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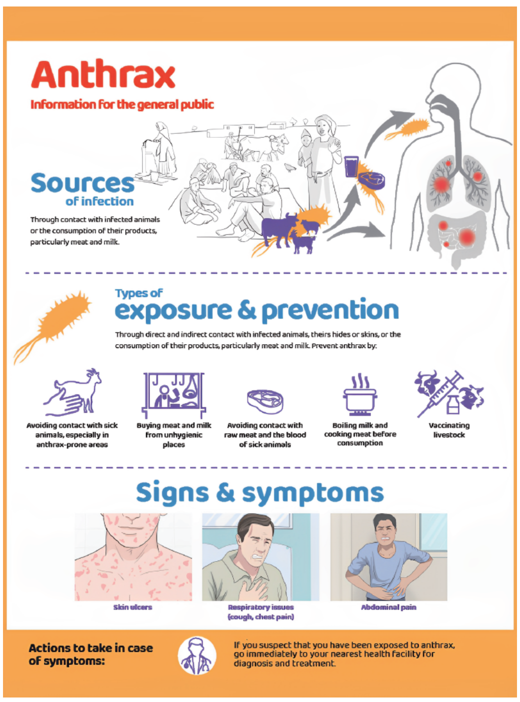

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Preplanned Studies

Sanitary Evaluation of Rural Water Supply Projects — China, 2020

Yunting Xia[1]; Hongxing Li[1,#]; Chuanlong Xiong[1,#]; Rong Zhang[1]

Summary

What is already known about this topic?

Over the last decade, the centralized water quality and supply have been substantially enhanced in rural China. However, compared with the urban water supply, most of the rural Water Supply Projects (WaSPs) are small in scale, simple in engineering facilities, and poor in management.

What is added by this report?

Most of the rural WaSPs have been basically guaranteed sustainable sources of water. More measures should be taken to improve water disinfection effects, water losses control, and operational and maintenance management. The WaSPs with water supply <3,000 m^3/d need to be paid more attention.

What are the implications for public health practice?

Laws and regulations requiring rural WaSPs to carry out a sanitary evaluation should be established. WaSPs should use tools such as World Health Organization Water Safety Plans to identify and control risks.

Safe drinking water is one of the most important factors affecting health (*1*). China's rural centralized water supply coverage has improved significantly since 2005. More than 9.31 million rural Water Supply Projects (WaSPs) have been constructed and the rate of central water supply directed at rural areas reached 88% by 2020 (*2*). Compared with the urban water supply, most of the rural WaSPs are smaller in scale, simpler in design, and poorly managed (*3*). This study aimed to understand the evidence provided by the Sanitary Evaluation of Rural Water Supply Projects (SERWaSP) using 160–180 typical rural WaSPs to identify potential water quality risks. The study was conducted between August and November, 2020 in 66 counties within 18 provincial-level administrative divisions (PLADs) in China. The results demonstrated that the rural water supply could be sustained and that most water sources and WaSPs were well protected. However, sanitation related to water disinfection effectiveness, water losses control, and Operations and Maintenance (O&M) management needs further improvement. Laws and regulations requiring rural WaSPs to carry out a sanitary evaluation should be established. WaSPs should use tools such as World Health Organization (WHO) Water Safety Plans to identify and control risks.

In total 178 rural WaSPs were evaluated in this study, of which 34.3% were in eastern China, 22.5% in central China, 43.3% in western China. In addition, 67.4% of samples came from surface water sources and 32.6% were from groundwater sources. Of the 178 rural WaSPs, 21.9% were built before 2005, 18.5% were built between 2005 and 2009, 27.0% were built between 2010 and 2014, and 32.6% were built after 2005. Meanwhile, 33.7% had a water supply of 3,000 m^3/d or above and 66.3% had less than a 3,000 m^3/d water supply. Together all 178 WaSPs provide water for about 5.6 million residents. The standardized evaluation process of each rural WaSP follows the directions and guidelines issued by *National Center for Rural Water Supply Technical Guidance* (NCRWSTG) from China CDC. The first procedure of SERWaSP is to organize an expert team and then do a data review, water quality assessment, and field survey. This study includes information on water source, water distribution system, water treatment process and technology, operation management, and other factors. The SERWaSP report based on the work above was done by an expert team and was returned to the evaluated WaSPs for their continued improvement. The data used in this study were collected by each WaSP expert team using the questionnaire made by NCRWSTG.

As presented in Table 1, the proportion of WaSPs with continuous water supply (i.e., 24 h × 7 day water supply) was 89.9% and the proportion of WaSPs with a guarantee probability of water supply higher than 90% was 94.3%. In addition, 91.0% of WaSPs were delineated source water protection areas as the *Technical Guideline for Delineating Source Water Protection Areas* requests, and 93.3% did not have pollutants in its primary protected area of drinking water source. About 92.1% of WaSPs had disinfection

TABLE 1. Key points from 178 rural Water Supply Projects evaluated in 2020 in China.

Segments	Risk points	≥3,000 m^3/d WaSPs			<3,000 m^3/d WaSPs			Total		
		N	Yes (%)	No (%)	N	Yes (%)	No (%)	N	Yes (%)	No (%)
Water supply	Continuity*	60	60 (100.0)	0 (0.0)	118	100 (84.7)	18 (15.3)	178	160 (89.9)	18 (10.1)
	Guarantee†	60	58 (96.7)	2 (3.3)	118	110 (93.2)	8 (6.8)	178	168 (94.3)	10 (5.6)
Water source	Protection areas	60	60 (100.0)	0 (0.0)	118	102 (86.4)	16 (13.6)	178	162 (91.0)	16 (9.0)
	Pollutants in first-grade protection zones	60	3 (5.0)	57 (95.0)	118	9 (7.6)	109 (92.4)	178	12 (6.7)	166 (93.3)
Treatment process	Disinfection procedures	60	60 (100.0)	0 (0.0)	118	104 (88.1)	14 (11.9)	178	164 (92.1)	14 (7.9)
	Disinfection equipment used properly	56	56 (100.0)	0 (0.0)	104	80 (76.9)	24 (23.1)	160	136 (85.0)	24 (15.0)
	Accurate dosage of disinfectants	55	54 (98.2)	1 (1.8)	90	77 (85.6)	13 (14.4)	145	131 (90.3)	14 (9.7)
	Filter material seriously worn or lost	53	0 (0.0)	53 (100.0)	78	2 (2.6)	76 (97.4)	131	2 (1.5)	129 (98.5)
	Well protection of regulating structures	60	54 (90.0)	6 (10.0)	118	91 (77.1)	27 (22.9)	178	145 (81.5)	33 (18.5)
Pipelines	High leakage§	58	28 (48.3)	30 (51.7)	111	40 (36.0)	71 (64.0)	169	68 (40.2)	101 (59.8)
	Long-term low disinfectant level of tap water	60	0 (0.0)	60 (100.0)	99	7 (7.1)	92 (92.9)	159	7 (4.4)	152 (95.6)
Plant area	Soak away toilets, pits or effluent discharges within 30 m	60	0 (0.0)	60 (100.0)	118	7 (5.9)	111 (94.1)	178	7 (3.9)	171 (96.1)
	Pile garbage, excrement or waste residue within 30 m	60	0 (0.0)	60 (100.0)	118	4 (3.4)	114 (96.6)	178	4 (2.2)	174 (97.8)
Management	Sanitary management systems	60	60 (100.0)	0 (0.0)	118	101 (85.6)	17 (14.4)	178	161 (90.4)	17 (9.6)
	Emergency response plan	60	52 (86.7)	8 (13.3)	118	89 (75.4)	29 (24.6)	178	141 (79.2)	37 (20.8)
	Cleaning, disinfection, operating and maintenance procedures	60	54 (90.0)	6 (10.0)	118	79 (66.9)	39 (33.1)	178	133 (74.7)	45 (25.3)
	Organized training for personnel	60	54 (90.0)	6 (10.0)	118	76 (64.4)	42 (35.6)	178	130 (73.0)	48 (27.0)
	Authorized hygienic license	60	49 (81.7)	11 (18.3)	118	45 (38.1)	73 (61.9)	178	94 (52.8)	84 (47.2)
Water quality examination	Detection by qualified organization before water-supply	60	56 (93.3)	4 (6.7)	118	105 (89.0)	13 (11.0)	178	161 (90.4)	17 (9.6)
	Index and frequency requirements	60	47 (78.3)	13 (21.7)	118	47 (39.8)	71 (60.2)	178	94 (52.8)	84 (47.2)

Abbreviation: WaSPs=Water Supply Projects; N=number.
* Continuity: 24 hour/day water supply.
† Guarantee: guarantee probability of water supply ≥90%.
§ High leakage: leakage rate of pipes >12%.

procedures, 90.3% of WaSPs used accurate disinfectant dosage, and 90.4% of WaSPs had sanitary management systems. Before formal supply water, 90.4% could be detected water quality by qualified organizations. All the WaSPs with water supply ≥3,000 m^3/d have established a 24 h/d water supply, source water protection areas, disinfection procedures, and sanitary management systems.

The SERWaSP also showed that the pipe leakage rate in 40.2% of the WaSPs was higher than 12%. As for management of WaSPs, 20.8% did not have an emergency response plan for unsafe drinking water conditions, 25.3% had no cleaning, disinfection, operating, or maintenance procedures, and 27.0% did not have regular training for personnel. The detection index and frequency of 47.2% of WaSPs did not meet the requirements according to *Technical Specification for Water Supply Projects in Towns and Villages* issued by Ministry of Water Resources in 2019. Of the WaSPs with water supply <3,000 m^3/d, 11.9% had no disinfection procedures, 23.1% could not use disinfection equipment properly, 14.1% could not measure disinfectants accurately, and 14.4% had not well-established their sanitary management systems.

According to the most recent water quality reports of these WaSPs provided by CDC, the qualified rates of finished water and tap water were 79.7% and 74.7%, respectively. Most qualified rates of water quality indices were higher than 90% except for microbial indices. Detailed data were shown in Table 2.

DISCUSSION

The National Rural Drinking Water Quality Monitoring System has shown that the qualified rate of drinking water quality in rural areas has increased but is still lower than that of urban areas. Overall, China's rural water supply has been improving, but there are still deficiencies.

The *Technical Specification for Water Supply Projects in Towns and Villages* issued in 2019 suggests that drinking water should be disinfected. Since this study evaluated the whole water treatment process at each WaSPs, we observed that while most WaSPs used a water treatment procedure, more than 10% of WaSPs' water supply with <3,000 m^3/d had no disinfection procedures and were used improperly. The disinfection procedure rate of 403 WaSPs in 6 PLADs of China in 2015 was found to be 39.5% (*4*). This may be the result of a higher proportion of small-scale WaSPs investigated in 2015 and therefore disinfection was given more attention. Water disinfection is efficient at inactivating pathogens (*5*). For drinking water safety, the WaSPs should be equipped with disinfection facilities and use disinfectants accurately.

In this study, we found that both large and small WaSPs have problems with high rates of pipeline leakage. The *Water Pollution Control Action Plan* issued in 2013 stated that the leakage rate in the public water supply network should be limited to 12% by 2017 and 10% by 2020. About two-fifths WaSPs do not meet this requirement. The high leakage rate increases the risk of microbial and chemical re-contamination and causes water resource waste and economic losses for water supply enterprises. The higher leakage rate could be attributed to aging pipes and gate valves, poor quality of pipes, unstable water pressure, or other reasons. The pipe leaks were also related to the year last serviced. The WaSPs with water supply ≥3,000 m^3/d had a higher ratio of leakage, which may be related to many of their pipelines running longer in this study. The reasons for the high leakage rate should be uncovered quickly and targeted measures such as pipeline renovation and replacement or water supply pressure control should be taken according to the actual situation.

Operations and Maintenance management remains a long-standing problem, as the studies of water safety plans implemented in 311 water systems of China from 2004 to 2018 revealed the prevalence of insufficient overall management capacity in rural WaSPs (*6*). O&M is fundamental to WaSPs because failure to adequately address O&M can result in process failures, contamination events, water-borne

TABLE 2. Water quality of 178 rural Water Supply Projects evaluated in 2020 in China.

Water types	Regular indices	≥3,000 m^3/d WaSPs		<3,000 m^3/d WaSPs		Total	
		N	Qualification (%)	N	Qualification (%)	N	Qualification (%)
Finished water							
	Toxicology	60	59 (98.3)	117	116 (99.1)	177	175 (98.9)
	Microbiology	60	56 (93.3)	117	93 (79.5)	177	149 (84.2)
	Physical and chemical parameters	60	56 (93.3)	117	110 (94.0)	177	166 (93.8)
	Disinfectants	60	59 (98.3)	117	116 (99.1)	177	175 (98.9)
	Total	60	52 (86.7)	117	89 (76.1)	177	141 (79.7)
Tap water							
	Toxicology	60	58 (96.7)	118	116 (98.3)	178	174 (97.8)
	Microbiology	60	51 (85.0)	118	87 (73.7)	178	138 (77.5)
	Physical and chemical parameters	60	56 (93.3)	118	111 (94.1)	178	167 (93.8)
	Disinfectants	60	59 (98.3)	118	117 (99.2)	178	176 (98.9)
	Total	60	48 (80.0)	118	85 (72.0)	178	133 (74.7)

Abbreviation: WaSPs=Water Supply Projects; N=number.

diseases, and economic losses (*7*). Nearly half WaSPs cannot carry out the necessary water quality index assessments at the frequency required. The regular monitorings by the WaSPs themselves are able to discover problems quickly. The detection and frequency of index assessments can be increased according to raw water quality, water treatment process, water supply scale, etc. When the results do not meet the standards, the risks should be quickly identified and countermeasures should be enacted. Emergency plans should be launched when necessary.

