



Excess Animal Bite Cases Associated with the COVID-19 Pandemic: Evidence from a Time Series Analysis (2016 - 2023) In Razavi Khorasan Province

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Abstract

Background: The advent of COVID-19 has profoundly impacted the welfare of both humans and animals.

Objectives: The objective of this study is to investigate the impact of the COVID-19 pandemic on animal bite trends in order to inform rabies prevention strategies.

Methods: Data on bite incidents were collected from the Canter Control Health Rabies between April 2016 and March 2023 in Razavi Khorasan province. The data from 2016 to 2020 were regarded as the baseline for comparison to assess changes in animal bite cases during the COVID-19 pandemic. A quantitative technique known as univariate time series analysis was used to analyze animal bite victims by their monthly occurrence, and excess cases were calculated.

Results: During the COVID-19 pandemic, 40,324 cases were registered, and 32,087.83 cases were estimated (16,481.87 - 47,693.78). Changes in trend were -5.07% in 2020 - 2021, 30.25% in 2021 - 2022, and 54.72% in 2022 - 2023. During the third year of the Coronavirus pandemic, women experienced a change of over 90%, middle-aged adults had an estimated 70.79%, seniors had an estimated 43.38%, and children aged 11 to 20 had an estimated 26.80%. An estimated 81.09% occurred for self-employed individuals, 69.30% for students, 67.75% for homemakers, and 91.14% and 34.11% for urban and suburban areas.

Conclusions: The COVID-19 pandemic exposed the fragility of our immunological defenses against a fatal zoonosis. Shifts in animal bite patterns directly reflect population exposure risk and the healthcare system's capacity to deliver time-sensitive, life-saving immunological interventions. This underscores the urgent need for resilient strategies, guided by a One Health framework, to ensure uninterrupted access to essential vaccines and immunoglobulins during public health crises.

Keywords: Trend Analysis, Animal Bite, Post-exposure Prophylaxis, COVID-19, One Health

1. Background

Rabies is a fatal viral disease that primarily affects mammals, including humans, by targeting the nervous system. This pathogenesis is characterized by the virus's remarkable ability to evade host immune surveillance. Following a bite, the rabies virus (RABV) often replicates locally in muscle tissue before entering peripheral

nerves and traveling retrograde towards the central nervous system (CNS), an immune-privileged site where it can cause devastating encephalitis before an effective immune response can be mounted (1). Transmission typically occurs through the saliva of infected animals via bites or scratches. The virus's interaction with the host's innate immune system at the wound site is a critical determinant of infection outcome, with RABV encoding proteins that can actively suppress early

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interferon responses, thereby facilitating its silent entry into the nervous system (2).

Immediate medical intervention following exposure, especially from wild or unfamiliar animals, is critical to prevent disease onset. This intervention, known as post-exposure prophylaxis (PEP), is a classic example of immunotherapy and active immunization working in concert. PEP involves thorough wound cleansing, administration of rabies immunoglobulin (RIG) to provide immediate passive immunity at the exposure site, and a series of inactivated RABV vaccinations to stimulate the patient's adaptive immune system. The primary goal is to induce a robust titer of rabies virus-neutralizing antibodies (RVNAs) before the virus can reach the CNS, as these antibodies are the established correlate of protection (3). The risk of contracting rabies, combined with injuries from animal bites and the disease's near-universal fatality once symptoms manifest, represents a significant public health challenge. To eliminate rabies, healthcare systems must enhance their prevention and management strategies (3).

The COVID-19 pandemic has profoundly impacted global health, economics, social structures, and daily living, resulting in severe disruptions and livelihood threats (4-6). Early in the pandemic, resources were reallocated to prioritize COVID-19 detection and treatment, jeopardizing a decade of progress against other diseases, including rabies (7). This crisis also created a unique immunological landscape. The widespread immune activation and potential immune modulation caused by SARS-CoV-2 infection or COVID-19 vaccination raised theoretical concerns about possible interference with the immunogenicity of concurrent vaccines, including rabies, highlighting a critical area of investigation at the intersection of virology, immunology, and pharmacology (4). This crisis has underscored the importance of sustainable disease control methods and reinforced the necessity of understanding the complex interactions between humans, animals, and the environment. Gathering robust epidemiological data on animal bites in humans is crucial for effective rabies surveillance, resource distribution, and improving health outcomes for both populations, particularly in developing countries where surveillance is hindered by underreporting and misdiagnosis (6, 8-10).

