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EPIDEMIOLOGICAL AND CLINICAL ASPECTS OF SNAKEBITE IN BELO HORIZONTE, SOUTHEAST BRAZIL

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SUMMARY

Epidemiologic and clinical aspects of 310 hospitalized snakebite patients and 310 matched controls were described, over a seven years period, from an emergency hospital in Belo Horizonte, Southeast Brazil. The diagnosis was based upon clinical picture or actual snake identification. Fifty six percent of victims were bitten by the snakes of genus *Bothrops*, 32.0% by *Crotalus*, 1.0% by *Lachesis* and 10.0% undetermined. During the study period, stable number of cases and marked seasonal variation were noted. In comparing cases of snakebite and controls, those from a rural area or who were involved in agricultural labor activity were identified as a high risk group, with an odds ratio (OR) of 14.7 and 6.7, respectively, in favor of being bitten. Upon treatment, snakebite patients were 13.5 times more likely to have had early anaphylactic reactions than their controls, with a higher association in the age group ≥ 20 years (OR = 30.3). Increased risks were also detected for pyrexia (OR = 11.7), with a marked association in the group under 19 years old (OR = 16.6). Severe cases of snakebite are an important treatable cause of morbidity in Brazil but therapy may be potentially life threatening. The higher case-fatality ratio encountered, compared to national statistics may be due the representativeness of the more severe cases who sought hospitalization. Preventing snakebite and early referral of those who are bitten is proposed.

KEYWORDS: Snakebite; Risk Factors; Case-control study; Epidemiological studies.

INTRODUCTION

Venomous snakebite is a worldwide problem, especially in tropical regions[1, 23, 27-28]. Annual incidence rates may vary according to geographical regions, from 4.8 - 125.7/10,000 in West Africa and 0.3 - 8.2/10,000 in New Guinea, to 1.4/10,000 in Brazil and 0.3/10,000 in the U.S. [6, 13, 22, 30]. The vast majority of cases of snakebite occurring in the Western hemisphere are due to the family Viperidae, sub-family Crotalidae, also known as pit vipers. In South America, the Crotalidae are represented by the genera *Bothrops* (now subdivided into a number of new genera), *Crotalus* and *Lachesis* [6, 9-10, 17, 28].

In Brazil, approximately 20,500 snakebite cases are reported annually. The case-fatality rate is about 0.5% and 0.4% of all cases developed serious sequelae. About 50% of all cases are reported from the Southeast region[6].

Risk factor for snakebite may provide important evidence regarding preventive interventions[24]. The present study proposes to report epidemiological features related to exposure and treatment outcomes of hospitalized snakebite patients and matched controls admitted to a referral public emergency care facility in Belo Horizonte, Minas Gerais, Southeast Brazil, over a seven year period.

MATERIAL AND METHODS

Study setting. The study was conducted at Hospital João XXIII, a state foundation hospital, which is the largest and most important public referral emergency care and toxicology center for the population living in the urban and rural area of Belo Horizonte, a capital of the third largest state (Minas Gerais) in Brazil. During the study period this tertiary center was the only toxicology referral center for treatment of snakebite and scorpion sting for the entire Metropolitan area of Belo Horizonte.

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The medical records from January 1980 through December 1986 were screened and all patients with a first discharge diagnosis of snakebite (E905.0)[33] were reviewed and included in the case group. Controls were patients in the same hospital randomly allocated by other emergency discharge diagnosis, who had never experienced a snakebite episode. Since young male adults have higher rates of snakebites, and are more related to agricultural work[6,10] in order to assure comparability betwen groups, controls were matched by sex and age (± 5 years). Date of hospital admission was included to assure time frame comparability.

Information on risk factors of being hospitalized, for both cases and controls, included socio-demographic background, residence, occupation, and circumstances or activity at the moment of the accident. Clinical diagnosis, treatment, tetanus and antibiotic prescriptions, duration of hospitalization and outcome were recorded. Early anaphylactic reactions were defined as the evidence of the following manifestations: itching, urticaria, bronchospasm, central cyanosis, cough, abdominal pain, diarrhea or hypotension[5, 31]. The definition was validated by treatment with adrenaline. Pyrogenic reactions were defined as an attack of fever and rigors following intravenous therapy[31].

