Epidemiology and time series analysis of snakebite incidence in Southwestern Iran (Shoushtar) 2017-2022

Abstract

Snakebite incidents are a serious concern. approximately 5.4 million snakebite incidents occur worldwide annually, resulting in 125,000 deaths. This study focused on epidemiological surveys and modeling the time series data of snakebites in Shoushtar City from 2017 to 2022. This study recorded data on 396 individuals who experienced snakebite incidents during the research period. Time series analysis in the medical field involves studying and analyzing data collected over time to identify patterns, trends, and relationships. Time series analysis and appropriate models were used to forecast the trend of cases for future months using BOX-Jenkins models. Findings revealed that the majority of snakebites occurred in men and rural areas. The trend remained constant until the end of 2019, and from the last months of 2019 to the end of 2020, it exhibited an increasing trend (during the peak of the COVID-19 pandemic). The data had a seasonal trend, with the highest occurrences in hot seasons and the lowest occurrences in cold seasons. The age groups of 25-44 years and 10-24 years constituted the largest portion of the victims. The most frequently affected body parts were the foot (58.8%) and hand (38.8%). The majority of individuals sought treatment without delay. The best-fitting model for the available data was a seasonal ARIMA model in the form of ARIMA (0,0,0) (1,0,1)12. Forecasting was carried out for the next 6 months using the selected model, suggesting a decrease in snakebite cases compared to previous periods. Overall, time series analysis in the medical field is crucial in improving patient care, enhancing public health strategies, and advancing medical research. It can also aid in resource allocation and healthcare planning.

Keywords: Epidemiology; Snake Bites; Time Series; Box Jenkins; Southwestern Iran

1. Introduction

Snakebite is a major and significant health problem. Snakes are among the most venomous animals in the reptile category, found in most parts of the world except for the South Pole (1). Snakebite is a significant medical emergency that can lead to immediate patient death. Additionally, it is one of the major causes of mortality and morbidity in tropical and subtropical regions of the world (2). The methods and consequences vary in different regions based on geographical location, season, lifestyle, socioeconomic status, housing conditions, general health of the victim (age, weight, medical history, and individual sensitivity), bite location, number of bites, depth of penetration, injected venom quantity, and other injected microorganisms accompanying the venom (3). The provision of healthcare services and snake species in the region also contribute to the variations. The Southeast Asia region has the highest incidence of snakebite cases worldwide (4). Since reporting snakebite cases is not mandatory in many regions worldwide, accurate global statistics on the incidence are not readily available. However, according to reports, approximately 5.4 million snakebite incidents occur worldwide annually, resulting in about 125,000 deaths, and an additional 400,000 people suffer from permanent complications despite receiving initial care (5).

In 2017, the WHO declared snakebite a critical situation and added it to the list of neglected diseases (6). Prevention and treatment of this complex issue require collaboration among public health, medical, ecological, and laboratory science sectors (7). Because of the increasing number of cases, the World Health Organization committed in 2019 to reduce snakebite-related deaths and disabilities by half by 2030 (8). Iran is also considered one of the countries with a high incidence of snakebites in the world, and the toxicity of 25 out of approximately 69 snake species present in Iran has been proven (9). The majority of cases are reported in the provinces of Sistan and Baluchestan and Khuzestan (10). The diagnosis of snakebite primarily relies on victim self-reporting, laboratory investigations, and a syndromic approach (11). Snakebite caused 63,400 deaths and 2.94 million years of life lost (YLL) globally in 2019. Snakebite occurs more frequently in men than women (12). Individuals engaged in wild environments or agriculture activities such as farming, forestry, fishing, mining, wildlife management, or outdoor work are more exposed to snake bites. Inadequate knowledge regarding initial actions and prompt treatment with antivenom may lead to serious health threats for the victims. Only a few countries have a reporting and registration system for snakebite cases. Additionally, snakebite incidents are more common in rural and remote areas, contributing to underreporting and a lack of accurate data on deaths and occurrences (6, 13). The impact and complications of snakebites depend on factors such as lifestyle, socioeconomic status, housing conditions, age, location and method of exposure, access to medical services, and snake species prevalent in each region. Therefore, studies and research are needed in different locations. In the hot and tropical regions of southern Iran, despite the higher incidence of snakebites compared to other parts of the country, there have been fewer comprehensive studies in this field, particularly regarding the temporal trend of their occurrences. Therefore, in this study, by identifying the time series behavior of snakebite incidents and determining a suitable model, we aim to identify the pattern of their occurrences and predict future trends. By doing so, we intend to assist relevant authorities in controlling and preventing snakebites in this region.

