made useful comments and suggestions.

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Revijalni rad

UDC: 616 001.49(497.11)
doi:10.5633/amm.2020.0413

UJEDI OTROVNIH ZMIJA U SRBIJI TOKOM 125 GODINA – ŠTA SVE (NE) ZNAMO U POREĐENJU SA SUSEDNIM ZEMLJAMA: PREGLED LITERATURE

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U Srbiji se mogu naći samo tri autohtone vrste otrovnih zmija; ujedi dveju mogu biti opasni ili čak fatalni po ljude. Sve tri vrste otrovnih zmija zaštićene su na nacionalnom i/ili međunarodnom nivou. Autorka je pronašla samo četiri publikacije, u kojima je opisan mali broj (ukupno 164) ujeda otrovnih zmija u Srbiji između 1893. i 2018 godine. Sa druge strane, samo tokom 2017. godine, zbog ujeda zmija, hospitalizovane su 94 osobe. Ipak, u desetogodišnjem periodu, prijavljena su samo četiri smrtna ishoda. Izgleda da do sada nije bilo pokušaja da se sistematizuju dugoročni podaci ovog tipa za celu Srbiju. Što se ostalih republika bivše Jugoslavije tiče, autorka je prikupila analize gotovo 4.000 slučajeva, za približno isti period. Ljudi često mešaju neotrovne zmije sa otrovnicama i plaše se svih. Još značajnije je to što se, iz dostupnih izvora, može zaključiti da ni lekari u Srbiji nisu uvek dovoljno dobro obavešteni o vrstama zmija, koje naseljavaju područja u kojima rade. Stoga je neophodna transdisciplinarna edukacija o ovoj temi, kako šire javnosti tako i medicinskog kadra. Osim toga, poželjno je da prikupljanje informacija o ujedima otrovnih zmija postane obavezno i centralizovano, a njihove analize bi se mogle periodično objavljivati. Iako envenomacija može biti ozbiljan medicinski problem, u Srbiji nema razloga za paniku po pitanju otrovnih zmija.

Acta Medica Medianae 2020;59(4):95-103.

Ključne reči: *ujedi otrovnih zmija, edukacija, međudisciplinarna saradnja*