The *Administrative Measures for Sanitary Evaluation of Rural Drinking Water Safety Projects (Trial)* issued in 2008 proposed sanitary evaluations should be carried out in rural WaSPs with water supply ≥3,000 m^3/d to ensure safe water supply. In addition, the document suggested that SERWaSP results were one of the important conditions for the water supply permissions in rural WaSPs. However, many of the WaSPs with water supply ≥3,000 m^3/d had not carried out SERWaSPs before they were put to use. The results showed WaSPs with a water supply <3,000 m^3/d had more problems during the process of SERWaSP, such as water source protection, disinfection procedures, water quality, and sanitary management. This study's findings point out that the laws and regulations on sanitary evaluation for centralized rural supply should be reinforced. Rural WaSPs covering both large and small, newly constructed, or reconstructed must pass SERWaSP before supplying water. WaSPs in use shall also be subjected to the sanitary evaluation, supervision, and inspection.

However, this study was subject to some limitations. First, the real-world WaSP conditions may be more challenging considering that more WaSPs with water purification treatment were selected in this study. Second, some water quality reports used to carry out SERWaSPs were from months ago, and the water quality might have changed. *Opinions on comprehensively promoting rural revitalization and accelerating the modernization of agriculture and rural areas* issued in 2021 call for the implementation of projects to ensure rural water supply and to strengthen the construction and protection of water sources such as small and medium-sized reservoirs (*8*). The implementation of SERWaSPs is a better choice for water supply safety, which can strengthen the sanitary management of the WaSP in O&M and analyze the water quality safety risks that should be addressed in priority order. The risk management tool, called Water Safety Plans (WSPs) proposed by the WHO, contributes to improving O&M by supporting the systematic assessment, prioritization, and management of risks from catchment to consumer, which might also be applied in rural WaSPs (*6*,*9*). Lastly, a multi-department management mechanism should be operated to promote the development of SERWaSPs and better serve the drinking water safety of rural residents.

Conflicts of Interest: No conflicts of interest reported.

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[#] Corresponding authors: Hongxing Li, lihx@ncrwstg.chinacdc.cn; Chuanlong Xiong, xiongcl@ncrwstg.chinacdc.cn.

[1] National Center for Rural Water Supply Technical Guidance, Chinese Center for Disease Control and Prevention, Beijing, China.

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REFERENCES

1. Zhang R, LI HX, Tao Y. Sanitary risk assessment on rural water supply facility in China. Chi J Public Health 2008;24(5):560 – 1. http://dx.doi.org/10.11847/zgggws2008-24-05-23. (In Chinese).
2. The Ministry of Water Resources and nine other departments issued guidelines on ensuring rural water supply. mwr.gov.cn, 2021 Aug 19. http://www.mwr.gov.cn/xw/slyw/202108/t20210819_1539912.html. [2021-12-8]. (In Chinese).
3. String GM, Singleton RI, Mirindi PN, Lantagne DS. Operational research on rural, community-managed Water Safety Plans: Case study results from implementations in India, DRC, Fiji, and Vanuatu. Water Res 2020;170:115288. http://dx.doi.org/10.1016/j.watres.2019.115288.
4. Zhang Q, Chen GL, Tao Y. Hygienic management status of rural drinking water supply in some areas of China. J Environ Health 2015;32(5):412 – 5. http://dx.doi.org/10.16241/j.cnki.1001-5914.2015.05.010. (In Chinese).
5. Chu CH, Ryberg EC, Loeb SK, Suh MJ, Kim JH. Water Disinfection in Rural Areas Demands Unconventional Solar Technologies. Acc Chem Res 2019;52:1187 – 95. http://dx.doi.org/10.1021/acs.accounts.8b00578.
6. Li HX, Smith CD, Cohen A, Wang L, Li Z, Zhang R, et al. Implementation of water safety plans in China: 2004 – 2018. Int J HygEnviron Health 2020;223(1):106 – 15. http://dx.doi.org/10.1016/j.ijheh.2019.10.001.
7. World Health Organization, International Water Association. Strengthening operations and maintenance through water safety planning. https://www.who.int/publications/i/item/WHO-CED-PHE-WSH-18.69. [2018-9-17].
8. Opinions on comprehensively promoting rural revitalization and accelerating the modernization of agriculture and rural areas. CPC Central Committee and the State Council, 2021 Jan 4. http://www.xinhuanet.com/politics/2021-02/21/c_1127122068.htm. [2021-2-21]. (In Chinese).
9. World Health Organization. Guidelines for drinking-water quality. 4th ed. Geneva: World Health Organization. 2011. https://www.who.int/water_sanitation_health/publications/drinking-water-quality-guidelines-4-including-1st-addendum/en/. [2021-12-8].

Preplanned Studies

Associations of Ambient NO_2 with Daily Hospitalization, Hospitalization Expenditure and Length of Hospital Stay of Cause-Specific Respiratory Diseases — Shanxi, China, 2017–2019

Dashan Zheng[1,&]; Dawei Cao[2,&]; Shiyu Zhang[1]; Huiqing Shen[2]; Yi Liu[2]; Qiyong Liu[3]; Jimin Sun[4]; Guangyuan Jiao[5]; Jianzhen Wang[2]; Xiaoran Yang[6]; Xinri Zhang[2,#]; Hualiang Lin[1,#]

Summary

What is already known about this topic?

Numerous epidemiological studies have documented the association between ambient nitrogen dioxide (NO_2) and mortality and morbidity of respiratory diseases, however, research on the effect of NO_2 on the length of hospital stay (LOS) and hospitalization expenditure is limited.

What is added by this report?

This study collected the respiratory hospitalization, hospital expenditure, and LOS for respiratory diseases from 2017–2019 in Shanxi, China, and comprehensively evaluated the association between ambient NO_2 exposure and respiratory hospitalization, expenditure, and LOS.

What are the implications for public health practice?

This study provides evidence on the association between ambient NO_2 and respiratory burden, suggesting that continuously reducing the NO_2 concentrations could prevent respiratory disease-associated hospital admissions and decrease the relative burden in Shanxi Province and other similar regions.

Nitrogen dioxide (NO_2) has been widely associated with respiratory morbidity and mortality. However, its association with hospitalization expenditure and length of hospital stay (LOS) is scarcely analyzed. Thus, we analyzed this association in Shanxi Province, which has famously high fuel combustion with residential and industrial regions centralized in basins and valleys, making it difficult for air pollutants to disperse (*1*). Daily air pollution exposures were estimated for each case using an inverse distance approach and then averaged for each city. City-specific associations of NO_2 with hospital admission, hospitalization expenditure, and LOS were assessed by general additive models. The overall effects were then pooled through a random-effects meta-analysis. The potentially avoidable values and population attributable fraction (PAF) for total respiratory disease, asthma and chronic obstructive pulmonary disease (COPD) were assessed by reducing the concentration to the standards of the World Health Organization (WHO) (25 μg/m^3) and Chinese government (40 μg/m^3). Significant associations between NO_2 and respiratory hospitalization, hospital cost, and LOS were observed. We estimated 198.73 million CNY [95% confidence interval (CI): 119.07–278.40] in hospital costs, and 272.00 thousand days (95% CI: 179.22–364.79) of LOS could be potentially avoided under the WHO's standards for Shanxi during 2017–2019. This study provides evidence for the association between NO_2 exposure and respiratory burden, suggesting that continually diminishing ambient NO_2 could effectively reduce respiratory burden.

This study collected hospital admission data for respiratory diseases from all the secondary and tertiary hospitals in Shanxi Province from February 2017 to November 2019. The information included general characteristics, residential address, date of admission and discharge, the principal diagnosis (based on the International Classification of Diseases, ICD-10), and hospital expenditures. The hospital expenditures included fees for drugs, clinical examinations, nursing care, and clinical operations. The LOS was calculated based on the admission date, and the LOS for each case was summed and regarded as the value for that day. We included the participants who had resided in Shanxi Province and excluded cases with missing information and those who had only received emergency or outpatient treatment and were then discharged.

Daily ambient air pollutant concentrations of NO_2, fine particulate matter, sulfur dioxide, and ozone at all state-controlled air quality monitoring stations in Shanxi from 2017 to 2019 were also obtained. Individual level exposure was assessed using reverse distance weighting (IDW) by geocoding patient addresses and monitoring station locations and averaging an individual's daily exposure for each city (*1–2*).

The daily mean temperature and relative humidity were extracted from ERA5-L and reanalysis data (*3*). A bilinear interpolation approach was used to estimate the daily meteorological exposure for each participant, and then average the exposure for each city.

The city-specific and overall associations between NO_2 and hospitalization, hospital cost, and LOS for respiratory diseases, COPD, and asthma were assessed using a two-stage statistical approach based on the time-series model. At the first stage, a generalized additive model (GAM) with a quasi-Poisson was built to explore the effect of NO_2 on daily hospital admissions for each city. Considering the normal distribution of LOS and cost, the GAM with a Gaussian link was applied to examine the association between NO_2 and those two indicators. Time trend was controlled by a penalty smoothing spline function of 6 degrees of freedom (df) per year. Daily mean temperature and relative humidity were adjusted using the same spline function with 6 df and 3 df. Public holidays and days of the week (DOW) were treated as categorical variables.

Considering the lag effect, the associations on single lag days of 0 to 5 and moving average days of 01 to 03 were also examined. Further, a random-effect meta-analysis based on the associations of all 11 cities was applied to obtain the overall effects of NO_2.

At the second stage, this study estimated the attributable value and PAF of respiratory hospitalization, cost, and LOS for overall respiratory disease, asthma, and COPD to elucidate the potential benefits by controlling NO_2 concentration to a certain level. The recommended concentrations by the WHO (25 μg/m^3) and Chinese government (40 μg/m^3) were used as reference concentrations. The formula and sensitivity analysis can be found in the Supplementary Materials (available in http://weekly.chinacdc.cn).

This analysis included 666,189 hospital admissions due to respiratory diseases, corresponding to a total of 5.54 million days of LOS and 4.58 billion CNY in hospital expenditures.

Figure 1 illustrates the positive effects of NO_2 on daily hospitalizations, hospital expenditures, and LOS across different lag days and moving average days at the provincial level. The effect was highest in lag03, every 10 μg/m^3 increment in NO_2 was associated with a 2.14% (95% CI: 1.39–2.89) increase in respiratory

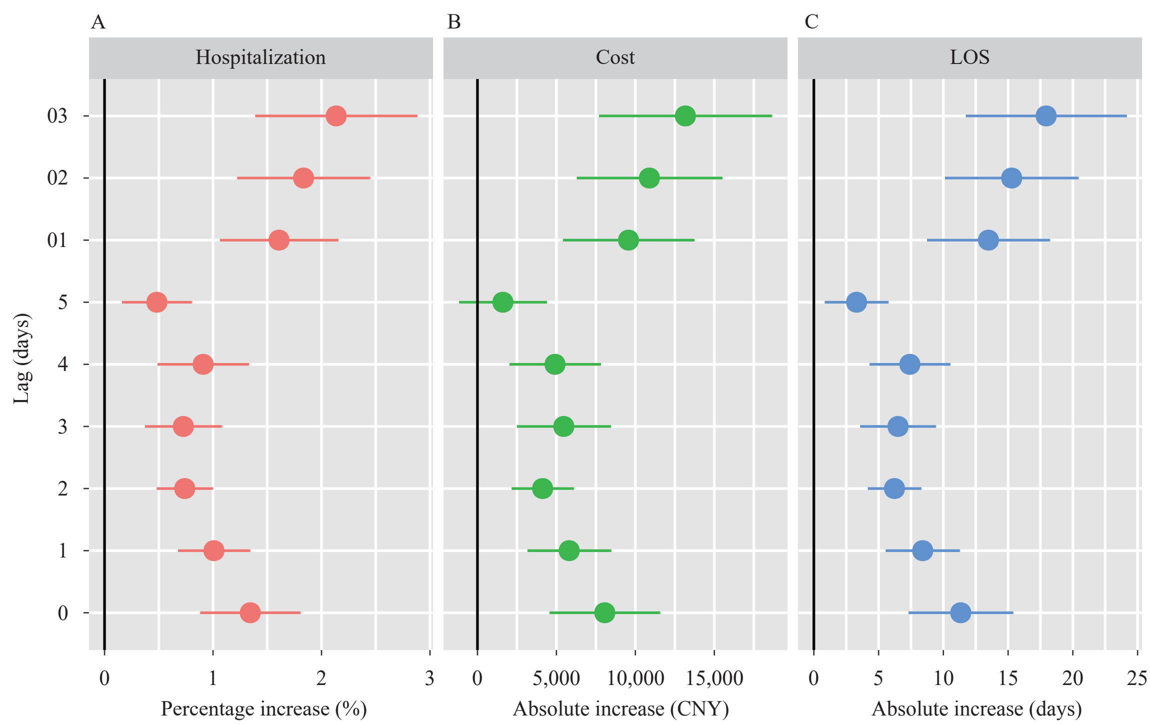

FIGURE 1. The provincial overall association of daily NO_2 (10 μg/m^3) with (A) hospital admission, (B) hospitalization expenditure, and (C) length of hospital stay (days) at different lag days including single lag days (lag0–5) and moving average days (lag01–03) from 2017 to 2019.
Abbreviation: CNY=Chinese Yuan; LOS=length of hospital stay.

hospitalization, 13,167.36 CNY (95% CI: 7,697.29–18,637.43) in hospital expenditures, and 17.94 days (95% CI: 11.74–24.14) increase of LOS. Supplementary Tables S1–S3 (available in https://weekly.chinacdc.cn) displayed the city-specific attributable values which vary across different cities.