2. Material and method

This descriptive-analytical and time series study of snakebite cases from April 2017 to March 2022 in Shushtar County, Khuzestan Province. Reported data from the local health center were used for analysis. The variables studied included age, gender, region, month of incidence, affected body part, time of incidence, delay in seeking medical care, history of snakebite, and administration of serum. Time series analysis and appropriate models were used to forecast the trend of cases for future months using BOX-Jenkins models.

The overall formula for time series analysis:

[$Y = \text{Trend} + \text{Seasonality} + \text{Residual}$]

(Y) represents the observed data in the time series, (Trend) captures the long-term increase or decrease in the data, (Seasonality) represents the repeating short-term fluctuations in the data, (Residual) is the random variation or error left after the Trend and Seasonality is accounted for.

formula is a basic framework used in time series analysis to decompose the data into its components for better understanding and forecasting.

The modeling process involved three stages: model identification, estimation of parameters for the selected model, and evaluation of the final model. Autocorrelation function (ACF) and partial autocorrelation function (PACF) plots were used to examine the stationarity in the mean and variance. The appropriate model was selected after differencing using autoregressive (AR) p and moving average (MA) q estimations, as well as the AUTO ARIMA command and AIC criterion. Data analysis was conducted using SPSS and R studio software.

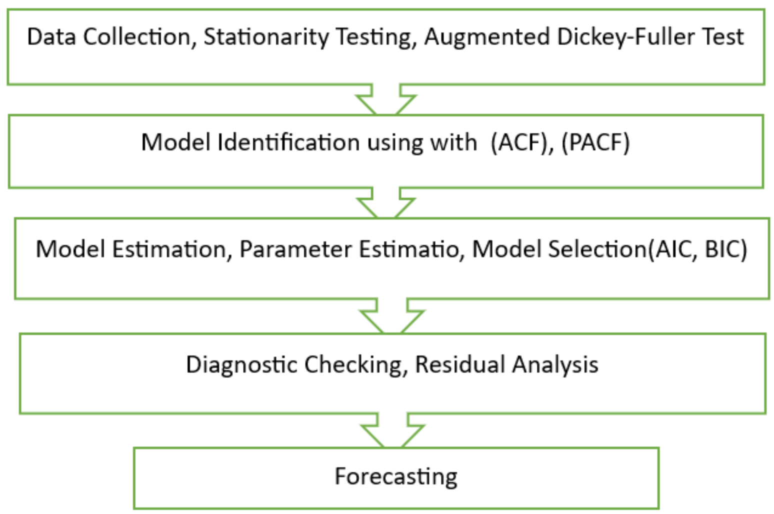

Figure 1: Stages of time series analysis

3. Result

During the study years, information on 396 individuals was recorded as snakebite incidents. The highest occurrence of snakebites was observed in men (79%) and rural areas (68.1%). A significant difference was found between snakebite incidence, gender, and the location of occurrence based on the Chi-square test ($p<0.001$). The age group of 25-44 years (48.9%) and 10-24 years (23.9%) comprised the majority of the victims. No significant difference was observed between age groups and snakebite occurrences. The foot (58.8%) and hand (38.8%) were the most frequently affected body parts. Snakebite incidents were more prevalent from 24:00 to 6:00. Most individuals sought treatment without delay, while (14.1%) experienced a delay of more than 3 hours. Throughout the study, only one fatality occurred in 1399 due to a delay of more than 3 hours in seeking medical attention.

Table 1. Frequency distribution of Snskebite cases by demographic variable in Shushtar County (2017-2022)

Variable	Group	N	%
Gender	Men	313	79
	Women	83	20.9
Bite area	City	126	31.8
	Rural	270	68.1
Age	0-9	26	6.5
	10-24	95	23.9
	25-44	194	48.9
	45-64	63	15.9
	65<	18	4.5
Bitten organ	Head and neck	4	1
	Hand	154	38.8
	Leg	233	58.8
	Trunk	5	1.2
Bite time	24-6	125	31.5
	6-12	89	22.4
	12-18	87	21.9
	18-24	95	23.9
Referral time	>1h	222	56.3
	1-2h	118	29.7
	3<	56	14.1
Recovery time	>6h	358	90.4
	<6h	38	9.5