Time series analysis offers a powerful tool to assess healthcare delivery by tracking error patterns, evaluating intervention outcomes at the population level, and simultaneously investigating intended and unintended effects (6, 11, 12). Using this approach, we

analyzed PEP cases for animal bites treated at the Anti-Rabies Clinic from April 2016 to March 2023.

The COVID-19 pandemic significantly altered animal bite trends in Razavi Khorasan, with initial lockdowns reducing cases, followed by a sharp increase as restrictions eased. This study identifies key demographic shifts and geographic patterns, highlighting the pandemic's indirect effects on human-animal interactions. These findings emphasize the need for a One Health approach to rabies prevention, focusing on responsible pet ownership, community engagement, and improved public health strategies to mitigate future outbreaks.

2. Objectives

The objective was to compare actual and projected cases during the COVID-19 pandemic period. The findings will inform the development of enhanced rabies prevention and control guidelines at Razavi Khorasan province.

3. Methods

3.1. Geographic Context and Data Sources for Animal Bite Incidents

Between April 2016 and March 2023, all individuals with animal bite injuries who presented to the Center for Control and Prevention of Rabies in Razavi Khorasan province, Iran, were included in this retrospective observational study. As all cases reported to the center during the study period were analyzed, no specific inclusion or exclusion criteria were applied.

Each patient's demographic information was collected, including age, sex, occupation, and location. The information was used to identify potential risk factors and patterns in animal bite incidents.

3.2. Statistical Analysis

Seasonal Autoregressive Integrated Moving Average (SARIMA) was constructed based on the monthly occurrence of cases during the study period. A SARIMA model consists of seven parameters, including (p,d,q), (P,D,Q), and s, where p is the number of autoregressive terms, d indicates the number of differences, q indicates the number of moving averages, P indicates the number of seasonal autoregressive terms, D indicates the number of seasonal differences or integrations, Q indicates the number of seasonal moving averages, and s indicates the length of the seasonal periods (s = 12 months in this study). To fit the model, the following steps were taken:

The first step was to assess stationarity in the variance using a diagram of the disease trend and the Box-Cox test. The number of animal bite cases in the model was transformed if there was non-stationarity in the variance. To test stationarity in the means of the series, we used the Dicky-Fuller test. First-order seasonal differencing ($D = 1$) with a period of 12 was used to remove the seasonality trend. All further analyses were conducted on stationary data.

The next step was to determine the parameters of the model AR (p , P) and MA (q , Q) using autocorrelation function (ACF) plots. In order to select the best and most parsimonious univariate model, different SARIMA models were compared using the likelihood ratio test. In order to evaluate the goodness-of-fit of the final model, we used the Ljung-Box (Q) test for residuals to determine if they are white noise, i.e., mean = 0 and constant variance (13-15).

The number of cases under "normal" circumstances occurring from March 2020 to March 2023 was based on the number of cases from April 2016 to February 2020, regressed with a 95% prediction interval: Excess cases = Reported cases - Expected cases.

The number of excess cases gives us a sense of scale, but it is less comparable across time, regions, and population subgroups. In order to make these comparisons, it is easier to compare reported cases with projected cases. This metric is called the P-score and we calculate it as follows: $P\text{-score} = (\text{Reported cases} - \text{Expected cases}) / (\text{Expected cases}) \times 100$.

When the observed number of cases falls below the baseline, the P-score can be negative. A yearly P-score is calculated by averaging 12 months' P-scores (15). All analyses were done with Stata14 software (StataCorp, College Station, TX, USA).