Data analysis. Frequency distributions were generated separately for cases and controls. Linear regression, medians, means and proportions were used to analyze the case distribution. Cases and controls were cross-classified with demographic and clinical variables. Association between exposure and disease was expressed as matched odds ratio (OR) with 95% confidence intervals to guide interpretation[29].

RESULTS

Cases. Three hundred and ten cases were selected. Table 1 shows demographic characteristics of cases. The median age was 29 years (range: 1-70 years), approximately 80% were males ($p < 0.01$) and non-white ($p < 0.01$), they similarly came from rural and urban areas.

TABLE 1
Demographic characteristics of 310 cases of snakebite (Southeast Brazil, Belo Horizonte, MG)

Characteristics	Number of cases (n = 310)	Proportions (%)
Age (years)*		
1-4	15	4.8
5-9	34	11.0
10-19	87	28.1
20-44	119	38.4
45-65	46	14.8
> 65	9	2.9
Sex		
Female	69	22.3
Male	241	77.7 *
Ethnic group†		
White	63	20.4
Non white	246	79.6*
Geographical region‡		
Rural	117	41.3
Urban	166	58.7

* $P < 0.01$ (x^2 Goodness of Fit)
† Missing information in one case
‡ Missing information in 27 cases

The identification of snake species was based upon the comparison between the clinical diagnosis at admission and at discharge, given that the actual identification of the offending snake by the hospital staff was performed in only 26 (8.4%) cases. The vast majority of patients were diagnosed as having been bitten by snakes from the family Viperidae, sub-family Crotalidae, also known as pit vipers. They were represented by the genera *Bothrops* (55.5%) and *Crotalus* (32.3%). In 1.0% of cases, the bite was thought to be due to the genus *Lachesis*. In 27% of cases, the species of snake was undetermined at the time of admission; 10% remained undetermined at the time of discharge. As can be seen in Table 2, good percent of agreement beyond chance was reached for the diagnosis according to this criteria (kappa statistic = 71.9%).

TABLE 2
Classification of the 310 snakebite cases diagnosed according to the clinical picture at the admission and discharge time (Southeast Brazil, Belo Horizonte, MG)

Diagnosis	Admission n	Admission (%)	Discharge n	Discharge (%)
Not stated	5	(1.6)	3	(1.0)
Bothrops	136	(43.9)	172	(55.5)
Crotalus	84	(27.1)	100	(32.3)
Lachesis	2	(0.6)	3	(1.0)
Undetermined	83	(26.8)	32	(10.3)

% agreement = 78.7; Kappa Statistic = 71.9%

The annual distribution of cases over seven year period is shown in Figure 1. Although an apparent ascendent trend was noticed , there was no statistically significant trend in the number of hospitalized cases during the study period. A distinct seasonal variation was observed (Figure 2), with the highest incidence in the rainy season (November - April). The median time of day for snakebites was around 12:00 noon. The activity at the moment of bite was recorded in only 13% (41 cases), but of those, 85.4% were work related.

The majority of snakebites (98.6%) occurred on the extremities, 260 (85.2%) on the lower and 36 (11.8%) on the upper extremity.

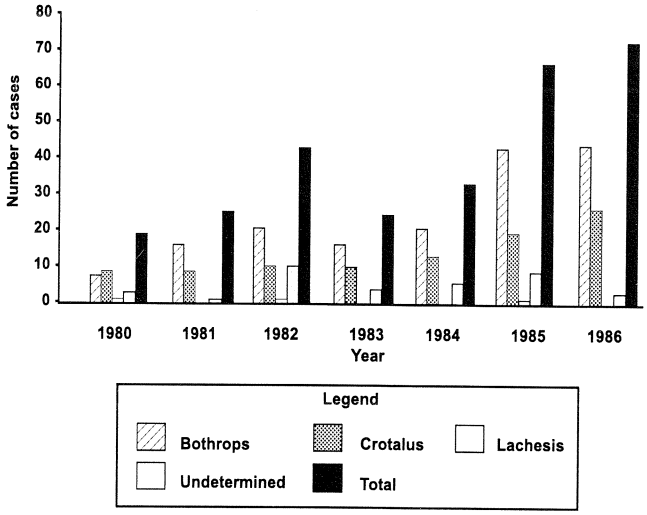

Fig. 1 - Annual distribution of snakebite cases according to discharge diagnosis in Belo Horizonte, Brasil, 1980-1986.