Time series analysis was used to analyze monthly snakebite data. In the data decomposition plot, Figure 2(A) displays the observed data series, and Figure 2(B) represents the underlying trend in the data. The trend remained constant until the end of 2019, and from the last months of 2019 to the end of 2020, it exhibited an increasing trend (during the peak of the COVID-19 pandemic). There was also a mild increase towards the end of 2021. Figure 2(C) illustrates seasonal variations in the data series. Snakebite cases increased in the first months of the year and then started to decrease. The lowest number of snakebite incidents was observed in November and December, followed by another increase from the month of Mars. Figure 2(D) represents the residual time series after removing trends and seasonal variations from the data, indicating that this part of the graph does not contain any specific patterns in the data

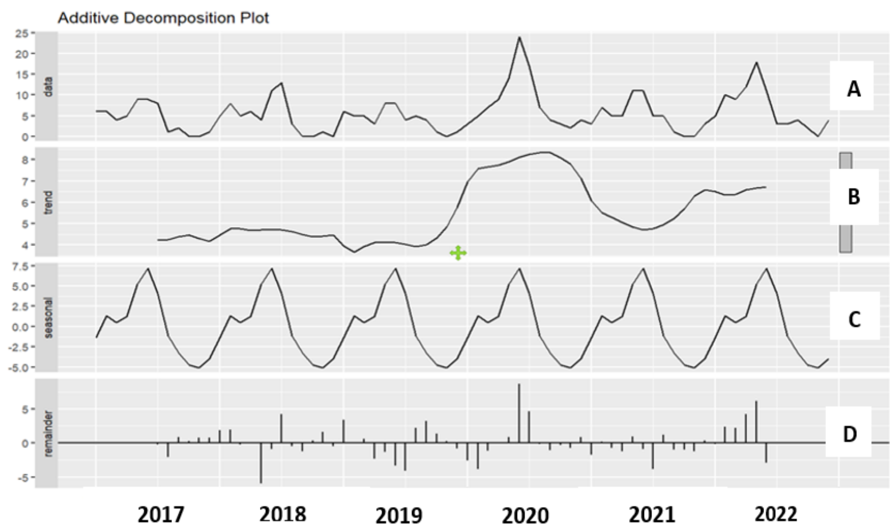

Figure 2: Decomposition of Snakebite cases time series components: trend, seasonality, and residuals

The lack of instability in variance was confirmed using the BOX-COX test, while instability in the mean was observed due to the presence of both increasing and decreasing trends in the data, as well as seasonal patterns. To address the mean instability in the series, a differencing method was applied. This involved performing first-order differencing on the series data once and seasonal differencing once. The resulting plots, including time series, autocorrelation, and partial autocorrelation, are shown after seasonal differencing. Seasonal differencing proved to be more effective in resolving the mean instability in the series.

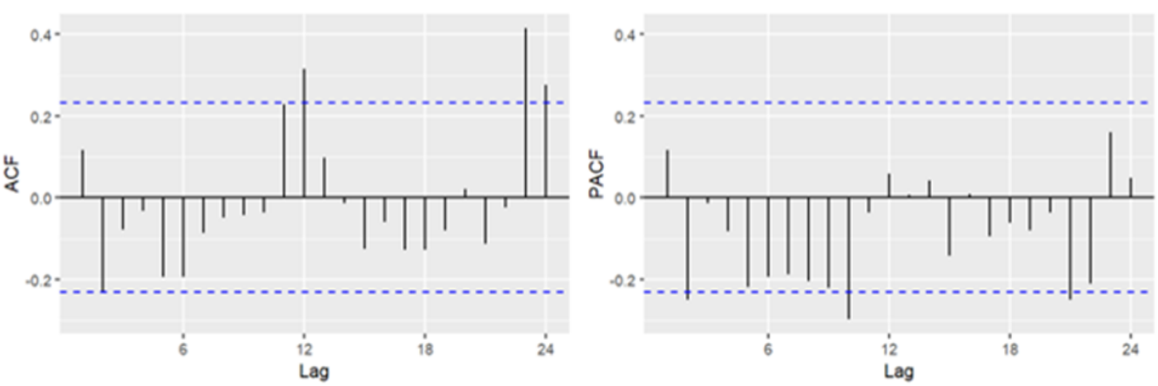

Figure 3: Plot of autocorrelation (ACF) and partial autocorrelation functions (PACF) for Snakebite cases after seasonal differentiation

To determine the initial parameters for Box-Jenkins modeling, autocorrelation, and partial autocorrelation plots were used after seasonal differencing. Considering the significance of the 10th lag in the partial autocorrelation plot and the significance of the 12th lag in the autocorrelation plot, the initial model was considered as a seasonal ARIMA(0,0,0)(1,0,1)12 model. Also, the command 'auto arima' was used to determine the appropriate model for this data. The best-chosen model by the above command was the ARIMA(0,0,0)(1,0,1)12 model. The coefficients and evaluation criteria for this model are shown in Table 2.