The potentially avoidable value and PAF by meeting different air quality standards are shown in Table 1. Under the WHO's standards, about 18.10 thousand (95% CI: 11.78–24.54) hospital admissions, 198.73 million CNY (95% CI: 119.07–278.40) hospital costs, and 272.00 thousand days (95% CI: 179.22–364.79) of LOS could be avoided.

The potentially avoidable cost and LOS per capita based on the two standards are demonstrated in Table 2. About 298.31 CNY (95% CI: 178.73–471.90) in hospital costs and 0.41 days (95% CI: 0.27–0.55) of LOS could be avoided for each respiratory case under the standards of WHO.

Supplementary Table S4 (available in https://weekly.chinacdc.cn) delineates the overall attributable burden of COPD and asthma due to NO_2. About 5.69 million CNY (95% CI: 0.72–10.65) for asthma and 50.66 million (95% CI: 25.06–776.26) for COPD could be prevented by decreasing ambient NO_2 concentrations to 25 μg/m^3, corresponding to PAFs of 5.40% (95% CI: 0.69%–10.11%) and 4.79% (95% CI: 2.37%–7.22%).

DISCUSSION

This analysis firstly demonstrated that higher NO_2 exposure was associated with increased respiratory hospitalization, higher hospital cost, and longer LOS. Furthermore, the results indicate that numbers of respiratory hospitalization, hospital costs, and length of hospital stay could be potentially saved by reducing the NO_2 concentrations. These findings provided ample evidence for formulating air pollution control policies, suggesting that continuously reducing NO_2 concentrations can decrease the burdens of respiratory diseases in Shanxi Province and other similar regions with high NO_2 pollution.

Our results indicate an adverse effect of ambient NO_2 on hospital burden due to respiratory diseases, which is in line with previous studies. For example, one study found an association between life expectancy of people living with respiratory diseases and air pollution (*4*). Furthermore, in Pennsylvania, the regions with more serious air pollution were found to have a higher hospital expenditure for respiratory diseases (*5*).

The potentially avoidable values and PAFs for cause-specific respiratory diseases in our analysis were also aligned with previous studies. For example, Guo et al. estimated that the asthma-induced economic cost attributed to NO_2 was 17.15 million dollars per year for Shanghai, China (*6*). Notably, the similar PAFs suggested that ambient NO_2 had an adverse effect on both chronic and allergic respiratory diseases.

Several mechanisms could help explain the observed adverse effect of NO_2 on the respiratory system. In one clinical trial, NO_2 caused mild airway inflammation in healthy subjects, which affected blood cells and

TABLE 1. Potentially avoidable values and population attributable fraction of hospital admission, hospitalization expenditure and hospital stay due to respiratory disease by reducing ambient NO_2 concentration to the recommended concentration by WHO (25 μg/m^3) and Chinese government (40 μg/m^3), 2017–2019.

Variable	Potential avoidable value (95% CI)		PAF (%, 95% CI)	
	25 μg/m^3	40 μg/m^3	25 μg/m^3	40 μg/m^3
Hospitalizations (thousand)	18.10 (11.78–24.54)	7.06 (4.60–9.55)	2.72 (1.77–3.68)	1.06 (0.69–1.43)
Hospitalization expenditure (million CNY)	198.73 (119.07–278.40)	72.81 (43.62–101.99)	4.34 (2.60–6.08)	1.59 (0.95–2.23)
Hospital stay (thousand days)	272.00 (179.22–364.79)	99.65 (65.66–133.64)	4.91 (3.23–6.58)	1.80 (1.18–2.41)

Abbreviation: WHO=World Health Organization; PAF=population attributable fraction; CI=confidence interval; CNY=Chinese Yuan.

TABLE 2. The potentially avoidable hospitalization expenditure and length of hospital stay for each respiratory case by controlling daily NO_2 concentrations to criteria of WHO (25 μg/m^3) and Chinese government (40 μg/m^3), 2017–2019.

Variable	Potentially avoidable values for each case (95% CI)	
	25 μg/m^3	40 μg/m^3
Hospitalization expenditure (CNY)	298.31 (178.73–417.90)	109.29 (65.48–153.10)
Hospital stay (days)	0.41 (0.27–0.55)	0.15 (0.10–0.20)

Abbreviation: WHO=World Health Organization; CI=confidence interval; CNY=Chinese Yuan.

increased susceptibility to respiratory virus infections in airway epithelial cells (*7*). Moreover, exposure to higher ambient NO_2 was confirmed to be associated with lung function, which could trigger or aggravate COPD (*8*).

Limitations should be considered. First, this was an ecological study and it is difficult to make a causal inference on the association between ambient NO_2 exposure and respiratory burden. Second, this study only included cases from secondary and tertiary hospitals in Shanxi Province but excluded those from primary hospitals and patients without hospital admission, which may create a representativeness issue and lead to an underestimate of the respiratory burden in Shanxi Province.

In conclusion, this study elaborated on the association between ambient NO_2 exposure and respiratory hospitalization, hospital cost, and hospital stay. The findings in this analysis identified that government's continued implementation of NO_2 concentration control can potentially reduce hospital admissions, saving a considerable amount of hospital expenditure for people in regions with high NO_2 pollution.

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[#] Corresponding authors: Xinri Zhang, ykdzxr61@163.com; Hualiang Lin, linhualiang@mail.sysu.edu.cn.

[1] School of Public Health, Sun Yat-sen University, Guangzhou City, Guangdong Province, China; [2] Department of Respiration, First Hospital of Shanxi Medical University, Taiyuan City, Shanxi Province, China; [3] Key Laboratory of Infectious Disease Prevention and Control, Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, National Institute for Communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, China; [4] Key Laboratory of Vaccine, Prevention and Control of Infectious Disease of Zhejiang Province, Zhejiang Provincial Center for Disease Control and Prevention, Hangzhou City, Zhejiang Province, China; [5] Department of Ideological and Political Education, School of Marxism, Capital Medical University, Beijing, China; [6] Department of Standards and Evaluation, Beijing Municipal Health Commission Policy Research Center, Beijing Municipal health Commission Information Center, Beijing, China.

[&] Joint first authors.

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REFERENCES

1. Cao DW, Zheng DS, Qian ZM, Shen HQ, Liu Y, Liu QY, et al. Ambient sulfur dioxide and hospital expenditures and length of hospital stay for respiratory diseases: a multicity study in China. Ecotoxicol Environ Saf 2022;229:113082. http://dx.doi.org/10.1016/j.ecoenv.2021.113082.
2. Cao DW, Li DY, Wu YL, Qian ZM, Liu Y, Liu QY, et al. Ambient $PM_{2.5}$ exposure and hospital cost and length of hospital stay for respiratory diseases in 11 cities in Shanxi province, China. Thorax 2021;76(8):743. http://dx.doi.org/10.1136/thoraxjnl-2020-215838.
3. Wang LJ, Liu C, Meng X, Niu Y, Lin ZJ, Liu YN, et al. Associations between short-term exposure to ambient sulfur dioxide and increased cause-specific mortality in 272 Chinese cities. Environ Int 2018;117:33 – 9. http://dx.doi.org/10.1016/j.envint.2018.04.019.
4. Yang Y, Qi JL, Ruan ZL, Yin P, Zhang SY, Liu JM, et al. Changes in life expectancy of respiratory diseases from attaining daily $PM_{2.5}$ Standard in China: a nationwide observational study. Innovation 2020;1(3):100064. http://dx.doi.org/10.1016/j.xinn.2020.100064.
5. Carpenter BH, Chromy JR, Bach WD, LeSourd DA, Gillette DG. Health costs of air pollution: a study of hospitalization costs. Am J Public Health 1979;69(12):1232 – 41. http://dx.doi.org/10.2105/AJPH.69.12.1232.
6. Guo HB, Chen MX. Short-term effect of air pollution on asthma patient visits in Shanghai area and assessment of economic costs. Ecotoxicol Environ Saf 2018;161:184 – 9. http://dx.doi.org/10.1016/j.ecoenv.2018.05.089.
7. Frampton MW, Boscia J, Roberts NJ Jr, Azadniv M, Torres A, Cox C, et al. Nitrogen dioxide exposure: effects on airway and blood cells. Am J Physiol Lung Cell Mol Physiol 2002;282(1):L155 – 65. http://dx.doi.org/10.1152/ajplung.2002.282.1.L155.
8. Hou DN, Ge YH, Chen CC, Tan Q, Chen RJ, Yang YJ, et al. Associations of long-term exposure to ambient fine particulate matter and nitrogen dioxide with lung function: a cross-sectional study in China. Environ Int 2020;144:105977. http://dx.doi.org/10.1016/j.envint.2020.105977.

SUPPLEMENTARY METHODS

Formular and Models

Attributable value= $\sum_{i=0}^{n}$(baseline hospital admission) × [exp(β×ΔCi) − 1]

Attributable hospital expenditure (or length of hospital stay)=$\sum_{i=0}^{n}(\beta \times \Delta Ci)$

Population attributable fraction $= \frac{\text{attributable value}}{\text{overall number}} \times 100\%$

Attributable value for each case $= \frac{\text{attributable value}}{\text{cases number}} \times 100\%$

where i is the observation days with a higher NO_2 concentration than the recommended concentration offered by the WHO or Chinese government. Ci is the difference between the daily NO_2 concentration and the reference concentration on day i.

SUPPLEMENTARY TABLE S1. The estimated avoidable number of hospital admissions for respiratory diseases in 11 cities in Shanxi, China, 2017–2019.

City	Overall (in thousand)	25 μg/m³		40 μg/m³	
		Avoidable value (in thousand) (95% CI)	Population attributable fraction (%, 95% CI)	Avoidable value (in thousand) (95% CI)	Population attributable fraction (%, 95% CI)
Datong	85.72	3.28 (2.06 to 4.53)	3.82 (2.40 to 5.29)	0.71 (0.45 to 0.97)	0.82 (0.52 to 1.13)
Jincheng	55.53	1.73 (1.07 to 2.41)	3.12 (1.93 to 4.33)	0.68 (0.42 to 0.95)	1.23 (0.76 to 1.71)
Jinzhong	90.42	2.24 (0.52 to 4.02)	2.48 (0.58 to 4.45)	0.97 (0.23 to 1.73)	1.07 (0.25 to 1.91)
Linfen	73.08	3.32 (2.28 to 4.40)	4.55 (3.12 to 6.02)	1.43 (0.98 to 1.88)	1.95 (1.35 to 2.58)
Lyuliang	64.97	3.19 (1.77 to 4.66)	4.91 (2.72 to 7.17)	0.95 (0.53 to 1.38)	1.46 (0.81 to 2.12)
Shuozhou	28.31	0.29 (0.11 to 0.47)	1.01 (0.38 to 1.65)	0.07 (0.03 to 0.11)	0.25 (0.09 to 0.40)
Taiyuan	74.04	2.14 (0.68 to 3.65)	2.89 (0.92 to 4.93)	1.15 (0.37 to 1.95)	1.55 (0.49 to 2.63)
Xinzhou	36.64	0.42 (−0.04 to 0.90)	1.15 (−0.12 to 2.45)	0.14 (−0.01 to 0.29)	0.37 (−0.04 to 0.79)
Yangquan	32.60	0.26 (0.01 to 0.50)	0.79 (0.04 to 1.54)	0.11 (0.10 to 0.22)	0.35 (0.02 to 0.68)
Yuncheng	47.20	0.92 (0.53 to 1.34)	1.96 (1.11 to 2.83)	0.43 (0.24 to 0.62)	0.91 (0.52 to 1.31)
Changzhi	77.67	1.90 (0.58 to 3.26)	2.44 (0.74 to 4.20)	0.59 (0.18 to 1.01)	0.76 (0.23 to 1.30)

Abbreviation: CI=confidence interval.