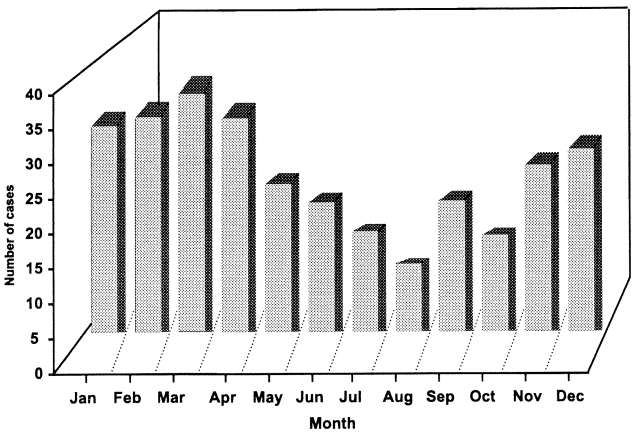

Fig. 2 - Monthly distribution of snakebite cases in Belo Horizonte, Brazil, 1980-1986.

Tourniquet application was recorded in 61 patients (19.6%), and 12 (3.8%) used topical substances such as alcohol or its derivatives. Median time from bite to hospitalization was four hours (range: 1-98 hours). During admission, 24.2% of patients presented with some bleeding (gingival, urinary, and upper gastrointestinal tract), and 26.1% presented with ptosis.

Antivenom was administered to 304 (98.1%) of patients, of whom, 42 (13.8%) presented some kind of early anaphylactic reactions and 36 (11.8%) pyrexia reactions.

Complications during the clinical course were recorded in 61 cases (19.6%) and are reported elsewhere[8].

Permanent sequelae were recorded in seven (2.3%) patients. Five of them had a *Bothrops* bite; four patients were amputated and one presented muscle contractions. The remained two patients who complicated had a diagnosis of renal failure; one due to *Crotalus* bite and the other one was undetermined.

Death was reported in three (0.9%) cases. According to the species, two deaths were reported due to a *Bothrops* bite and one was undetermined.

Controls. Three hundred and ten controls matched by sex, age, and date of admission were selected. They represented all type of diagnosis characterized as a medical emergency, with a remarked proportion (36.5%) in the group labelled as injuries and poisonings.

Cases and controls. Table 3 shows selected risk factors among cases and controls. Cases were more likely to be from rural areas than controls. The frequency of agricultural occupation was higher in cases than controls. Using a univariate matched analysis, cases from rural areas had almost 15 times higher the risk of being bitten than controls (OR = 14.7, 95% CI: 6.8 - 31.6, $p < 0.01$); agricultural occupation was also significantly associated with a snakebite episode, with a risk of almost seven in favor of being bitten (OR = 6.7, 95% CI: 3.5 - 13.0, $p < 0.01$).

Cases also differed from controls regarding some procedures during hospitalization. They had a shorter length of stay at the hospital (mean: 11.3 ± 3 (SD) days for cases compared with 15.6 ± 1.5 (SD) days for controls, $p< 0.05$); they were given antibiotics (24.2%) and tetanus prophylaxis (42.9%) in a smaller propor-

TABLE 3
Comparisons of cases of snakebite with matched controls according to some characteristics related to rural exposure (Southeast Brazil, Belo Horizonte, MG)

Characteristics	Cases		Controls		Odds ratio *	95% CI*
	+/n	(%)	+/n	(%)		
Rural residence	110/268	(41.0)	15/262	(5.7)	14.7	6.8-31.6
Agricultural occupation	96/294	(32.7)	26/272	(9.6)	6.7	3.5-13.0

* Odds Ratio and Confidence Interval (CI) presented are results of matched analysis .

TABLE 4
Age-related association of early anaphylactic and pyretic reactions between cases of snakebite and matched controls (Southeast Brazil, Belo Horizonte, MG)

Characteristics	Cases		Controls		Odds ratio *	95% CI*
	+/n	(%)	+/n	(%)		
Early anaphylactic reactions (n = 612)	42/304	(13.8)	3/308	(1.0)	13.5	7.2-25.1
1-19 years (n=272)	17/134	(12.7)	2/138	(1.4)	4.7	2.2-10.3
≥ 20 years (n=340)	25/170	(14.7)	1/170	(0.6)	30.3	10.5-86.2
Pyretic reactions (n=611)	36/303	(11.9)	3/308	(1.0)	11.7	6.2-22.1
1-19 years (n=272)	23/134	(17.2)	1/138	(0.7)	16.6	5.9-46.3
≥ 20 years (n=339)	13/169	(7.7)	2/170	(1.2)	8.7	3.6-21.5

* Odds Ratio and Confidence Interval (CI) presented are results of matched analysis

tion than controls; however, cases and controls had the same proportion of intravenous therapy (99.0%).