Table 2. ARIMA models Final Estimates of Parameters

	SAR1	SMA1
Coef	.8317	-.5408
SE	.1455	.2257
P-Value	0.01	0.00

Log-likelihood	-188.42
AIC	382.85
BIC	389.63

To assess the suitability of the selected model, the residuals of the model were examined by plotting residual graphs and autocorrelation function (ACF) (Figure 4). The results indicated that the distribution of residuals was random and did not exhibit any specific pattern, and no significant autocorrelation was observed in the residuals. The histogram plot of the model residuals showed that they followed a normal distribution.

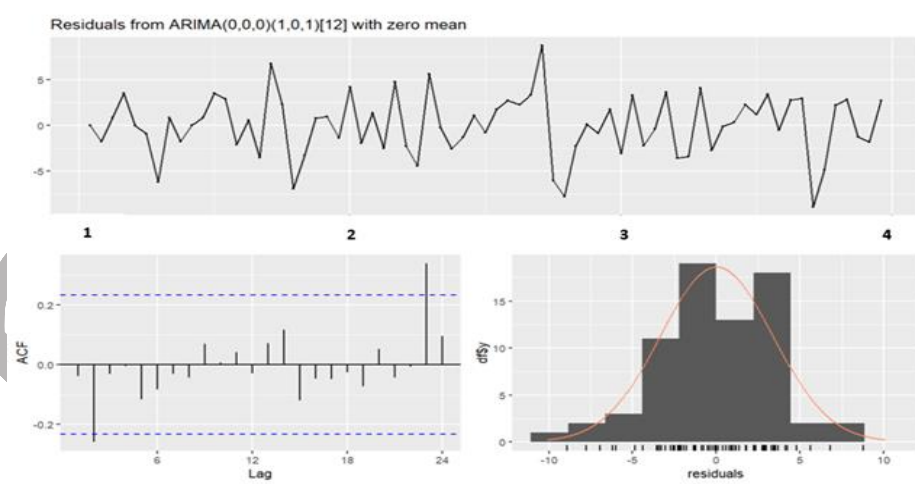

Figure 4: Plot of Autocorrelation function and histogram for the model's residuals.

After examining the remaining components of the model, the monthly snakebite cases were predicted for the next 6 months using the aforementioned model. According to the prediction, the number of cases is expected to decrease compared to the past, and a seasonal trend is also observable in predicting future cases.

Figure 5: Prediction of Snakebite cases with the model for the next 6 months.

4. Discussion

Snakebite is a health problem in poor and developing countries. So fewer studies have been conducted to determine the incidence and influencing factors of this issue. The results of the present study showed a seasonal trend in the occurrence of snakebites, with higher cases in the warm months and fewer cases in the cold months. The incidence rate increased from the last months of 2019 to the end of 2020 (during the peak of the COVID-19 pandemic). In the study by Ebrahimi, Brunda, and Hmimou, the highest number of snakebite cases occurred in the warm months (14.15.16). The increase in snakebite incidents during the hot season can be attributed to the animal's physical conditions, where it is most active at temperatures ranging from 25-32 degrees Celsius. Additionally, the hot seasons in southern regions of Iran coincide with the agricultural season and working in the fields, which can increase human encounters with snakes. The higher rate of snakebites, especially during the peak of the COVID-19 pandemic, could be due to fear of infection and restricted presence in closed spaces, resulting instead visiting gardens and outdoor spaces, which are prone to snake presence. Most cases of snakebite occurrence in men and the age group of 25-44 years was higher. Additionally, in the study conducted by Mulay, Buranasin, and Dehghani, the highest number of snakebite cases was observed in men and the age group of 10-44 years (17, 18). The higher prevalence of snakebites in men and the active age group of the community could be due to the higher involvement of men in farming and agriculture, as well as their presence in snake habitats. Additionally, men may engage in more risky activities compared to women. The higher incidence of snakebites in rural areas can be attributed to various factors such as inappropriate rural environments, suitable conditions for snakes to hide and live in, and the presence of farms and orchards. snakebites were observed to have a uniform distribution over the 24 hours, with slightly elevated from midnight to 6 am. This discovery contradicted the findings of the research conducted by Leite (19). Similarly, Ebrahimie's study in Haji-Abad, southern Iran, found that snakes exhibited higher levels of activity during the late-night to early-morning period (16).