SUPPLEMENTARY TABLE S2. The estimated avoidable hospital cost for respiratory diseases in 11 cities in Shanxi, China, 2017–2019.

City	Overall (million CNY)	25 μg/m³		40 μg/m³	
		Avoidable value (million CNY, 95% CI)	Population attributable fraction(%, 95% CI)	Avoidable value (million CNY, 95% CI)	Population attributable fraction (%, 95% CI)
Datong	683.11	26.40 (12.07 to 40.74)	3.87 (1.77 to 5.96)	5.22 (2.39 to 8.05)	0.76 (0.35 to 1.18)
Jincheng	314.07	16.98 (5.94 to 28.02)	5.41 (1.89 to 8.92)	6.27 (2.20 to 10.35)	2.00 (0.70 to 3.30)
Jinzhong	546.70	23.18 (−0.17 to 46.53)	4.24 (−0.03 to 8.51)	8.95 (−0.06 to 17.97)	1.64 (−0.01 to 3.29)
Linfen	479.07	36.35 (21.96 to 50.73)	7.59 (4.58 to 10.59)	13.66 (8.25 to 19.07)	2.85 (1.72 to 3.98)
Lyuliang	405.99	35.98 (1635 to 55.62)	8.86 (4.03 to 13.70)	11.72 (5.32 to 18.11)	2.89 (1.31 to 4.46)
Shuozhou	151.05	3.23 (−1.38 to 7.83)	2.14 (−0.91 to 5.19)	0.75 (−0.32 to 1.82)	0.50 (−0.21 to 1.21)
Taiyuan	724.98	23.75 (−8.98 to 56.48)	3.28 (−1.24 to 7.79)	11.74 (−4.44 to 27.91)	1.62 (−0.61 to 3.85)
Xinzhou	300.82	14.73 (−0.94 to 30.41)	4.90 (−0.31 to 10.11)	4.99 (−0.32 to 10.30)	1.66 (−0.11 to 3.42)
Yangquan	274.49	6.05 (−6.62 to 18.73)	2.21 (−2.41 to 6.82)	2.35 (−2.58 to 7.28)	0.86 (−0.94 to 2.65)
Yuncheng	237.83	14.16 (7.24 to 21.07)	5.95 (3.05 to 8.86)	5.44 (2.78 to 8.10)	2.29 (1.17 to 3.40)
Changzhi	462.84	7.19 (−8.31 to 22.69)	1.55 (−1.80 to 4.90)	2.36 (−2.73 to 7.46)	0.51 (−0.59 to 1.61)

Abbreviation: CNY=Chinese Yuan; CI=confidence interval.

Sensitivity Analysis

Several sensitivity analyses were performed to examine the robustness of our results. We conducted two-pollutant models to control for the potential confounding effect of other air pollutants, including $PM_{2.5}$, O_3, and SO_2 in Supplementary Table S5. We also changed the df of temporal trend in the range of 5–8 and that of daily temperature and relative humidity in the range of 4–6 to examine the robustness of models (Supplementary Table S6).

The results of the sensitivity analysis indicated that our results were robust. Our two-pollutant models (Supplementary Table S5) suggest that the association was robust to the adjustment of co-pollutants (O_3, SO_2, and $PM_{2.5}$). In Supplementary Table S6 compared with our main models, the associations between NO_2 concentrations and outcomes were also generally similar by changing the dfs for the adjustment of meteorological factors and temporal trend.

SUPPLEMENTARY TABLE S3. The estimated avoidable length of hospital stays (LOS) for respiratory diseases in the 11 cities in Shanxi, China, 2017–2019.

City	Overall (thousand days)	25 μg/m^3		40 μg/m^3	
		Avoidable value (thousand days, 95% CI)	Population attributable fraction (%, 95% CI)	Avoidable value (thousand days, 95% CI)	Population attributable fraction (%, 95% CI)
Datong	866.97	39.18 (22.58 to 55.79)	4.52 (2.60 to 6.44)	7.74 (4.46 to 11.02)	0.89 (0.51 to 1.27)
Jincheng	430.01	25.93 (14.79 to 37.06)	6.03 (3.44 to 8.62)	9.58 (5.46 to 13.69)	2.23 (1.27 to 3.18)
Jinzhong	684.28	25.79 (4.22 to 47.37)	3.77 (0.62 to 6.92)	9.96 (1.63 to 18.30)	1.46 (0.24 to 2.67)
Linfen	578.60	37.52 (24.41 to 50.63)	6.49 (4.22 to 8.75)	14.10 (9.18 to 19.03)	2.44 (1.59 to 3.29)
Lyuliang	491.85	31.01 (13.05 to 48.97)	6.31 (2.65 to 9.96)	10.1 (4.25 to 15.94)	2.05 (0.86 to 3.24)
Shuozhou	234.09	7.82 (1.67 to 13.96)	3.34 (0.71 to 5.96)	1.82 (0.39 to 3.25)	0.78 (0.17 to 1.39)
Taiyuan	667.01	35.56 (9.65 to 61.47)	5.33 (1.45 to 9.22)	17.57 (4.77 to 30.38)	2.63 (0.72 to 4.55)
Xinzhou	309.92	13.38 (-0.06 to 26.81)	4.32 (-0.02 to 8.65)	4.53 (-0.02 to 9.08)	1.46 (-0.01 to 2.93)
Yangquan	304.5	9.87 (0.02 to 19.71)	3.24 (0.01 to 6.47)	3.84 (0.01 to 7.66)	1.26 (0.00 to 2.52)
Yuncheng	379.06	30.77 (20.22 to 41.32)	8.12 (5.33 to 10.90)	11.82 (7.77 to 15.88)	3.12 (2.05 to 4.19)
Changzhi	597.57	14.45 (-1.67 to 30.56)	2.42 (-0.28 to 5.11)	4.75 (-0.55 to 10.05)	0.79 (-0.09 to 1.68)

Abbreviation: CI=confidence interval.

SUPPLEMENTARY TABLE S4. Avoidable values and attributable fractions of COPD and asthma by controlling ambient NO_2 according to standards by 25 μg/m^3, 40 μg/m^3 in Shanxi Province, 2017–2019.

Disease	Variable	Avoidable value (95% CI)		Population attributable fraction (%, 95% CI)	
		25 μg/m^3	40 μg/m^3	25 μg/m^3	40 μg/m^3
COPD	Hospital cost (million CNY)	50.66 (25.06 to 76.26)	18.56 (9.18 to 27.94)	4.79 (2.37 to 7.22)	1.76 (0.87 to 2.64)
	Hospital stay (thousand day)	56.01 (30.49 to 81.54)	20.52 (11.17 to 29.87)	5.06 (2.76 to 7.37)	1.85 (1.01 to 2.70)
Asthma	Hospital cost (million CNY)	5.69 (0.72 to 10.65)	2.08 (0.27 to 3.90)	5.40 (0.69 to 10.11)	1.98 (0.25 to 3.70)
	Hospital stay (thousand day)	7.65 (3.45 to 11.85)	2.80 (1.26 to 4.34)	6.14 (2.77 to 9.52)	2.25 (1.02 to 3.49)

Abbreviation: CNY=Chinese Yuan; COPD=Chronic obstructive pulmonary disease; CI=confidence interval.

SUPPLEMENTARY TABLE S5. Sensitivity analyses on the PAF of NO_2 for hospital admission, hospital cost, and length of hospital stay at lag03 in two-pollutant models by meeting 25 μg/m^3.

Two-pollutant model	Daily respiratory hospitalization	Hospitalization cost (thousand CNY)	Length of Hospital stay (days)
NO_2+SO_2	2.13 (1.17, 3.09)	13.46 (7.15, 19.76)	18.79 (10.98, 26.60)
NO_2+O_3	1.94 (1.26, 2.61)	12.07 (7.02, 17.11)	16.28 (10.55, 22.02)
NO_2+$PM_{2.5}$	1.84 (1.19, 2.50)	7.84 (4.39, 11.27)	12.76 (8.32, 17.21)

Abbreviation: CNY=Chinese Yuan; PAF=population attributable fraction.

SUPPLEMENTARY TABLE S6. Sensitivity analyses of the association between daily NO_2 and hospital admissions, hospital cost, and length of hospital stay by changing the degree of freedom in the smoothing functions.

Models	Daily respiratory hospitalizations	Hospitalization cost (thousand CNY)	Length of Hospital stay (days)
Varying df for temporal trend			
df=5	2.23 (1.44 to 3.02)	13.25 (8.09 to 18.42)	18.70 (12.21 to 25.18)
df=7	1.89 (1.25 to 2.53)	11.72 (7.07 to 16.36)	16.00 (10.72 to 21.28)
df=8	1.78 (1.20 to 2.37)	11.83 (7.57 to 16.08)	15.30 (10.55 to 20.05)
Varying df for temperature			
df=5	2.00 (1.32 to 2.69)	12.08 (7.20 to 16.97)	16.49 (10.87 to 22.10)
df=7	1.98 (1.30 to 2.66)	11.81 (6.98 to 16.65)	16.45 (1075 to 22.15)
df=8	2.00 (1.31 to 2.68)	11.86 (7.02 to 16.71)	16.59 (10.87 to 22.32)
Varying df for relative humidity			
df=4	1.99 (1.30 to 2.68)	11.95 (7.13 to 16.76)	16.56 (10.88 to 22.23)
df=5	1.99 (1.29 to 2.68)	12.12 (7.18 to 17.07)	16.60 (10.93 to 22.27)
df=6	1.99 (1.30 to 2.68)	12.06 (7.11 to 17.01)	16.60 (10.92 to 22.29)

Abbreviation: CNY=Chinese Yuan.

Vital Surveillances

Epidemiological Characteristics of Human Anthrax — China, 2018–2021

Huijuan Zhang[1,2,&]; Enmin Zhang[1,2,&]; Mu Guo[3]; Jinrong He[1,2]; Wei Li[1,2]; Jianchun Wei[1,2,#]

ABSTRACT

Introduction: The epidemic of human anthrax is at a low level in China in recent years, but the reported incidence increased in 2021. In order to understand the current landscape of research and knowledge about anthrax in China, the epidemiological characteristics of anthrax in humans from 2018 to 2021 were analyzed and the prevention and control suggestions were proposed.

Methods: Surveillance data of anthrax in humans and livestock, together with human outbreaks data during 2018–2021, were collected and analyzed by descriptive statistics methods. The number and proportion of outbreaks, cases and deaths by provincial-level administrative divisions (PLADs), clinical types, and contributing factors were calculated.

Results: A total of 1,244 cases of human anthrax and 53 outbreaks were reported from 2018 to 2021 in China. While the incidence of anthrax declined from 2018 to 2020, it increased in 2021. The regions of anthrax were mainly located in the west and the northeast PLADs of China, though cases were reported in some central and eastern PLADs in 2021. Young and middle-aged men involved in animal husbandry were found to be at a higher risk of anthrax. All the reported outbreaks were associated with the exposure of infected livestock. A total of 296 livestock anthrax cases were reported.

Conclusions: The increased incidence and wider geographical distribution of human anthrax in 2021 were found to be the result of inadequate supervision of diseased animals as well as updated diagnostic criteria. As such, the monitoring of risk factors and emergency preparation procedures should be strengthened at the national level. In addition, it is also critical to strengthen health education for high-risk occupational groups and strengthen professional training for local clinicians. Finally, more measures should be carried out to strengthen anthrax surveillance in livestock husbandry.

Anthrax is an acute, infectious, zoonotic disease caused by *Bacillus anthracis* (*B. anthracis*) that can form spores, is resistant to extreme environmental conditions, and can persist for long periods of time in soil or hay. Anthrax mostly infects susceptible herbivores, such as cattle, mules, sheep, horses, and donkeys. Humans become infected through contact with diseased animals or by inhaling spores from contaminated animal products accidentally (*1*). The emergence of injectional anthrax among heroin users in Europe highlights the possibility of new routes of the spread of human anthrax (*2*). In addition, *B. anthracis* can be used as a biological weapon, and several anthrax-related bioterrorism events have occurred — resulting in intentional outbreaks (*2*).

Anthrax is still prevalent in many countries in Asia and Africa, as well as in some countries in Europe and America (*3*). In China, the national anthrax surveillance project has been gradually scaled up since 2005; alongside this, the number of human anthrax cases has gradually decreased over the last three decades, though a few comparatively larger anthrax outbreaks still occurred (*4*–*6*). Currently, anthrax remains a threatening endemic disease in China, and a considerable number of human anthrax cases are reported every year (*7*). In 2021, human anthrax outbreaks were reported in more than 20 counties in China, some of which belonged to historically low-incidence areas (*8*), and some of which happened in places where no anthrax cases had been reported for many years. In order to understand the current knowledge of anthrax in China, the national epidemiological surveillance data of anthrax in humans and livestock from 2018 to 2021 were analyzed. Sourced from this analysis, corresponding risk factors were identified and recommended policy measures are outlined at the conclusion.