Early anaphylactic reactions, recorded in 45 patients, started significantly early for cases than controls (median time of 2.1 hours for cases and 518.0 hours for controls, $p < 0.01$). Pyrexia developed in 39 patients, and also occurred earlier for cases (median 5.8 hours for cases and 48.6 hours for controls, $p < 0.01$). Table 4 describes the overall and age groupwise relationship of anaphylactic and pyretic reactions among cases and controls. Early anaphylactic reactions were significantly more frequent among snakebite patients, nearly 14 times higher for cases than controls in a matched analysis ($p < 0.01$). The paired estimated of the odds ratio across the age strata showed that the risk of early anaphylactic reactions was eight times higher for cases who were ≥ 20 years old and 30 times higher for cases who were ≥ 20 years old, compared with controls. Cases were 12 times more likely to have pyrexia than controls. Younger cases (< 20 years old) had a higher risk of pyrexia than older cases (≥ 20 years), when compared with controls.

Deaths, reported in three (0.9%) cases and 37 (11.9%) controls, were associated with other medical condition but snakebite, with an odds ratio of 18.0 (95% CI 4.3-74.8).

DISCUSSION

Snakebite is an important public health problem in Brazil, [6, 8, 10] and this study suggests a stable trend of snakebite cases over time. Snakebites are more frequent among young non-white males who have been exposed to rural areas and who have had an agricultural occupation. The occurrence of early anaphylactic reactions in bitten patients was high as well as pyrogenic reactions.

Though these data may not represent populations, as a hospital-based study, the ascending non-significant trend of snakebites overtime has the same pattern described in official reports in Brazil[6]. Factors such as an increased human being exposure either due to expansion in agriculture-related activities or in actual increase in the relative number of poisonous snakes through deforestation and change of habitat may be associated to this trend in Brazil, as described elsewhere[13]. Differential referral patterns over time may be another source for the increased trend observed. In the middle of the 80's, a shortage in the commercial production of antivenom in Brazil, was followed by a massive governmental response program on snakebite, resulting in a expansion of the national surveillance program. A better surveillance system, referring bitten patients to specific treatment centers, might be operation in this setting, perhaps accounting for some increase in the number of hospitalizations due to snakebite. The described seasonal pattern of snakebite, with an increase in the rainy season, has been explained as due to an increased activity of both snakes and humans during this period[16, 17, 23, 25, 26, 31]. The distribution of cases by age, sex, time of day and anatomical site was consistent with other reports [1-3, 6, 10, 14, 17, 21, 23, 25, 26, 31].

Epidemiological data on snakebite is often difficult to interpret because of different criteria used for the diagnosis, especially when an adequate identification and documentation of the offending snake are usually lacking [13, 17, 21, 31]. The criteria adopted for case ascertainment, based upon the high agreement between the diagnosis at the admission and discharge, although subject to some misclassification, seemed to be suitable for the purpose of this study. The reliability of these observations could be verified by comparison with the neurotoxic manifestations of envenomation by different species of snakes [19]. There was an agreement between the number of patients with reported ptosis and the proportion given the discharge diagnosis of *Crotalus* bite [25].

The time interval between the accident and arrival at the hospital indicated a delay in treatment which may have contributed to the related complications [8]. Unorthodox treatment, with tourniquets and topical substances, might contribute to the delay in the specific treatment [17, 31]. The use of antibiotic prophylaxis was not standardized in this setting, and tetanus prophylaxis might be innapropriate [19].

Despite the limitations in comparing snakebite cases and controls, the higher odds for those from rural area and exposed to an agricultural labor may confirm that young males, who are involved in agricultural activity during the day, have a higher chance of being bitten. Bites on the extremities are probably due to the terrestrial and arboring habits of snake, [17] and may possibly be attributed to the absence of an adequate protection during labor activity [4].

