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Preplanned Studies

Status and Correlates of Hypersomnia in Hospitalized Patients with Unipolar Depression — Beijing, Henan, and Shandong, China, August 2019–March 2021

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Summary

What is already known about this topic?

Hypersomnia is an atypical characteristic of unipolar depression (UD), indicating a high risk of bipolar depression. Identifying the symptom should be prioritized in patients with UD. However, the status and correlated factors of hypersomnia greatly varied across investigations.

What is added by this report?

Among inpatients with UD, the rate of hypersomnia was roughly 28.1% (39/139). Younger age (18–35 years) and recurrent depression were independent correlates of hypersomnia in hospitalized patients with UD.

What are the implications for public health practice?

Understanding the high rate and independent correlates of hypersomnia in hospitalized patients with UD will help clinicians and policymakers to identify characteristics of depression, strengthen the management capacity and improve the quality of treatment and control programs.

Depression remains a serious public health problem around the world, including China. Globally, depression accounts for the biggest share of the total burden of disease with an estimated 76.4 million years lost to the disability (*1*). According to the data from the China Mental Health Survey, which was launched nationally in 2012, depressive disorder was the most common mood disorder, and its weighted lifetime prevalence was up to 6.8% (*2*), thus bringing heavy disease burden in Chinese population. Previously, the clinical and health management of unipolar depression (UD) emphasized symptoms of mood and interest but ignored the recognition of sleep disturbance, especially hypersomnia. Hypersomnia is an atypical characteristic of depressive disorder and it is significant for the early

identification of bipolar depression from UD (*3*). However, the rate and correlates of hypersomnia greatly varied across investigations. In the study, we investigated hospitalized patients with UD from 3 hospitals in Beijing Municipality, Henan Province, and Shandong Province and found that the rate of hypersomnia was roughly 28.1% (39/139), and younger age (18–35 years) and recurrent depression were independent correlated factors of hypersomnia in hospitalized patients with UD. The result reminded us of the necessity of paying attention to hypersomnia in UD patients.

The investigation was a cross-sectional study, and a total number of 139 inpatients with UD were recruited from Peking University Sixth Hospital, Zhumadian Second People's Hospital, and Liaocheng Fourth People's Hospital from August 2019 to March 2021. The research protocol was approved by the Ethics Committee of Peking University Sixth Hospital, and all participants signed informed consent. All inpatients met the unipolar depressive disorder diagnostic criteria of the International Classification of Diseases-10th Version (ICD-10) and were confirmed by the Mini-International Neuropsychiatric Interview (M.I.N.I.). They were all 18 years old or older and had primary education or above. All inpatients scored more than or equal to 20 in the Mini Mental State Examination. Patients with serious impairment of cardiac, hepatic, nephritic, and respiratory function or other serious diseases were excluded from the study. The general demographic data and clinical characteristics were obtained, including the Epworth Sleepiness Scale (ESS), the 9-item Patient Health Questionnaire (PHQ-9), the 7-item Generalized Anxiety Disorder Scale (GAD-7), the Brief Psychiatric Rating Scale (BPRS), and the Montreal Cognitive Assessment (MoCA); the suicide module of M.I.N.I. Hypersomnia was determined by a score of more than or equal to 10 in ESS (*4*) (total score range is between 1–24), all

participants were divided into groups of inpatients with and without hypersomnia depending on the scores of ESS.

Measurement data of normal distribution were expressed as $\bar{x} \pm s$, and an independent sample t-test was used for comparison between the two groups. Measurement data of non-normal distribution was represented by M (Q$_1$, Q$_3$), and the Mann-Whitney U test was used for comparison between the two groups. Count data were expressed as n (%), and χ^2 test was used for comparison. A multiple logistic regression model was used to obtain the independent correlates of hypersomnia. All statistical methods were adopted by the two-tailed test, and $P<0.05$ was considered statistically significant. All statistical analyses were performed using SPSS software (Version 21.0. IBM Corp., Armonk, NY, USA).

Among all hospitalized patients with UD, 41.7% (58/139) of participants were male and 58.3% (81/139) were female. The age of all the patients had a mean value of 43.45±16.37 years old. The rate of hypersomnia in hospitalized patients with UD was roughly 28.1% (39/139), scoring more than or equal to 10 in ESS. The rate of recurrent depression in the UD inpatients was 46.8% (65/139). Depression above the threshold was defined by a score of more than or equal to 10 in PHQ-9 (5), and its rate was 71.2% (99/139).