METHODS

The reported cases and outbreaks of anthrax in humans were collected from the China Information System for Disease Control and Prevention. All clinically-diagnosed cases and laboratory-confirmed cases during 2018–2021 were included in this study. These cases were identified according to the anthrax case definitions issued by the National Health Commission of the People's Republic of China. It should be noted that, before November 2020, human anthrax cases were identified according to the *Diagnostic Criteria for Anthrax* (WS 283–2008). After November 2020, the diagnostic criteria for anthrax were updated in China, so the human anthrax cases after November 2020 were diagnosed according to the new diagnostic criteria (WS 283–2020) (*9*). In addition to previous methods, polymerase chain reaction methods for specific genes of *B. anthracis*, the detection of antibodies or antigens of *B. anthracis*, as well as documented anthrax environmental exposure were included in the new criteria.

The definition of an anthrax outbreak in this research is based on the following standards: the case(s) in a potential outbreak either needed to involve an inhalational or fur processing related anthrax case or more than 3 cutaneous or gastrointestinal anthrax cases in a week in a limited area (e.g., in a village, a school, etc.). Such an anthrax outbreak was required to be reported as an anthrax public health event. Since 2021, one of the items about anthrax outbreaks was added, i.e. when a cutaneous or gastrointestinal anthrax case was found in a county or in a district where no cases were reported over the past 5 years, it was also considered as an anthrax outbreak and required to be reported.

Routine surveillance of livestock anthrax is organized by the Ministry of Agriculture and Rural Affairs of the People's Republic of China and corresponding data are published monthly on the Official Veterinary Bulletin (*10*).

RESULTS

A total of 1,244 human anthrax cases with 7 deaths were reported in China from 2018 to 2021, with 336 reported in 2018, 297 in 2019, 224 in 2020, and 387 in 2021. These cases were distributed across 19 provincial-level administrative divisions (PLADs) in China. The majority of cases (76.8%, or 955/1,244 cases) were located in western and northeastern China, such as Sichuan Province, Gansu Province, Qinghai Province, Inner Mongolia Autonomous Region, and Xinjiang Uygur Autonomous Region. Notably, the 51 total cases in 2021 were sourced from Shandong Province (22 cases), Anhui Province (8 cases), and Shanxi Province (21 cases). This was significant because there were no human anthrax cases reported in these 3 provinces in the past 5 years — save for 1 case

TABLE 1. General characteristics of reported cases of human anthrax in China, 2018–2021.

Variable	2018		2019		2020		2021		Total	
	Number of cases	Proportion (%)	Number of cases	Proportion (%)	Number of cases	Proportion (%)	Number of cases	Proportion (%)	Number of cases	Proportion (%)
Total	336	100.0	297	100.0	224	100.0	387	100.0	1,244	100.0
Age (years)										
0–24	39	11.6	36	12.1	18	8.0	33	8.5	126	10.1
25–49	213	63.4	180	60.6	124	55.4	219	56.6	736	59.2
50–	84	25.0	81	27.3	82	36.6	135	34.9	382	30.7
Sex										
Male	248	73.8	232	78.1	139	62.1	295	76.2	914	73.5
Female	88	26.2	65	21.9	85	37.9	92	23.8	330	26.5
Occupation										
Herdsmen	167	49.7	156	52.5	129	57.6	177	45.7	629	50.6
Farmers	121	36.0	109	36.7	79	35.3	167	43.2	476	38.3
Others	48	14.3	32	10.8	16	7.1	43	11.1	139	11.2
Clinical type										
Cutaneous	331	98.5	290	97.6	221	98.7	382	98.7	1,224	98.4
Inhalational	0	0.0	0	0.0	1	0.4	1	0.3	2	0.2
Others	5	1.5	7	2.4	2	0.9	4	1.0	18	1.4

being reported in Shanxi in 2020. The characteristics of the cases are listed in Table 1. The proportion of cases in persons aged 25–49 years old was 59.2%. About 73.5% of cases were in men. About 50.6% of cases were herdsmen and 38.3% of cases were farmers. In terms of the clinical types of cases, 98.4% of the cases were cutaneous anthrax, with 4 deaths and a fatality rate of 0.3% (4/1,224); two cases were inhalational anthrax with no deaths; and about 1.4% of the cases (18 cases) belonged to other clinical types, including intestinal anthrax, septicemia, and meningitis anthrax, with 3 deaths and a fatality rate of 16.7% (3/18). Figure 1 shows the monthly reported cases of anthrax in humans and livestock in China from 2018 to 2021. Human anthrax cases occurred throughout the year, and peaked around July or August. A total of 296 livestock anthrax cases were reported: 77.4% (229/296) of which originated from cattle.

There were a total of 53 human anthrax outbreaks involving 224 cases reported from 2018 to 2021. The year with the fewest was 2020 (4 outbreaks), while the year with the most was 2021 (24 outbreaks) (Table 2). These outbreaks occurred from July to September, with a peak in August. The epidemiological investigation revealed that the majority of these outbreaks were sourced from being exposed to livestock anthrax as a result of slaughtering, skinning, or eating poorly-cooked, contaminated meat. Notably, before 2021, anthrax outbreaks mainly occurred in areas that historically suffered from epidemic anthrax in China, such as Inner Mongolia, Gansu, and Sichuan PLADs. However, in 2021, some provinces with lower historical anthrax incidence reported anthrax outbreaks, including 2 outbreaks in Anhui, 1 outbreak in Shanxi, and 8 outbreaks in Shandong. One outbreak in Shandong Province even involved the death of a 14-year-old student (meningitis anthrax), which aroused great public concern at that time. Because inhalational anthrax is defined as a public health event and is required to be managed as a class A infectious disease in China, more public concern is also aroused by an inhalational anthrax case in Beijing in 2021. In fact, this was the second inhalational anthrax case to have sought treatment in Beijing recently: the former occurred in 2020. Another noteworthy issue is that anthrax outbreaks occurred in 3 consecutive years (2019, 2020, and 2021) in Henan Province, while it had been 16 years before 2019 without reported cases. In addition, some special clinical types of anthrax have

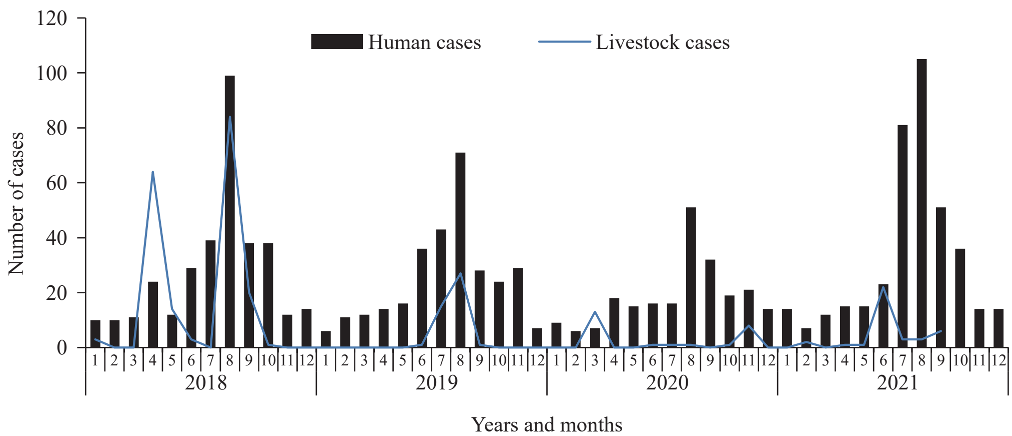

FIGURE 1. The monthly reported cases of anthrax in humans and livestock in China, 2018–2021.

TABLE 2. Reported human anthrax outbreaks, PLADs and cases involved in China, 2018–2021.

Year	Number of outbreaks (n)	Involved PLADs (n)	Involved cases (n)
2018	11	8	60
2019	14	9	57
2020	4	4	12
2021	24	11	95
Total	53	16	224

Abbreviation: PLADs=provincial-level administrative divisions.

occurred in recent years, such as one intestinal anthrax outbreak in Sichuan in 2018, inhalational anthrax in Hebei in 2020 and 2021, and meningitis and septicemia anthrax in Shandong in 2021.

CONCLUSIONS

Generally, human anthrax epidemics in China have showed a steadily decreasing trend over the past three decades, with occasional small-scale rebounds in certain years (*7*). This study shows that the reported incidence of human anthrax in China decreased year by year from 2018 to 2020, but increased in 2021, with an increase of 35.3 percent compared to the average incidence of the previous three years. At present, the annual reporting numbers are less than 400 in China, which is a low incidence level. West and northeast China are the highest-risk areas for human anthrax. However, corresponding risks in the central and eastern regions of China increased in 2021. The young and middle-aged men engaged in agriculture and animal husbandry in the western and northeastern regions are at risk of anthrax, and should be monitored and trained. Meanwhile, monitoring of outbreaks and risk factors in other regions of China should be strengthened.

Human cases of anthrax usually result from contact with infected livestock during the slaughtering, butchering, and skinning processes. Nevertheless, this study found the number of reported livestock anthrax cases was comparatively much lower than human anthrax in China, which indicates that anthrax surveillance and reporting in livestock husbandry is inadequate. Regular livestock supervision is the fundamental way to control the transmission of anthrax in humans. Vaccination of livestock, more effective quarantine and inspection measures for livestock, and harmless disposal of dead livestock in affected areas are very essential. As a public health response, offering some joint approaches between livestock and human countermeasures could contribute to controlling anthrax outbreaks in the future.

In general, some noteworthy features of human anthrax occurred in 2021, including a greater number of reported cases, wider geographical spread, and more diversity of clinical types. One reason for these features may be the update of diagnostic criteria for human anthrax cases, which could contribute to the incomparability of the data to some extent. On the other hand, a relatively truer picture of anthrax epidemics was revealed due to the new diagnostic criteria. The high-sensitivity gene testing in new criteria can improve positive detection in clinical samples. More laboratory assays and evidence promote more human anthrax cases to obtain laboratory diagnostic support and increase the number of laboratory-confirmed anthrax cases. Another reason for the unusual features of anthrax cases in 2021 may be ongoing personnel training in anthrax diagnostic capacity, along with gradual improvement in public awareness about anthrax prevention and control, and more patients seeing doctors in time — which allows doctors to make diagnoses more quickly and correctly. These efforts contributed to early detection and treatment of cases. However, it is still necessary to continue strengthening training in this area, because this study found that the higher fatality rate of other clinical types, excepting cutaneous anthrax, may be related to delays in seeking medical attention, as well as to the special pathogenesis. Therefore, further studies on the etiology and treatment of varying clinical types should be strengthened in the future.

This study was subject to some limitations. First, the update of diagnostic criteria for human anthrax cases affected the comparability of the data. Second, this study did not investigate molecular epidemiological characteristics, which needs to be carried out in the future. Third, the development of livestock husbandry influences the incidence of human anthrax, but this study did not acquire general information on livestock breeding, transportation, vaccination, quarantine, etc.

In conclusion, this study's results showed that the epidemic of human anthrax was at a low level in China, but the increased incidence and the wider geographical distribution in 2021 suggest that the monitoring of risk factors and emergency preparation procedures should be strengthened at the national level. Most cases were farmers, shepherds, and employees in the slaughtering industry, so health education for them is still an important way to prevent anthrax. In addition, professional training for local clinicians should be strengthened to enable them to recognize and identify various clinical anthrax cases earlier. On the other hand, anthrax surveillance and reporting in livestock husbandry were inadequate; as such, more measures and policies should be carried out to strengthen the monitoring of anthrax in livestock husbandry.

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Corresponding author: Jianchun Wei, weijianchun@icdc.cn.

[1] National Institute for Communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, China; [2] State Key Laboratory of Infectious Disease Prevention and Control, Beijing, China; [3] Yunnan Institute for Endemic Disease Control and Prevention, Dali City, Yunnan Province, China.
[&] Joint first authors.