4. Results

In the periods April 2016 - February 2020 and March 2020 - March 2023, Razavi Khorasan province reported 36,277 and 40,324 dog bite incidents, with 69,898 (91.25%) being bites by dogs. Table 1 shows the goodness-of-fit evaluation of the models using the Ljung-Box (Q) test and AIC. For each series of animal bite incidents between April 2016 and February 2020, best fit models were developed and forecasted between March 2020 and March 2023, regressed with a 95% prediction interval and compared with reported cases using the P-scores given in Table 2.

In Table 2, the trends of animal bites are shown based on the demographic characteristics of the victims. From March 2020 to March 2023, there has been a clear

increase in the number of all cases. However, victims' characteristics experienced varying changes. It was found that an exponential increase in animal bites occurred in the first year of the COVID outbreak and continued in the second year. In the last two years, women were about twice as vulnerable as men.

The age was broken down into 10-year intervals. P-scores for ages 0 - 10 are more stable from March 2020 to 2023. The P-score for animal bites in ages 11 - 20 dropped in 2020, but in 2021 and 2022 it sharply increased. As well as in 2020, the P-score of animal bites among ages 11 - 20 and 31 - 40 dropped, but rose sharply in 2021 and 2022. P-scores for animal bites in ages 21 - 30 declined in 2020 and 2021, but spiked in 2022. P-scores for animal bites in ages 41 and over have increased in the current three consecutive years, especially in the elderly.

Those who work with animals, such as veterinarians, animal control workers, and laboratory personnel, are considered at risk of contracting rabies. According to the findings of this study, the risk of animal bites changed over time in different kinds of work. As compared to earlier times, P-scoring of animal bites in farmers and animal husbandry decreased from March 2020 to 2023. In 2020, the P-score of animal bites in housekeepers declined, but in 2021 and 2022, it soared. Over the past two years, students have also increased their P-scores for animal bites. Additionally, this event has increased for the last three consecutive years in workers/municipal workers. The report noted that self-employment was one of the more sensible jobs, especially in the last year. There were increases in P-scores for other categories of jobs as well.

It also illustrates the local distribution of animal bite victims. In rural areas, this event decreased in the first year of the outbreak, but slightly increased two years later. Throughout the current three continuous years, animal bite victims have increased in both semi-urban and urban areas. However, people in urban areas have experienced worse conditions.

5. Discussion

This study examines the patterns of animal bite incidents spanning from April 2016 to March 2023, emphasizing notable differences before and during the COVID-19 pandemic by applying optimized predictive models tailored to each victim category. Dog bites constituted over 90% of new reported cases at the Anti-Rabies Clinic, consistent with findings from previous research indicating that trends in overall animal bite incidents largely reflect dog bite occurrences (16, 17).

From an immunological and pharmacological perspective, each animal bite represents a potential

Table 1. Characteristics of the Best Seasonal Autoregressive Integrated Moving Average Fitted Models' Series of Animal Bite Victims from April 2016 to February 2020

Characters of Victims	The Best Model ^a	Ljung-Box (Q) Test (P-Value) ^b	ALC
Total	SARIMA (2,0,0), (1,0,0,12)	0.52	208
Gender			
Male	SARIMA (1,0,1), (1,0,0,12)	0.43	211
Female	SARIMA (1,0,0), (1,0,0,12)	0.56	265
Age groups (y)			
≤ 10	SARIMA (2,0,1), (1,0,1,12)	0.80	192
11 - 20	SARIMA (3,0,1), (1,0,1,12)	0.88	209
21 - 30	SARIMA (2,0,1), (1,0,0,12)	0.49	243
31 - 40	SARIMA (2,0,2), (1,0,0,12)	0.99	187
41 - 50	SARIMA (2,0,2), (1,0,0,12)	0.47	305
51 - 60	SARIMA (2,0,2), (1,0,0,12)	0.56	218
61 - 70	SARIMA (3,0,1), (1,0,0,12)	0.68	310
≥ 71	SARIMA (2,0,1), (1,0,0,12)	0.81	268
Nature of work			
Farmer and animal husbandry	SARIMA (3,0,1), (1,0,0,12)	0.91	318
Housewife	SARIMA (1,0,1), (1,0,0,12)	0.32	286
Student	SARIMA (2,0,0), (1,0,0,12)	0.40	328
Worker/municipal worker	SARIMA (1,0,1), (1,0,1,12)	0.57	353
Self-employed	SARIMA (2,0,1), (1,0,1,12)	0.58	217
Others	SARIMA (3,0,1), (1,0,1,12)	0.54	293
Habitat of the victims			
Rural	SARIMA (3,0,1), (1,0,1,12)	0.84	197
Semi-urban	SARIMA (3,0,1), (1,0,1,12)	0.76	245
Urban	SARIMA (3,0,2), (1,0,0,12)	0.16	302