In terms of demographic characteristics, compared with inpatients without hypersomnia, inpatients with hypersomnia were younger, aged with a median value of 31 years ($Z=-3.77$, $P<0.001$). After stratifying by age, inpatients with hypersomnia also had high rate of younger age (18–35 years) (66.7% vs. 28.0%, $P<0.001$). Gender distribution had no significant difference between two groups. (Table 1)

For the clinical characteristics, there were no significant differences in the duration of depression, family history of mental disorders, history of modified electroconvulsive therapy (MECT), histories of smoking and alcohol consumption, and use of medications between UD inpatients with and without hypersomnia. The hypersomnia group had a higher rate of recurrent depression, but the difference was not statistically significant (59.0% vs. 42.0%, $P=0.072$). Compared with participants without hypersomnia, those with hypersomnia had higher scores of MoCA. However, the rate of mild cognitive impairment, defined by the score of less than 26 in MoCA, showed no significant difference between the two groups. Also, there were no significant differences in BPRS scores,

GAD-7 scores, and rates of comorbidity with anxiety and current suicide risk between inpatients with and without hypersomnia. UD inpatients with hypersomnia scored significantly higher in PHQ-9 than those without hypersomnia ($P<0.05$), indicating severer depressive symptoms. Patients with hypersomnia had a higher rate of depression above the threshold, but the statistical difference was not significant (82.1% vs. 67.0%, $P=0.078$).

In the multiple logistic regression model, age, recurrent depression, and depression above the threshold (PHQ-9≥10) were entered as potential contributors to hypersomnia in hospitalized patients with UD. As presented in Table 2, being aged 18–35 years [odds ratio (OR)=6.73, 95% confident interval (CI): 1.91–23.75] and recurrent depression (OR=2.96, 95% CI: 1.25–6.99) were independently correlated with hypersomnia in hospitalized patients with UD (all $P<0.05$). However, the factor of depression above the threshold was not an independent correlate of hypersomnia.

DISCUSSION

The study was a multicenter cross-sectional epidemiological investigation that found that the rate of hypersomnia in UD inpatients was roughly 28.1%, and patients with hypersomnia were associated with severer depressive symptoms. Younger age (18–35 years) and recurrent depression were independently associated with hypersomnia.

A previous study had reported the prevalence of increased sleep in major depressive disorder was 24.0% (3), which was similar to the rate of hypersomnia in hospitalized patients with UD. After controlling the effect of medication types, our study revealed younger age (18–35 years) and recurrent depression were independent correlates of hypersomnia in patients with UD. Several studies have illustrated that atypical depression might serve as a nosological bridge between UD and type II bipolar depression and indicate the possibility of "soft bipolarity". Bipolar depression is so similar to UD in its clinical manifestation that often obscures the differential diagnosis and accurate recognition. Clinical misdiagnosis may lead to incorrect intervention and poor prognosis, such as iatrogenic mania/hypomania switching and higher suicide risk, and thus higher healthcare burdens for individuals and the government. Bipolar disorders brought heavy disease burden worldwide and are ranked as being a heavier health burden in younger

TABLE 1. Comparisons of demographic and clinical characteristics in unipolar depressive inpatients with and without hypersomnia.

Characteristics	Inpatients with hypersomnia (n=39)	Inpatients without hypersomnia (n=100)	$t/\chi^2/Z$ value	P value
Demographic characteristics				
Gender [Male/Female, n (%)]	17/22 (43.6/56.4)	41/59 (41.0/59.0)	0.08	0.781
Age (Years, M (Q_1, Q_3)]	31.00 (22.00, 47.00)	51.00 (34.00, 57.75)	−3.77	<0.001
18–35 years [n (%)]	26 (66.7)	28 (28.0)		
36–59 years [n (%)]	9 (23.1%)	51 (51.0)	17.67	<0.001
>60 years [n (%)]	4 (10.3%)	21 (21.0)		
Clinical characteristics				
Duration of depression (Years, M (Q_1, Q_3)]	3.00 (1.00, 9.75)	3.00 (1.00, 10.00)	−0.56	0.578
Recurrent depression [n (%)]	23 (59.0)	42 (42.0)	3.25	0.072
Family history of mental disorders [n (%)]	7 (17.9)	26 (26.0)	1.01	0.316
History of alcohol consumption [n (%)]	36 (92.3)	83 (83.0)	1.97	0.160
History of smoking [n (%)]	33 (84.6)	75 (75.0)	1.50	0.221
History of MECT [n (%)]	35 (89.7)	82 (82.0)	1.26	0.261
Medication [n (%)]				
Antipsychotics	22 (56.4)	46 (46.0)	1.22	0.270
Antidepressants	39 (100)	98 (98.0)	0.79	0.374
Sedative hypnotics	27 (69.2)	69 (69.0)	0.001	0.979
Mood Stabilizers	2 (5.1)	5 (5.0)	0.001	0.975
MoCA score [M (Q_1, Q_3)]	25.00 (22.00, 28.00)	23.00 (20.00, 26.75)	−1.97	0.049
Mild cognitive impairment (MoCA score<26) [n (%)]	23 (59.0)	66 (66.0)	0.60	0.438
BPRS score ($\bar{x} \pm s$)	32.46±6.68	32.57±5.27	0.10	0.920
PHQ-9 score [M (Q_1, Q_3)]	16.00 (12.00, 23.00)	13.00 (8.00, 20.00)	−1.99	0.047
Depression (PHQ-9 score≥10) [n (%)]	32 (82.1)	67 (67.0)	3.10	0.078
GAD-7 score [M (Q_1, Q_3)]	11.00 (6.00, 16.00)	8.00 (5.00, 14.00)	−1.45	0.149
Anxiety (GAD-7 score≥10) [n (%)]	22 (56.4)	42 (42.0)	2.35	0.126
Current suicide risk [n (%)]	30 (76.9)	68 (68.0)	1.07	0.300