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REFERENCES

1. World Health Organization. The control of neglected zoonotic diseases: from advocacy to action: report of the fourth international meeting held at WHO Headquarters, Geneva, Switzerland, 19–20 November 2014. Geneva: World Health Organization; 2015. https://apps.who.int/iris/handle/10665/183458.
2. Doganay M, Demiraslan H. Human anthrax as a re-emerging disease. Recent Pat Anti-Infect Drug Discov 2015;10(1):10 – 29. http://dx.doi.org/10.2174/1574891X10666150408162354.
3. World Health Organization, Food and Agriculture Organization of the United Nations & World Organisation for Animal Health. Anthrax in humans and animals. 4th ed. Geneva: WHO. 2008. https://apps.who.int/iris/handle/10665/97503.
4. Li S, An X, Huang Y, Pei G, Cao D, Mi Z, et al. Source tracking of an anthrax outbreak in northeastern China using complete genome analysis and MLVA genotyping. Eur J Clin Microbiol Infect Dis 2015;34(1): 89 – 100. http://dx.doi.org/10.1007/s10096-014-2195-7.
5. Liu DL, Wei JC, Chen QL, Guo XJ, Zhang EM, He L, et al. Genetic source tracking of an anthrax outbreak in Shaanxi province, China. Infect Dis Poverty 2017;6(1):14. http://dx.doi.org/10.1186/s40249-016-0218-6.
6. Zhang EM, Zhang HJ, He JR, Li W, Wei JC. Genetic diversity of *Bacillus anthracis* Ames lineage strains in China. BMC Infect Dis 2020;20(1):140. http://dx.doi.org/10.1186/s12879-020-4867-5.
7. Zhang HJ, Zhang EM, He JR, Li W, Wei JC. Genetic characteristics of *Bacillus anthracis* isolated from northwestern China from 1990 to 2016. PLoS Negl Trop Dis 2018;12(11):e0006908. http://dx.doi.org/10.1371/journal.pntd.0006908.
8. Yu XL, Zhang LF, Fang M, Liang H, Zhang Q, Yin XS, et al. Two confirmed patients of anthrax - Binzhou City, Shandong Province, China, August 2021. China CDC Wkly 2021;3(38):808 – 10. http://dx.doi.org/10.46234/ccdcw2021.185.
9. National Health Commission of the People's Republic of China. Diagnosis for anthrax. 2020. http://www.nhc.gov.cn/wjw/s9491/202005/7ab2722f726541a6aae5bf427406764b/files/595e704eb44143d8b37db4d6e0633a6a.pdf. (In Chinese).
10. Ministry of Agriculture and Rural Affairs of the People's Republic of China. Official Veterinary Bulletin. http://www.moa.gov.cn/gk/sygb/202111/P020211117598373488251.pdf. (In Chinese).

Vital Surveillances

Epidemiological Analysis of Foodborne Botulism Outbreaks — China, 2004–2020

Hongqiu Li[1]; Yunchang Guo[1]; Tian Tian[2]; Wanhua Guo[3]; Changqing Liu[4]; Xiaocheng Liang[5]; Jikai Liu[1]; Weiwei Li[1]; Ping Fu[1,#]

ABSTRACT

Introduction: Foodborne botulism is a rare, potentially fatal illness resulting from the ingestion of foods contaminated with preformed botulinum neurotoxin types A, B, E, or F, produced by *Clostridium botulinum*. The descriptive epidemiology of foodborne botulism outbreaks in China during 2004–2020 was performed to inform public health response strategies.

Methods: Data from 22 of 31 provincial-level administrative divisions (PLADs) of the National Foodborne Disease Outbreaks Surveillance System during 2004–2020 and Embase, China National Knowledge Infrastructure (CNKI), Wanfang Data, and Chinese Science and Technique Journals (CQVIP) from January 2004 to December 2020 to identify indexed publications in the Chinese literature using the following search terms "botulism," or "botulinum toxin," or "Clostridium botulinum." The number and proportion of outbreaks, illnesses, and deaths by PLAD, food types, and contributing factors were calculated.

Results: During 2004–2020, a total of 80 foodborne botulism outbreaks occurred in China, involving 386 illnesses and 55 deaths; most outbreaks were reported between June and August, with a sharp peak in January; 22 out of 31 PLADs reported foodborne botulism outbreaks, Xinjiang reported the largest number of outbreaks (20), followed by Qinghai (13); the most commonly implicated foods were home-prepared traditional processed stinky tofu and dried beef, accounting for 51.25% events. Improper processing and improper storage in contributing factors accounted for 77.50% outbreaks. Initial misdiagnosis occurred in 27.50% of cases.

Conclusions: Outbreaks of foodborne botulism had a high case-fatality rate. Targeted food safety and popularization education to farmers and herdsmen in Xinjiang and Qinghai related to botulism prevention should be carried out, and timely outbreak investigation and hospital surge capacity should be improved.

Belgian scholars in consumers of sausages first described botulism in 1896 (*1*). It was confirmed that the growth and germination of toxins occurred only under particular conditions in an anaerobic low salt, low-acid environment. People who ingest food contaminated with botulinum neurotoxin (BoNT) produced by botulinum toxin can have a potentially fatal outcome (*2*). Outbreaks have been reported worldwide. In Canada, the first Clostridium botulinum type E outbreak in 1944 in Nanaimo, British Columbia was reported in 1947 (*3*); In China, Wu et al. first reported botulism in Xinjiang in 1958 due to edible semi-finished noodle sauce (*4*). A better understanding of the epidemiology of botulism outbreaks can help tailor local prevention and public health response strategies. Here, we reviewed surveillance data on outbreaks, illnesses, and deaths of botulism in China from 2004 to 2020.

METHODS

Data were collected from 22 provincial-level administrative divisions (PLADs) in the mainland of China, and surveillance data of 50 outbreaks were abstracted from the database of the National Foodborne Disease Surveillance Network. Handsearching identified 30 publications from Embase, China National Knowledge Infrastructure, Wanfang Data, and Chinese Science and Technique Journals from January 2004 to December 2020 to identify indexed publications in the Chinese literature using the following search terms: "botulism," "botulinum toxin," or "Clostridium botulinum" combining "outbreaks." Foodborne botulism outbreaks were performed by descriptive statistical analyses. We analyzed the number and proportion of outbreaks, illnesses, deaths and case-fatality rate, date of the outbreak, regional distribution, implicated food(s), contributing factors, locations of food preparation, serotype, and circumstances of occurrence. Statistical analysis of the data was done in SPSS (version 19, IBM, Armonk, NY, USA), and significance was defined as $P<0.05$.

RESULTS

From 2004 to 2020, a total of 80 foodborne botulism outbreaks occurred in China, involving 386 illnesses and 55 deaths; a 14.25% overall case-fatality rate of foodborne botulism outbreaks was reported in China (Table 1). Also, the case-fatality rate dramatically decreased from 57.69% (15/26) in 2004 to 38.46% (5/13) in 2020. Households had the largest proportion of outbreaks, accounting for 90.00% (72/80), and the most commonly implicated foods were home-prepared traditional processed stinky tofu in Xinjiang and dried beef in Qinghai households, accounting for 43.06% (31/72) of the total.

Nationwide, most cases were reported between June and August, but with a sharp peak in January (Figure 1). During 2004–2020, the mean annual number of outbreaks was 5 (range: 3 to 11 outbreaks). Xinjiang had the largest number of outbreaks (20), followed by Qinghai (13) (Qinghai accounted for the greatest number of illnesses (101, 26.17%) and deaths (18, 32.73%). Between the top two PLADs with the most outbreaks, there was no statistically significant difference in case fatality rate between Qinghai and Xinjiang (χ^2=2.22, P>0.05). Among the 54 identified types of botulinum toxin, BoNT type A (28, 51.85%) was the most frequently identified toxin type, followed by type B (18, 33.33%). However, initial misdiagnosis occurred in 27.50% of cases (Table 1).

Table 2 shows that stinky tofu and dried beef were the primary sources of botulism, accounting for 41 out of 80 (51.25%) outbreaks in China. Among the top two foods with the most outbreaks, there was no statistically significant difference in case fatality rate between stinky tofu and dried beef (χ^2=1.61, P>0.50). Improper processing (32) and improper storage (30) were the main contributing factors of food-borne botulinum, accounting for 77.50% (62/80) of the total.

CONCLUSIONS

Foodborne botulism is an intoxication caused by ingestion of food containing botulinum neurotoxin. Cases of foodborne botulism are usually sporadic (single, unrelated), but outbreaks of two or more cases occur. Foodborne botulism remains a public health issue in China (*5*). From 2004 to 2020, the median number of outbreaks per year was 5 (range: 3 to 11 outbreaks). Whereas Xinjiang accounted for the highest number of outbreaks (20, 25.00%), Qinghai had the highest number of illnesses and deaths. This may be related to the fact that local farmers and herders especially in Xinjiang and Qinghai prepared traditional foods (home-made ethnic foods such as stinky tofu, soybean paste stew, and air-dried raw beef from households) using inappropriate/unsafe production processes (*6*); the study revealed that the primary cause of foodborne botulism was improper food handling practices and improper storage (55, 68.75%). For example, the fermentation process of home-made tempeh and soybean paste stew, etc. (placed in airtight containers) likely fostered an anaerobic environment, and suitable temperature (fermented for 10–15 days by the stove or radiator) was a necessary condition for toxin growth and production (*7*). Whereas some herders in Qinghai slaughtered cattle and sheep on the grass around their tents, put beef and mutton contaminated by botulinum toxin in the soil into pockets, and placed them outside the tent to air dry, the deeper part of the meat that was not completely air-dried still had some certain water content and the spores likely multiplied in the deeper part of the meat once the temperature was raised, providing conditions for the growth of botulinum toxin (*8*). Most reported cases mainly occurred from June to August in the study due to the high ambient temperature and high humidity at that time, which was compatible with the temperature required for botulinum to multiply and produce toxins. Our study highlighted the key characteristics of foodborne botulism outbreaks that could inform clinicians and public health officials in the development of preparedness and response plans (*9*). Therefore, targeted continuous education is needed to inform farmers and herdsmen in Xinjiang and Qinghai of the potential risks of botulism from ingesting homemade traditional native foods. It is necessary to standardize the management of processing, storage, and consumption of food raw materials. Preventive messages should focus on not using unsanitary and

TABLE 1. Number and proportion of foodborne botulism outbreaks, illnesses, deaths, serotype, and setting by PLAD, China, 2004–2020.

PLADs	No. of outbreaks (%)	No. of illnesses (%)	No. of deaths (%)	Annual average	No. of misdiagnoses*	Case-fatality rate† (%)	Serotype§		Setting¶	Adjusted χ^2**	p
							Type A	Type B	Household		
Xinjiang††	20(25.00)	53(13.63)	4(7.27)	4	3	8.00	11	4	18	0.64	0.14
Qinghai	13(16.25)	101(26.17)	18(32.73)	13	4	17.82	0	0	13		
Hebei	9(11.25)	23(5.96)	0(0.00)	8	2	0.00	1	3	9		
Gansu	5(6.25)	17(4.40)	9(16.36)	3	2	52.94	0	0	4		
Guizhou	4(5.00)	14(3.63)	4(7.27)	4	0	28.57	1	2	4		
Henan	3(3.75)	15(3.89)	0(0.00)	5	1	0.00	1	2	3		
Guangdong	3(3.75)	6(1.55)	0(0.00)	2	1	0.00	1	1	2		
Shaanxi	3(3.75)	10(2.59)	1(1.82)	3	2	10.00	5	2	3		
Tibet	2(2.50)	42(10.88)	3(5.45)	21	0	7.14	1	0	2		
Jiangxi	2(2.50)	8(2.07)	0(0.00)	4	1	0.00	0	0	2		
Shanxi	2(2.50)	5(1.30)	0(0.00)	3	0	0.00	0	0	2		
Anhui	2(2.50)	17(4.40)	6(1.25)	9	0	35.29	1	0	2		
Sichuan	2(2.50)	19(4.92)	9(16.36)	10	0	47.37	1	1	2		
Yunnan	2(2.50)	27(6.99)	1(1.82)	14	1	3.70	0	0	1		
Hunan	1(1.25)	2(0.52)	0(0.00)	2	1	0.00	1	1	0		
Jiangsu	1(1.25)	1(0.26)	0(0.00)	1	1	0.00	1	0	1		
Guangxi	1(1.25)	2(0.52)	0(0.00)	2	1	0.00	1	1	1		
Shandong	1(1.25)	4(1.04)	0(0.00)	4	1	0.00	1	1	1		
Ningxia	1(1.25)	11(2.85)	0(0.00)	11	1	0.00	0	0	1		
Jilin	1(1.25)	3(0.78)	0(0.00)	3	0	0.00	0	0	1		
Beijing	1(1.25)	2(0.52)	0(0.00)	2	0	0.00	1	0	0		
Inner Mongolia	1(1.25)	4(1.04)	0(0.00)	4	0	0.00	0	1	0		
Total	80(100.00)	386(100.00)	55(100.00)	5	22	14.25	28	18	72		

Abbreviation: PLAD=provincial-level administrative division.

* Misdiagnosis: Patients with botulism can be misdiagnosed as having other illnesses such as Guillain-Barré Syndrome, common cold, malnutrition and myasthenia gravis.

† Case-fatality rate = number of deaths / number of illnesses.

§ Serotype: the remaining includes 26 serotypes not identified and 3 type E, 2 type AB, 2 types Mangan and 1F.

¶ Setting: the remaining 2 outbreaks occurred in unit canteens, 1 outbreak occurred in school canteens, supermarkets, stores and large restaurants respectively; 2 outbreaks not identified.

** The Adjusted chi-square test (χ^2) of case-fatality rate between Xinjiang and Qinghai was performed and the result was: Adjusted χ^2=2.22, P>0.05.

†† 20 cases of botulism in Xinjiang include 3 in Xinjiang Production and Construction Corps.