Abbreviations: ALC, Akaike criterion; SARIMA, Seasonal Autoregressive Integrated Moving Average.

^a SARIMA (p, d, q), (P, D, Q, s).

^b The portmanteau test for residuals white noise.

exposure event that demands a rapid and effective medical countermeasure: PEP. A pronounced downturn in bite cases was observed during the initial year of the COVID-19 outbreak, primarily due to government-imposed lockdowns limiting human mobility. However, this reduction may also reflect diminished access to these critical anti-rabies services amid broader disruptions in healthcare provision (5, 18, 19). This disruption has profound implications, as delays in administering PEP critically narrow the window of opportunity to prevent the fatal neuroinvasion of the RABV (1).

The subsequent resurgence in bite incidences as restrictions eased placed renewed strain on PEP delivery systems. The efficacy of this regimen relies on a two-pronged immunological strategy: The immediate provision of passive immunity via RIG to neutralize the virus at the wound site, and the induction of active, long-lasting immunity through a series of vaccinations that stimulate the production of RVNAs (3). The pandemic raised critical questions about potential

immune interference; widespread SARS-CoV-2 infection and vaccination created a unique immunological landscape, with theoretical concerns that the systemic immune activation or dysregulation could alter the immunogenicity of concurrent vaccines (4). As restrictions eased, there was a moderate to sharp resurgence in bite incidences over the next two years, likely driven by increased movement and other pandemic-related factors, coupled with a rising dog population.

According to our study, the age, gender, region, and occupation of the victims clearly changed over time. The high-risk groups shifted towards children, women, the elderly, and urban areas and occupations that had lower statistics in the past. These transitions likely result from complex interactions involving changes in human and animal behavior, environmental conditions, healthcare access, and socio-economic factors during the pandemic. Notably, pet ownership – especially of dogs and cats – increased markedly during this period (20). Despite the upward trend in animal bites and escalating

Table 2. Patterns of Animal Bite Victims Reported Versus Projected and P-Scores from April 2016 to March 2023^a