Abbreviations: MECT=modified electroconvulsive therapy; MoCA=montreal cognitive assessment; BPRS=brief psychiatric rating scale; PHQ-9= 9-item patient health questionnaire; GAD-7=7-item generalized anxiety disorder scale.

TABLE 2. Independent correlates of hypersomnia in hospitalized unipolar depressive patients (n=139).

Items	B value	S.E. value	Wald χ^2 value	OR (95% CI)	P value
Age (years)					
>60				1	
36–59	0.041	0.666	0.004	1.042 (0.282–3.844)	0.951
18–35	1.906	0.644	8.766	6.726 (1.905–23.751)	0.003
Recurrent depression					
No				1	
Yes	1.084	0.439	6.102	2.956 (1.251–6.987)	0.014

Abbreviations: S.E.=standard error; OR=odds ratio; CI=confidence interval.

populations (6), which may be a consequence of the early age of onset and recurrent nature of bipolar disorder (7). Therefore, it can be inferred that UD patients with hypersomnia have some inherent characteristics that may be associated with bipolar depression and may develop into bipolar disorder in

the future. However, the mechanisms of the relationship between the two have not been clarified, and further longitudinal research and exploration are still needed.

This study was subject to at least three limitations. First, the cross-sectional study design could only present correlated factors of hypersomnia, and it is difficult to avoid recall bias and cannot reveal the influencing factors and causal relationships. Second, ESS only revealed the subjective sleep quality in the last several months, which cannot fully reflect the long-term circumstances and objective performance. Finally, the relatively small sample size limited the reliability of the study, so further investigations with larger sample sizes are necessary.

In conclusion, hypersomnia is common in hospitalized patients with UD. We should pay close attention to the evaluation of hypersomnia in UD to help guide clinical practice and health management.

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Preplanned Studies

Assessing Impacting Factors of Dog Owners' Adoption of Dog Vaccination Against Rabies: A Cross-sectional Survey in Rural Areas — Guangxi Zhuang Autonomous Region, China, 2021

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Summary

What is already known about this topic?

Rabies is fatal while preventable. More than 99% of human rabies cases were caused by dog bites worldwide. Mass dog vaccination could interrupt dog-mediated rabies if achieving and maintaining a minimum coverage rate of 70%.

What does this report contribute?

The results of this study show that roughly 23.7% of households owned dogs in Guangxi Zhuang Autonomous Region, China but only about 19.1% of these households reported having their dogs vaccinated. Possible positive factors were injury history of dog bites, awareness of the necessity, and policy help for the costs of dog vaccination, but negative factors were negative attitude and inaccessibility.

What are the implications for public health practices?

Much more effort should be made to improve dog vaccination coverage in rural areas in Guangxi Zhuang Autonomous Region, China. Well-designed free mass vaccination campaigns with more accessibility and awareness campaigns are important to improve coverage.

Although rabies is an almost 100% fatal zoonotic disease once symptoms appear, rabies can be prevented by vaccines. More than 99% of human rabies cases were caused by dog bites worldwide (*1*). However, achieving and maintaining a minimum dog vaccination coverage of 70% has been proven to interrupt dog-mediated rabies (*1*). Southern China is a rabies-endemic region, with most human rabies cases occurring in rural areas of this region (*2*). In 2015, the World Health Organization, the World Organisation for Animal Health, and the Food and Agriculture Organization of the United Nations (FAO) in collaboration with Global Alliance for Rabies Control

proposed eliminating dog-mediated rabies globally by 2030 ("zero by 2030"). Although the vaccination coverage among registered dogs is required to meet 90% by the National Animal Rabies Prevention and Control Plan (*3*), current low vaccination coverage in dogs was the main obstacle for China to eliminate dog-transmitted rabies (*4*). Therefore, it is important to know the impacting factors associated with low dog vaccination rates in rural areas to design well-targeted rabies control programs. This study conducted a household survey on evaluating influencing factors of dog vaccination against rabies using a uniform structural questionnaire to interview 533 dog-owning households out of 2,432 households surveyed in 127 villages of Guangxi Zhuang Autonomous Region, a provincial-level administrative division (PLAD) with 24.26 million rural residents in China in 2021, based on a multistage random sampling method. Results indicated that facilitating factors for dog vaccination were injury history of dog bites, awareness of the necessity, and policy help for the costs of dog vaccination, while hindering factors were negative attitudes and inaccessibility to dog vaccinations. It is recommended to scale up free and more accessible mass dog vaccinations, as well as conduct an awareness campaign to improve dog rabies vaccination coverage in rural China.