This is likely due to nocturnal resting in open areas in rural regions caused by hot weather in these areas. Most injured individuals had sought treatment within the first 2 hours. In the study by Jamshidi and Tavares, the majority of the injured had visited the medical center in less than 1.5 hours (20, 21). In the study by Ebrahimi, 75% of the injured had sought treatment in less than 3 hours (16). The majority of victims seeking medical attention in less than 2 hours indicates the importance of the issue and awareness of its urgency in this county. Since the time interval between snakebite incidents and the administration of anti-venom is crucial for saving the victim's life, there should continue to be a general public education on the need for timely treatment and emphasis on the importance of the issue. Moreover, considering the climate of Shush, and the hot weather, activities are mostly conducted in the warm seasons after sunset. Additionally, since snakes often prefer dark places and their highest activity and hunting occur during the night, an increase in encounters with snakes during this period seems natural. The most affected body parts were the feet and then the hands. In the study by Hati, Ochola, and Kassiri, most snakebites occurred on the lower limbs and then the hands (22, 23, 24). Walking barefoot in snake-prone areas and the increased use of these areas during work and activity can be some of the reasons for the higher incidence of snakebites in these regions, even without protection (such as boots and gloves).

Based on time series analysis and the ARIMA(0,0,0)(1,0,1)12 model, the forecast indicated a decrease in cases for the next 6 months. However, according to Ebrahimi's study, the ARIMA(1,0)(1,1)12 model was found to be the best for prediction, which differed from the fitted model in this study where AR=1 (16). In Zamani's study, the appropriate model was determined to be the first-order moving average (AR=1) with the first-order autoregressive (MA=1) (25)In all three studies, the presence of seasonal patterns in the data was also highlighted. Therefore, it can be concluded that incorporating seasonal factors in the models provides the best approach for identifying and predicting the time series patterns used in this analysis. The occurrence pattern in each region differs according to its climatic and ecological conditions, and a limitation of this study is its narrow focus on a specific area without considering a broader region.

Acknowledgment
The authors express their gratitude to the staff of Shushtar Health Center for their valuable contributions to this study.

Conflict of interest
The author(s) declare that they have no competing interests.

Funding
This research did not receive any specific funding from public agencies, or commercial or not-for-profit organizations

Ethics
The present research was supported and approved by the Shoushtar Faculty of Medical Sciences (IR.SHOUSHTAR.REC.1398.006).

Author Contributions

Study concept and design: F. R, S A. M
Acquisition of data: H. R
Analysis and interpretation of data: F. R, S A. M
Drafting of the manuscript: F. R, S A. M, L. S, H. R
Critical revision of the manuscript for important intellectual content: S A. M, L. S, H. R
Statistical analysis: F. R, S A. M
Study supervision: S A. M, L. S, H. R

References

1. Dehghani R, Dadpour B, Mehrpour O. Epidemiological profile of snakebite in Iran, 2009-2010 based on information of Ministry of Health and Medical Education. International journal of medical toxicology and forensic medicine. 2014;4(2):33-41.

2. Kasturiratne A, Lalloo DG, de Silva HJ. Chronic health effects and cost of snakebite. Toxicon: X. 2021;9:100074.

3. Hasson S, Al-Jabri A, Sallam TA, Al-Balushi MS, Mothana RA. Antisnake venom activity of Hibiscus aethiopicus L. against Echis ocellatus and Naja n. nigricollis. Journal of Toxicology, 2010:8.

4. Patra A, Mukherjee AK. Assessment of snakebite burdens, clinical features of envenomation, and strategies to improve snakebite management in Vietnam. Acta Tropica. 2021;216:105833.

5. Bhaumik S, Beri D, Jagnoor J. The impact of climate change on the burden of snakebite: Evidence synthesis and implications for primary healthcare. Journal of Family Medicine and Primary Care. 2022;11(10):6147.

6. Bawaskar HS, Bawaskar PH, Bawaskar PH. The global burden of snake bite envenoming. SAGE Publications Sage UK: London, England; 2021. p. 7-8.