Cause of Victims	2016 - 2019			2020 - 2021			2021 - 2022			2022 - 2023		
	Reported Cases	Predicted Cases	P-Score	Reported Cases	Predicted Cases	P-Score	Reported Cases	Predicted Cases	P-Score	Reported Cases	Predicted Cases	P-Score
Total	36277	36299.68 (24370.05 - 48029.32)	0.21	10898	11480.83 (6811.80 - 16149.86)	-5.07	13086	10046.29 (4807.09 - 15285.48)	30.25	16340	10560.7 (4862.97 - 16258.44)	54.72
Gender												
Male	26872	26880.85 (17780.97 - 35980.73)	0.01	8801	8629.05 (4968.88 - 12289.23)	0.27	10221	7334.16 (3316.07 - 11352.26)	36.25	12315	7859.07 (3504.87 - 12213.27)	53.79
Female	6725	6709.09 (3826.22 - 9591.96)	0.09	2068	2026.70 (1301.25 - 2752.15)	0.37	2865	1830.11 (1044.66 - 2555.56)	51.68	4025	1934.48 (1148.57 - 2720.39)	99.07
Age groups (y)												
≤ 10	5427	5491.26 (3126.39 - 7856.13)	-0.02	1530	1426.37 (598.59 - 2254.14)	-0.20	2085	1331.32 (436.70 - 2225.93)	0.09	2569	1475.10 (481.70 - 2468.50)	0.12
11 - 20	6184	6131.68	0.53	1997	2106.99 (1372.63 - 2841.34)	-7.39	2470	2171.07 (1064.67 - 3057.46)	11.78	2880	2248.11 (973.28 - 3262.94)	26.80
21 - 30	7523	7479.15 (5091 - 9866.64)	0.58	1980	2415.89 (1553.76 - 3278.01)	-0.19	2191	2178.75 (1208.69 - 3148.82)	-1.48	2703	2274.34 (1206.8 - 3341.88)	16.64
31 - 40	6780	6659.57 (4165.12 - 9154.01)	1.77	2179	2439.94 (1621.16 - 3258.73)	-10.21	2497	2294.77 (1245.79 - 3343.74)	5.50	3167	2331.28 (1074.93 - 3587.63)	12.07
41 - 50	4200	4199.43 (2426.68 - 5972.18)	0.14	1372	1283.01 (630.37 - 1935.64)	7.30	1643	1118.3 (422.11 - 1814.47)	42.08	2121	1207.51 (453.29 - 1961.72)	70.79
51 - 60	3360	3368.92 (1877.75 - 4860.1)	-5.8	1028	950.56 (475.08 - 1426.04)	8.19	1202	860.61 (351.51 - 1369.71)	12.78	1555	910.874 (356.15 - 1465.59)	14.00
61 - 70	1817	1815.14 (820.30 - 2809.97)	-0.31	546	526.08 (213.22 - 838.93)	4.12	685	481.45 (153.0 - 809.91)	16.12	926	516.84 (160.87 - 872.82)	37.81
≥ 71	985	983.05 (408.45 - 1557.66)	0.13	265	265.95 (95.90 - 436.0)	3.46	311	254.95 (81.28 - 428.61)	20.77	419	275.02 (86.85 - 463.19)	43.38
Nature of work												
Farmer and animal husbandry	4703	4731	-0.32	1462	1503.33 (756.77 - 2240.88)	-4.08	1290	1291.15 (510.80 - 2071.50)	-0.51	1200	1264.73 (483.78 - 2045.68)	-3.86
Housewife	3961	3951.06 (2194.9 - 5707.23)	0.25	1128	1152.17 (636.30 - 1668.02)	-1.10	1415	1039.62 (465.02 - 1614.22)	30.25	1931	1114.12 (488.46 - 1739.77)	67.75
Student	6824	6782 (4303.93 - 9262.72)	0.55	2412	2311.98 (1446.96 - 3177.0)	1.41	3151	2108.9 (1061.67 - 3156.13)	47.27	3799	2173.15 (985.56 - 3360.74)	69.30
Worker/municipal worker	193	463.09 (0 - 464.13)	0.72	76	149.28 (22.61 - 188.13)	9.08	169	189.70 (0 - 183.10)	16.00	241	225.12 (0 - 194.60)	11.54
Self-employed	8909	8772.16 (5351.9 - 12192.4)	1.47	3098	2921.37 (1801.38 - 4041.35)	4.5	3764	2697.74 (1446.1 - 343.32)	36.37	5133	2758.94 (1370.88 - 4145.99)	81.09
Others	2016	2018.73 (993.57 - 3043.87)	-0.22	686	6339.56 (339.86 - 939.26)	8.51	797	580.61 (263.94 - 897.27)	17.95	876	606.21 (260.93 - 951.5)	14.65
Habitat of the victims												
Rural	14272	14290.6 (9579.8 - 19001.4)	-0.22	4389	4419.97 (2518.58 - 6321.36)	-1.19	4931	3896.98 (1822.19 - 5971.77)	5.39	5500	4129.94 (1872.31 - 6387.57)	9.37
Semi-urban	3180	3169.49 (1381.99 - 4956.99)	0.34	1166	848.26 (221.39 - 1475.13)	14.25	1338	810.79 (41.86 - 1479.72)	32.31	1468	878.92 (154.05 - 1603.8)	34.11
Urban	13627	13568.6 (7943.89 - 19193.4)	0.45	4193	3985.28 (2271.72 - 5698.84)	4.41	5854	3789.83 (1981.3 - 5598.37)	52.97	7837	3903.89 (1919.13 - 5888.65)	91.14

^a Values are expressed as confidence intervals.

pet populations, studies specifically addressing this issue remain limited.