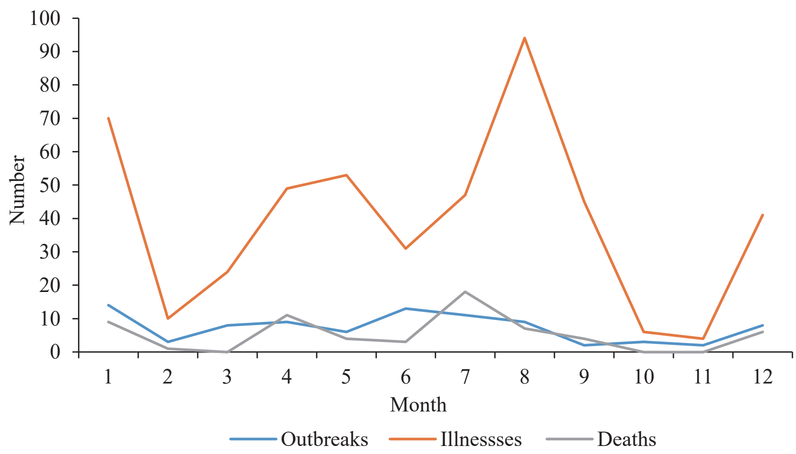

FIGURE 1. Foodborne botulism outbreaks, illnesses, deaths by month, China, 2004–2020.

TABLE 2. Attribution analysis of food types and contributing factors of foodborne botulism, China, 2004–2020.

Food types	Contributing factors				Total
	Improper processing	Improper storage	Raw material contamination	Unknown etiology	
Stinky tofu	12	9	1	2	24
Dried beef	8	4	5	0	17
Soybean paste stew	6	1	2	0	9
Meat products	3	5	2	1	11
Tempeh	1	6	0	0	7
Mixed food	1	0	0	1	2
Homemade pickles	0	2	0	0	2
Soy products	0	2	0	0	2
Unknown etiology	1	1	0	4	6
Total	32	30	10	8	80

traditional food processing, changing the bad eating habits of eating raw or half-raw meat, heating and boiling native foods thoroughly to destroy toxins and prevent *Clostridium botulinum* poisoning.

Foodborne botulism is rare, thus some physicians are unfamiliar with the disease (*10*), and delayed diagnosis or misdiagnosis potentially leads to severe fatal illness in clinical settings (*11*). Botulinum toxin poisoning has a high mortality rate of 14.25%, possibly related to the inability to diagnose correctly in time. In the study, initial misdiagnosis occurred in 27.50% of cases. Here, misdiagnosis means that patients with botulism can be misdiagnosed as having other illnesses, such as Guillain-Barré syndrome, common cold, malnutrition, and myasthenia gravis. Between the top two PLADs with the most outbreaks, the case fatality rate in Qinghai was higher than that in Xinjiang, which may be due to initial misdiagnosis or delayed diagnosis. Hospitals and provincial and local public health officials should incorporate stocking up on a certain amount of botulinum antitoxin into emergency planning. Professional prevention and treatment of food-borne botulism outbreaks should provide clinicians in hospitals with clinical, laboratory diagnosis and emergency preparedness precautions for botulism in the clinical guidelines to improve the recognition, diagnosis, and treatment of botulinum toxin poisoning; the need to rapidly identify patients in danger of respiratory failure must be anticipated (*12*). The provision of botulinum antitoxin should be ensured early and adequately used to avoid death.

We analyzed surveillance data from 50 outbreaks, and manual searches identified 30 publications of laboratory-confirmed outbreaks. They were merged and analyzed to make the data more representative and the analysis results more reliable. However, data elements were incomplete in much existing literature where clinical symptoms, incubation period, and some laboratories lacked the ability to differentiate between botulinum toxin and serum. Therefore, the epidemiological survey data and the quality of data reporting food-borne *Clostridium botulinum* surveillance should be improved; a better understanding of the epidemiology of botulism outbreaks can help tailor local prevention and public health response strategies.

This study is subject to certain limitations that may influence the generalizability of the findings. First, for many reported outbreaks, information on certain aspects of the outbreaks was missing or incomplete, so the conclusions might not be representative of unknown etiologies or food categories. Second, reported foodborne botulism outbreaks cannot represent all actual outbreaks occurred, since underreporting existed for various reasons, such as administrative intervention, insufficient ability of outbreak investigation, etc.

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[#] Corresponding author: Ping Fu, fuping@cfsa.net.cn.

[1] National Health Commission Key Laboratory of Food Safety Risk Assessment, China National Center for Food Safety Risk Assessment, Beijing, China; [2] Xinjiang Uygur Autonomous Region Center for Disease Control and Prevention, Urumqi City, Xinjiang Uygur Autonomous Region, China; [3] Qinghai Center for Disease Prevention and Control, Xining City, Qinghai Province, China; [4] Hebei Provincial Center for Disease Control and Prevention, Shijiazhuang City, Hebei Province, China; [5] Gansu Provincial Center for Disease Control and Prevention, Lanzhou City, Gansu Province, China.

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REFERENCES

1. Van Ermengem E. A new anaerobic bacillus and its relation to botulism. Rev Infect Dis 1979;1(4):701 – 19. http://dx.doi.org/10.1093/clinids/1.4.701.
2. Liu YP, Yuan XH, Men XY. Prevention and education of Clostridium botulinum poisoning. Guide China Med 2011;9(3):118 – 9. http://dx.doi.org/10.15912/j.cnki.gocm.2011.03.009. (In Chinese).
3. Leclair D, Fung J, Isaac-Renton JL, Proulx JF, May-Hadford J, Ellis A, et al. Foodborne botulism in Canada, 1985–2005. Emerg Infect Dis 2013;19(6):961 – 8. http://dx.doi.org/10.3201/eid1906.120873.
4. Wu CR, Lian ZH, Chen WJ, Liu YZ, Liang X, Li WH, et al. Botulism poisoning-investigation of “Chabuchar disease”. Nat Med J China 1958;44(10):932–8. http://rs.yiigle.com/CN112137195810/844135.htm. (In Chinese).
5. Liu DJ, Guo XB, Zhou HW. Epidemiological analysis of twelve botulism in Qinghai province. Mod Prev Med 2016;43(6):1017–9. https://d.wanfangdata.com.cn/periodical/xdyfyx201606017. (In Chinese).
6. Fleck-Derderian S, Shankar M, Rao AK, Chatham-Stephens K, Adjei S, Sobel J, et al. The epidemiology of foodborne botulism outbreaks: a systematic review. Clin Infect Dis 2017;66(S1):S73 – 81. http://dx.doi.org/10.1093/cid/cix846.
7. Sobel J, Rao AK. Making the best of the evidence: toward national clinical guidelines for botulism. Clin Infect Dis 2018;66(S1):S1 – 3. http://dx.doi.org/10.1093/cid/cix829.
8. Li X, Shao X. Epidemiological analysis of botulism in Ba Zhou, Xinjiang from 1998 to 2000. Chin J Prev Med 2002;36(3):171. http://dx.doi.org/10.3760/j:issn:0253-9624.2002.03.026. (In Chinese).
9. Luo JZ, Xu WY. The epidemic situation and preventive measures of botulism in Xinjiang. Mod Prev Med 2002;29(1):97 – 8. https://kns.cnki.net/kcms/detail/detail.aspx?dbcode=CJFD&dbname=CJFD2002&filename=XDYF200201065&uniplatform=NZKPT&v=ITI1-G2lsNKtSdFccpJ-ofHQI0CILKoRlPuH6AUA0o0l-xmFiKmadNsJPLAf3oXQ. (In Chinese).
10. Juliao PC, Maslanka S, Dykes J, Gaul L, Bagdure S, Granzow-Kibiger L, et al. National outbreak of type a foodborne botulism associated with a widely distributed commercially canned hot dog chili sauce. Clin Infect Dis 2013;56(3):376 – 82. http://dx.doi.org/10.1093/cid/cis901.
11. Tuerdi G, Gao PY, Sun H, Sun XH, Li XY, Lu XC, et al. An investigation of a botulism poisoning event in Urumqi, Xinjiang. Dis Surveill 2022;37(1):45 – 9. http://dx.doi.org/10.3784/jbjc.202009170320. (In Chinese).
12. Lúquez C, Edwards L, Griffin C, Sobel J. Foodborne botulism outbreaks in the United States, 2001-2017. Front Microbiol 2021;12:713101. http://dx.doi.org/10.3389/fmicb.2021.713101.

Vital Surveillances

Epidemiological Characteristics of Human Rabies — Shandong Province, China, 2010–2020

Xiaomei Zhang[1]; Xueying Tian[1]; Bo Pang[1]; Zhiqiang Wang[1]; Wenji Zhai[1]; Xiaolin Jiang[1]; Zengqiang Kou[1,#]; Shujun Ding[1,#]; Xianjun Wang[1]

ABSTRACT

Introduction: Rabies is a viral zoonotic disease that causes progressive and fatal inflammation in the brain. Rabies has caused more than 5,000 human deaths in Shandong Province since 1955. This study aimed to analyze the epidemiological characteristics of human rabies in Shandong Province from 2010 to 2020 and to provide a scientific basis for policy changes.

Methods: The data of reported human rabies cases from 2010 to 2020 were obtained from China's National Notifiable Disease Reporting System, and data related to exposure and post-exposure prophylaxis (PEP) of the cases were acquired through case investigation.

Results: A total of 414 human rabies cases were reported in Shandong Province from 2010 to 2020. Out of the 414 total cases, 87.20% were primarily farmers; 83.10% were over 40 years old. 70.29% (265/377) belonged to category Ⅲ exposure; and 96.67% (377/390) were exposed to the virus through infected dogs. The vaccine inoculation rate of these cases after exposure was only 8.85%; 1.03% (4/390) had been vaccinated with rabies immunoglobulin, developing the disease 11 to 13 days after category Ⅲ exposure.

Conclusions: Dogs were still the primary animal hosts. Most rabies patients died due to no or inadequate post-exposure prophylaxis. Vaccine inoculation rates for dogs should reach the target of 70% as soon as possible. Health departments should improve the accessibility and quality of PEP; and improve the health literacy of the elderly in rural areas.

Rabies is a viral zoonotic disease that causes progressive and fatal inflammation of the brain (*1*). China has been working on the control and elimination of human rabies. Since 1955, rabies became one of the notifiable infectious diseases in China. A total of 5,632 human rabies cases were reported comprising 4 epidemic peaks in Shandong Province from 1956 to 2020. In 2007, a total of 133 cases were reported and the number of cases reached the fourth peak in recent years (*2*). This study analyzed epidemiological characteristics and risk factors of human rabies in Shandong Province from 2010 to 2020. The data provided essential information and suggestions for adjustments to the rabies control policy in Shandong Province.

METHODS

Historical data of human rabies cases from 2010 to 2020 in Shandong Province were collected through China's National Notifiable Disease Reporting System (NNDRS) from January 1, 2010 to December 31, 2020. The questionnaire about every case was filled out through a face-to-face interview with a family member of the patient by trained public health physicians at the county-level CDC and sent to the Shandong Provincial CDC. The questionnaire included patient information (gender, age, occupation), clinical manifestations, wounds caused by animals, and post-exposure prophylaxis (PEP) at the local clinics, etc. Reverse transcription-polymerase chain reaction (RT-PCR) and fluorescence quantitative PCR were carried out on patients' saliva, urine, blood specimens and so on. Epidata (version 3.1, Epidata Association, Denmark) was used for data entering and ArcGIS (version 10.0, Esri Inc, California, USA) was used for making regional distribution graphics.

RESULTS

A total of 414 human rabies cases were reported in Shandong Province from 2010 to 2020, and the incidence of human rabies decreased rapidly year over year, except for a small rebound in 2011 and 2015. The reported incidence rate decreased from 0.10/100,000 population in 2011 to 0/100,000 in

2020 with the mean incidence rate of 0.04/100,000 from 2010–2020. Overall, 74 and 91 cases were reported in 2010 and 2011, respectively, and the number of new cases reached 0 in 2020 (Figure 1). Only 15.22% (63/414) of specimens from cases were collected and confirmed in the lab. Among these 63 cases, 16 cases were laboratory-confirmed with a positivity rate of 25.40%. Also, 73.42% (304/414) of cases were recorded between March and October with a peak season in October. After 2015, rabies cases gradually reduced, and the peak season was not obvious.

These 414 human rabies cases were distributed widely in 16 municipal areas and 84 counties. Among the 414 human cases, 51 cases were reported from Heze, 48 cases from Linyi, 45 cases from Qingdao, 40 cases from Dezhou, 39 cases from Yantai, accounting for 53.86% of cases in 2010–2020 in Shandong Province. Pingdu City (16 cases), Cao County (14 cases), Laiyang City (12 cases), Junan County (12 cases), and Mudan District (12 cases) were the top five counties in the number of cases, accounting for 15.94% of the total cases in the whole province. All cases occurred in rural areas.