The exceptionally high risk of early anaphylactic reactions in bitten patients could be induced either by the snake venom or the antivenon treatment. The allergic reactions due to the snake venom has been described in a few cases, usually after a previous episode of envenomation [15, 18]. Since all patients had no prior history of being bitten, and all episodes were recorded after the beginning of antivenom treatment, this explanation seems less likely. Early anaphylactic reactions to equine serum proteins has a broad range from 3% to 87% [7, 11, 12, 20]. An increased proportion of early anaphylactic reactions observed in adults in our series may be explained, at least in part, by the fact that snakebite patients were more frequently from rural areas where previous sensibilization following horse exposure might be higher. However, some early anaphylactic reactions, also called anaphylactoid reactions, are mediated by IgA rather than IgE. Anaphylactoid reactions are clinically indistinguible from anaphylactic reactions and are neither related to previous exposure to antigens nor predicted by hypersensitivity tests [20]. Although allergic reactions are potentially life threatening, antivenom is the only specific treatment of snakebite patients, and the risk of these reactions should not delay its administration. However, for a successfully therapy, its administration should be carefully monitored.

Pyrogens in the manufactured antivenoms have been responsible for pyretic reactions, rather than characteristics of the host [8, 31]. The higher risk of pyretic reaction in younger snakebite patients when compared with controls may need further confirmation. Studies comparing the frequency of the pyretic reactions before and after standardization of antivenom production in Brazil may provide further information regarding this aspect.

The case-fatality ratio of this series, similar to another hospital-based series in Brazil [21, 25] is almost twice as higher as official statistics[6]. This finding may be possibly attributed to the more severe cases who eventually sought help[1, 8, 21, 24]. The permanent disability despite specific treatment represents a considerable loss of productivity especially when the majority of victims are young and active. The mortality associated with snakebite was not as high as that among matched controls suffering from other acute conditions, suggesting that the severe cases of snakebite are an important treatable cause of morbidity in Brazil. The effectiveness of antivenom in reducing the severity of cases has been discussed elsewhere[8, 31, 32], however, for a successful therapy, the access to a treatment must be considered a priority in allowing immediate care, reducing morbidity from this injury.

Snakebite is an important preventable disease in tropical areas. By identification of high risk groups represented by those who are exposed to rural areas and have agricultural occupational, this study offers a strategy for a primary intervention in this population. The inclusion of snakebite in the list of occupational diseases, with adequate protective policies, may be an approach in public health not only for prevention, but also for an early referral of those who are bitten, decreasing mortality and disability caused by this condition.

RESUMO

Aspectos epidemiológicos e clínicos de acidentes ofídicos atendidos em hospital referência em Belo Horizonte, Minas Gerais, Brasil (1980-1986)

Um estudo clínico-epidemiológico, comparando 310 pacientes hospitalizados por acidentes ofídicos (casos) e 310 pacientes hospitalizados por outras causas (controles), pareados por idade e sexo, durante um período de sete anos, foi conduzido em um hospital de emergências em Belo Horizonte, MG. O diagnóstico dos casos foi baseado no quadro clínico ou na identificação do ofídio. Destes, 56% foram vítimas de serpentes do gênero *Bothrops*, 36% de *Crotalus*, 1% de *Lachesis* e 10% de serpentes não identificadas. Durante o período de estudo, apesar de um aparente aumento, o número de casos manteve-se estável do ponto de vista estatístico, porém com marcada flutuação sazonal. Comparando casos e controles, aqueles de origem rural ou relatando atividade agrícola mostraram riscos de acidentes ofídicos, estimado pela "odds" relativa (OR), de 14,7 e 6,7, respectivamente, sendo portanto identificados como um grupo de alto risco. Com relação ao tratamento, casos mostraram um risco de reações anafiláticas precoces 13,5 maior quando comparados aos respectivos controles; este risco subiu para 30,3 no grupo etário ≥ 20 anos. Casos apresentaram também um maior risco de pirexia (OR = 11,7), mostrando uma associação mais acentuada no grupo etário menor de 19 anos (OR = 16,6). Embora exista tratamento eficaz contra casos graves de acidentes ofídicos no Brasil, este tratamento pode vir acompanhado de efeitos colaterais importantes, chegando algumas vezes a ameaçar a sobrevivência do paciente. A taxa de letalidade descrita, mais alta que as estatísticas oficiais publicadas, mas consistente com outros trabalhos utilizando dados hospitalares, pode ser devida ao fato de que casos graves tendem a procurar hospitalização. Prevenção de acidentes ofídicos e tratamento precoce dos casos é sugerida.

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