The COVID-19 pandemic has profoundly influenced both human and animal health (21), indirectly impacting veterinary services and disease control efforts due to economic instability and movement restrictions (12, 22). Coronaviruses can infect a range of animal species, including livestock and companion animals, causing respiratory and gastrointestinal disease, though there is no direct evidence linking infection to increased biting behavior (23-26).

Several factors may explain the observed rise in animal attacks during the pandemic. Stress induced by public health measures altered dog behavior, elevating bite risk, particularly amid lockdown conditions (22). Behavioral studies reported increased anxiety and attachment behaviors in dogs during the pandemic period, although results on interventions to mitigate

these effects were inconclusive (23). Additionally, pathogen-induced sickness behavior in animals and humans – manifesting as sleep disturbances, anorexia, and cognitive impairment – could contribute to elevated aggression (23, 25).

Moreover, social distancing and movement restrictions have intensified emotional and economic stress within households, potentially amplifying family violence and indirectly affecting animal behavior (19, 26-28). Dogs, sensitive to their owners' emotional states, may respond to increased household tension with heightened aggression or biting incidents (26).

While most evidence regarding pandemic-related changes in animal bite epidemiology originates from countries with distinct cultural contexts, Iran has experienced a substantial rise in pet ownership, especially dogs and cats, although official data are scarce. This growth, while beneficial in some respects,

raises concerns about zoonotic disease risks due to gaps in owner knowledge about appropriate pet care and hygiene, potentially increasing bite incidents and disease transmission.

The study provides valuable insight into how the COVID-19 pandemic influenced animal bite incidents, but certain limitations must be acknowledged. Since the research relied on data from a single health facility, it may not fully capture broader regional trends. A more extensive dataset covering multiple healthcare centers would offer a more comprehensive perspective. Furthermore, while the study suggests an indirect link between the pandemic and shifts in bite patterns, isolating specific causal factors remains challenging due to the complex interaction between human behavior, animal dynamics, and environmental influences. Additionally, although the findings indicate that the pandemic affected bite trends, definitive proof of causation is lacking, as local policies and socioeconomic conditions may have also contributed to observed changes.

Despite these limitations, the study has several notable strengths. The application of time-series analysis provides a rigorous method for evaluating patterns and trends in bite incidents over time. One of the key contributions is the identification of demographic and geographic shifts in bite cases, underscoring the pandemic's broader implications on human-animal interactions. The research further highlights the necessity of considering indirect pandemic effects when shaping public health interventions. To address the multifaceted challenges posed by zoonotic diseases, the study reinforces the importance of a multi-sectoral One Health approach, emphasizing responsible pet ownership, community engagement, and collaborative efforts across health sectors.

In conclusion, our findings highlight significant demographic and behavioral shifts in animal bite victims, but more fundamentally, they reveal the fragility of our immunological defenses against a fatal zoonosis during a global crisis. The observed fluctuations in bite cases are not merely epidemiological curiosities; they directly reflect the population's exposure risk and the healthcare system's capacity to deliver a time-sensitive, life-saving immunological intervention. This underscores the urgent need for resilient prevention strategies, robust community education on PEP, and policies that ensure uninterrupted access to essential vaccines and immunoglobulins. Adopting a One Health framework – integrating human, animal, and environmental health

perspectives – is crucial for the effective control of rabies and related zoonoses in this evolving context.

Footnotes

AI Use Disclosure: The authors declare that no generative AI tools were used in the creation of this article.

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Data Availability: The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

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