Overall, 71.01% (292/414) of cases were male, and 28.99% (122/414) cases were female. The gender ratio of cases was 2.39∶1. The average age was 52.30±17.04 years old, with a range from 2 to 89 years old. In total, 83.10% (344/414) cases were more than 40 years old. Most human rabies cases from 2010 to 2012 were among the age group from 40 to 49 (62/232, 26.72%), while most human rabies cases from 2013 to 2015 and 2016 to 2020 were among the age group from 50 to 59 (35/124, 28.23%) and from 60 to 69 (24/58, 41.38%), respectively (Table 1). The higher-risk population was born between 1954 and 1972. By occupation, 87.20% (361/414) of cases occurred in farmers, followed by 3.62% (15/414) in students, 3.14% (13/414) in homemakers and unemployed individuals, 2.17% (9/414) in preschool children, and 3.86% (16/414) others.

The fatality rate was 100.00%. Overall, 407 questionnaires of human rabies cases were obtained and the response rate was 98.31% (407/414). The median course of disease was 4 days, ranging from 0 to 28 days; 91.40% (372/407) of patients died within one week. Most cases showed typical rabies symptoms such as agitation, hydrophobia, fearing of wind, convulsion, and photophobia, etc.

In the study, categories of exposure were recorded in 377 cases (92.63%); 265 (70.29%) of reported fatalities were category Ⅲ exposure. Location of exposure and exposure modes were recorded in 396 cases (97.30%). The wounds injured mostly occurred on the extremities, and the frequent exposure sites were hands (224 cases, 55.04%), followed by the lower limbs below the knee (78 cases, 19.16%). In 18 cases, there was more than one wound; 343 (86.62%) human cases that died from rabies were due to animal bites; 390 (95.82%) fatalities had reported wounding animal and animal origin; 139 cases (35.64%) were injured by stray animals; and 231 cases (59.23%) by domestic animals (belonging to the family of the case or a neighbor and raised in free range). Overall, 96.67% (377/390) of the cases were injured by dogs, and only 1.89% (4/212) of domestic dogs had been vaccinated against rabies (Table 2).

Of the 389 (95.58%) cases with available PEP treatment, 216 (55.53%) cases had no wound treatment post exposure at all. Another 137 (35.22%) cases treated the wound by themselves. In total, there were 353 (86.73%) fatalities without proper wound treatment. Only 36 (9.25%) cases had their wounds treated in medical institutions, mostly in village clinics

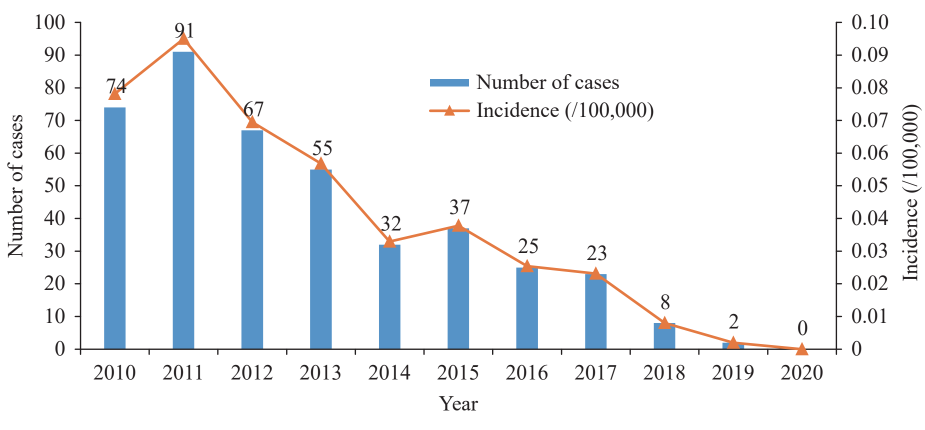

FIGURE 1. The number of cases and incidence rate of human rabies in Shandong Province, China, 2010–2020.

TABLE 1. Age distribution of human rabies cases in Shandong Province, 2010–2020.

Age group (years)	2010–2012		2013–2015		2016–2020	
	Number of cases	Proportion (%)	Number of cases	Proportion (%)	Number of cases	Proportion (%)
0–	4	1.72	2	1.61	0	0.00
5–	5	2.16	6	4.84	0	0.00
10–	6	2.59	0	0.00	2	3.45
20–	8	3.45	3	2.42	0	0.00
30–	26	11.21	5	4.03	3	5.17
40–	62	26.72	17	13.71	12	20.69
50–	53	22.84	35	28.23	10	17.24
60–	42	18.10	34	27.42	24	41.38
70–	22	9.48	18	14.52	6	10.34
80–	4	1.72	4	3.23	1	1.72

(21/36) (Table 2). Regarding the post-exposure vaccination, the rabies vaccine coverage rate was 8.85% (36/407), and 23 cases were vaccinated at village clinics or private clinics. Of the 11 cases who received the full vaccination, 10 cases classified as category Ⅲ exposure did not receive rabies immunoglobulin as recommended by the WHO guidelines. Among the 25 cases who were not fully vaccinated, 17 died before vaccination was completed.

Among the reported cases, 4 patients who were bitten by stray dogs came to county-level medical institutions for wound treatment and were injected with rabies vaccine and anti-rabies immunoglobulin within 12 hours. Among them, 2 cases were over 60 years old, and another 2 cases were pre-school children, all of whom were exposed as category Ⅲ and died before vaccination completed.

CONCLUSION

Rabies is a vaccine-preventable disease. By taking measures to strengthen disease surveillance, conduct technical training, and standardize the clinic treatment for PEP (*1*,*3*), the number of human rabies cases in Shandong declined significantly from 2011 to 2020, which was consistent with the epidemic trend of human rabies in China (*4*–*5*). First, every reported human rabies case was investigated and the specimens were collected as soon as possible. The case survey rate was almost always 100%. Second, a special training class on rabies was conducted for staff from all over the whole province every year by Shandong CDC. Third, Shandong Province has gradually standardized the construction of PEP clinics since 2001. A series of documents such as construction standards of PEP

TABLE 2. Characteristics of exposure history and post-exposure prophylaxis, according to data from case investigations, Shandong Province, 2010–2020.

Exposure characteristics	Number of human rabies cases	Proportion (%)
Age group (years)		
<20	24	5.90
20–39	42	10.32
40–59	189	46.44
≥60	152	37.35
Gender		
Male	289	71.01
Female	118	28.99
Occupation		
Farmers	359	88.21
Students/preschool children	23	5.65
Others	25	6.14

TABLE 2. (Continued)

Exposure characteristics	Number of human rabies cases	Proportion (%)
Exposure level*		
Ⅰ	18	4.77
Ⅱ	94	24.93
Ⅲ	265	70.29
Exposure mode*		
Bite	343	86.62
Scratch	33	8.33
Others	20	5.05
Animal source*		
Domestic animal	231	59.23
Stray animal	139	35.64
Others	20	5.13
Animal vector*		
Dog	377	96.67
Cat	7	1.79
Others	6	1.54
Exposure reason*		
Active attack by the vector	211	56.42
Defensive attack by the vector	59	15.78
Playing with the vector	72	19.25
Other	32	8.56
Bite more than one person*		
Yes	59	15.69
No	317	84.31
Exposure site		
Head	33	8.11
Neck	4	0.98
Hand	224	55.04
Trunk	10	2.46
Arm	38	9.34
Lower limb above the knee	11	2.70
Below the knee	78	19.16
Wound treatment*		
Untreated	216	55.53
Self-treated	137	35.22
Treated in medical facilities	36	9.25
Rabies immunoglobulins administered		
Yes	4	0.98
No	403	99.02
Vaccination administered		
Yes	36	8.85
No	371	91.15

* Variables with missing values.

clinics, were first issued in 2007. And now, there are more than 2,000 qualified rabies PEP clinics in Shandong Province, and they can provide timely services for people. Fourth, health education is indispensable for people.

The study indicated that people over 40 years old and farmers were still the main high-risk groups in Shandong in the past decade (*5*–*7*). Before 2013, the number of human rabies cases was the highest in the 40–49 age group, but in the following years, it gradually changed to the group of 50–69 years old. 11.52% (47/408) were young students and preschool children from 2003 to 2007 (*2*), declining to only 5.80% from 2010 to 2020.

This change indicated the elder people in rural areas need additional protection. Therefore, health education should be focused on the rural elderly. The main reasons for human rabies fatalities were failure to carry out timely and standardized wound treatment and immunization prevention after exposure. In the study, 353 (90.75%) cases died without proper wound treatment and 371 (91.15%) fatalities did not receive vaccination. The vaccination rate (8.85%) of the cases was lower than that in other studies (*8*). Most cases were treated with PEP in village clinics. These findings suggested that it is important to ensure the quality of PEP at village clinics and establish a transfer system to higher-level hospitals in case of complications. Since 2016, only 2 cases failed to complete the immune program, indicating that the standardized management of rabies vaccination has played an important role in the prevention and control of human rabies (*3*,*8*). A total of 4 cases received PEP due to category Ⅲ exposure on heads died before the vaccine procedure completion with an incubation period of 11 to 13 days. It is important for people to seek standardized PEP immediately after exposure, especially for wounds on the head. The physicians should also participate in training courses and pay more attention to serious wounds on the head and face (*1*).

The result showed that Shandong had a higher rate of dog-related injuries among the cases when compared with the national average level (96.67% *vs.* 91.46%) cases (*5*). The majority of attacking animals were domestic animals, with only 1.89% vaccinated for rabies, which was similar to a national study (*5*). These findings indicate that dog-related injuries are still a primary risk factor for human rabies in Shandong despite the sharp decline in the number of cases, and it is necessary to manage and vaccinate domestic dogs in rural areas as well as stray dogs.

This study was subject to some limitations. First, 7 of 414 human rabies cases have failed to carry out case investigation for missing data rate of 1.69% (7/414). Second, the survey response rate was not 100%, but still above 92.5%. Third, most human rabies cases were clinically diagnosed because no specimens were collected immediately and no laboratory results.

In conclusion, to achieve zero human deaths from rabies, management and vaccination of dogs in rural areas should be prioritized to reach the 70% vaccination target (*9*), as well as by improving the accessibility and quality of PEP in rural areas from the health departments in Shandong.

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Corresponding authors: Zengqiang Kou, jack-cou@163.com; Shujun Ding, dsj_jn@126.com.

[1] Shandong Provincial Key Laboratory of Communicable Disease Control and Prevention, Department of Communicable Disease Control and Prevention, Shandong Center for Disease Control and Prevention, Jinan, Shandong, China.

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REFERENCES

1. Rohde RE, Rupprecht CE. Update on lyssaviruses and rabies: will past progress play as prologue in the near term towards future elimination? Fac Rev 2020;9:9. http://dx.doi.org/10.12703/b/9-9.
2. Wang XJ, Ding SJ, Li Z, Wang LS, Kou ZQ, Feng KJ, et al. Human rabies epidemiology in Shandong Province, China. Jpn J Infect Dis 2010;63(5):323–6. https://pubmed.ncbi.nlm.nih.gov/20858997/.
3. Zhou H, Li Y, Chen RF, Tao XY, Yu PC, Cao SC, et al. Technical guideline for human rabies prevention and control (2016). Chin J Epidemiol 2016;37(2):139 – 63. http://dx.doi.org/10.3760/cma.j.issn.0254-6450.2016.02.001. (In Chinese).
4. Zhang XM, Ding SJ, Wang ZQ, Zhai WJ, Wang XJ. Surveillance of human rabies in Shandong province, 2010. Dis Surveill 2012;27(1):54 – 6. http://dx.doi.org/10.3784/j.issn.1003-9961.2012.1.017. (In Chinese).
5. Liu JJ, Duo L, Tao XY, Zhu WY. Epidemiological characteristics of human rabies in China, 2016–2018. Chin J Epidemiol 2021;42(1):131 – 6. http://dx.doi.org/10.3760/cma.j.cn112338-20200116-00037. (In Chinese).
6. Li YL, Liu XQ, Yang HT, Zhang LF, Yang SM. Analysis on rabies epidemiology in Yunnan province, 2005-2017. Dis Surveill 2018;33(12):1014 – 7. http://dx.doi.org/10.3784/j.issn.1003-9961.2018.12.011. (In Chinese).
7. Qi L, Su K, Shen T, Tang WG, Xiao BZ, Long J, et al. Epidemiological characteristics and post-exposure prophylaxis of human rabies in Chongqing, China, 2007-2016. BMC Infect Dis 2018;18(1):6. http://dx.doi.org/10.1186/s12879-017-2830-x.
8. Wang DL, Zhang XF, Jin H, Cheng XQ, Duan CX, Wang XC, et al. Post-exposure prophylaxis vaccination rate and risk factors of human rabies in mainland China: a meta-analysis. Epidemiol Infect 2019;147:e64. http://dx.doi.org/10.1017/S0950268818003175.
9. World Health Organization. WHO expert consultation on rabies: third report. Geneva: World Health Organization; 2018. WHO Technical Report Series, No. 1012. Licence: CC BY-NC-SA 3.0 IGO. http://apps.who.int/iris/bitstream/handle/10665/272364/9789241210218-eng.pdf;jsessionid=4B6D3213741157D26420E607664AA215?sequence=1.

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