7. Chippaux, J.-P. Snakebite envenomation turns again into a neglected tropical disease! J. Venom. Anim. Toxins Incl. Trop. Dis. 23, 38 (2017).

8. Seifert SA, Armitage JO, Sanchez EE. Snake envenomation. New England Journal of Medicine. 2022;386(1):68-78.

9. Nejadrahim R, Sahranavard M, Aminizadeh A, Delirrad M. Snake envenomation in North-West Iran: A three-year clinical study. Int J Med Toxicol Forensic Med. 2019;9:31-8.

10. Kassiri H, Dehghani R, Khodkar I, Ahmad FA, Kassiri A. Epidemiological profile of venomous animal bites and stings (A neglected problem) in the north of Sistan-Baluchistan province, South-Eastern Iran. Journal of Entomological Research. 2022;46(4):917-21.

11. Knudsen C, Jürgensen JA, Føns S, Haack AM, Friis RU, Dam SH, et al. Snakebite envenoming diagnosis and diagnostics. Frontiers in immunology. 2021;12:661457.

12. Roberts NLS, Johnson EK, Zeng SM, Hamilton EB, Abdoli A, Alahdab F, et al. Global mortality of snakebite envenoming between 1990 and 2019. Nature Communications. 2022;13(1):6160.

13. Chippaux JP. Snake-bites: an appraisal of the global situation. Bulletin of the World Health Organization. 1998;76(5):515.

14. Brunda G, Sashidhar R. Epidemiological profile of snake-bite cases from Andhra Pradesh using the immunoanalytical approach. Indian journal of medical research. 2007;125(5):661-8.

15. Hmimou R, Soulaymani A, Mokhtari A, Arfaoui A, Eloufir G, Semlali I, Soulaymani BR. Risk factors caused by scorpion stings and envenomations in the province of Kelâa Des Sraghna (Morocco). J. Venom. Anim. Toxins incl. Trop. Dis 2008; 14(4): 628-40.

16. Ebrahimi V, Hamdami E, Khademian MH, Moemenbellah-Fard MD, Vazirianzadeh B. Epidemiologic prediction of snake bites in tropical south Iran: Using seasonal time series methods. Clinical Epidemiology and Global Health. 2018 Dec 1;6(4):208-15.

17. Mulay DV, Kulkarni VA, Kulkarni SG, Kulkarni ND, Jaju RB. Clinical profile of snake bites at SRTR Medical College Hospital, Ambajogai (Maharastra). Indian Med Gazette 1986; 131: 363-6.

18. Buranasin P. Snake bites at Maharat Nakhon Ratchasima Regional Hospital. Southeast Asian J Trop Med Public Health 1993; 24: 186-92.

19. Leite RD, Targino IT, Lopes YA, Barros RM, Vieira AA. Epidemiology of snakebite accidents in the municipalities of the state of Paraíba, Brazil. Ciência & Saúde Coletiva. 2013;18:1463-71.

20. Jamshidi, Alizadeh Barzian, Kazem, Alizadeh Barzian, Mohammad, Danshi, Karimian Souq, Jamshidi, Berem Sabz. Investigation of snakebite in patients referred to medical centers in Behbahan city in 2016-2017. stupid 2022 Jan 21;25(4).

21. Tavares AV, Araújo KA, Marques MR, Vieira AA, Leite RD. The epidemiology of snakebite in the Rio Grande do Norte state, northeastern Brazil. Revista do Instituto de Medicina Tropical de São Paulo. 2017 3;59.

22. Hati AK, Mandal M, De MK, Mukherjee H, Hati RN. Epidemiology of snake bite in the district of Burdwan, West Bengal. Journal of the Indian Medical Association. 1992 Jun 1;90(6):145-7.

23. Ochola FO, Okumu MO, Muchemi GM, Mbaria JM, Gikunju JK. Epidemiology of snake bites in selected areas of Kenya. Pan African Medical Journal. 2018;29(1):1-4.

24. . Kassiri H, Khodkar I, Kazemi S, Kasiri N, Lotfi M Epidemiological analysis of snakebite victims in southwestern Iran Journal of Acute Disease 2019;8(6):260.

25. Zamani Alvijeh Fareshte, Dehdari Tahereh, Ahmadi Angali Kambiz, Taghi Rahdari Mina, Azar Abdar Tahereh, Ashrafi Hafez Asghar, Babaei Hyderabadi Akbar. Epidemiological study of

24 months and estimation of snake and scorpion bites among patients at 22 Bahman Hospital in Masjid Sulaiman based on time series model.