The study calculated the sample sizes using the formula given by Thrusfield as follows: $N=Z^2 P (1 – P)/M^2$. The Z value is 1.96 at the confidence interval (CI) of 95%, P is the estimated domestic dog vaccination coverage percentage, set at 50% in this study, and M is the standard error set at 0.05. The minimum required sample size was 384 households, and this research investigated 533 dog-owning households in total. A multistage random sampling method was used to select 2,432 households in rural areas of Guangxi Zhuang Autonomous Region in China for investigation. The household survey was

conducted from January to March 2021. The interviewer asked the selected households whether their family owns any dogs; if the answer was no, then the interview would end; if the answer was yes, then the questionnaire was continued. The family head or a substitute family member aged above 18 years old was interviewed face-to-face. The information collected for each interviewee included the demographical characteristics such as gender, age, education level, reasons for raising dogs, dog vaccination status, the reasons of failing to vaccinate if that was the case, awareness of rabies, and the local dog rabies vaccination cost policy. R software (version 4.0.4, University of Auckland, New Zealand) was used to perform chi-squared tests to do univariate analysis and binary logistic regression model to control the confounding factors, with $P<0.05$ was considered statistically significant.

Among the 2,432 households surveyed, 578 households reported owning dogs. The household dog-owning rate was 23.7% (578/2,432). Overall, 45 households failed to answer the vaccination status of the dogs and were excluded. Finally, there were 533 dog-owning households that were investigated. Only 102 out of these 533 households reported having their dogs vaccinated against rabies, with a coverage rate of 19.1% (102/533). The main reasons for owning dogs were guarding the house (84.8%) and liking dogs (32.9%). The main reasons of failing to get their dogs vaccinated against rabies included not knowing the dogs needed to be vaccinated against rabies (51.1%), thinking the process was too troublesome (44.6%), and not knowing where to vaccinate (31.5%) (Table 1).

Out of the 533 responders from theses 533 households, 257 responders (48.2%) were male and 276 responders (51.8%) were female. The majority of these responders were young adults and middle-aged people with a median age of 46.2 years old [interquartile range (IQR): 35.0–58.0 years old]. The educational level of the responders was mainly primary school and below (43.5%), and junior middle school (33.4%). The awareness rates of single rabies related knowledge points among respondents ranged from 34.2% to 70.0%, while 13.9% of them had history of injury due to dog bites in the past year.

Univariate analyses results showed that age, education level, awareness of rabies, and injury history of dog bites in the past year were related to dog vaccination status (Table 2). Further binary logistic regression found several promoting factors of dog vaccinations (Table 3). The dog owners who had an injury history of dog bites in the past year were more likely to vaccinate dogs (OR=2.124, 95% CI: 1.059–4.205, $P<0.05$), compared with those without dog-bite history. Awareness of the necessity and cost policy of dog vaccination were also found to influence dog vaccination. Compared with their respective counterparts, the dog owners who knew that dogs should be vaccinated against rabies (OR=4.956, 95% CI: 2.387–10.914, $P<0.01$), the dog owners who knew local free policy of dog vaccines against rabies, (OR=3.290, 95% CI: 1.285–8.296, $P<0.05$), and the dog owners who knew the price of dog vaccination against rabies (OR=1.915, 95% CI: 1.048–3.543, $P<0.05$) were more likely to vaccinate dogs.

DISCUSSION

This study revealed high dog-owning rates and low dog vaccination coverage in Guangxi Zhuang Autonomous Region, and that injury history of dog bites, awareness of the necessity, and policy help for the costs of dog vaccination were identified as promoting factors for dog owners' adoption of dog vaccination, while negative attitude and inaccessibility to dog vaccination were hindering factors.

People with injury history of dog bites had received rabies knowledge through this unpleasant experience,

TABLE 1. Given reasons why households did not vaccinate their dogs in rural areas of Guangxi Zhuang Autonomous Region, China, 2021 (n=419*).

Reason	Households in which dogs were not vaccinated	
	Number	Proportion (%)
Did not know dogs need to be vaccinated against rabies	214	51.1
Did not know where to vaccinate for dogs	132	31.5
Thought that vaccinating dogs was too troublesome	187	44.6
Vaccination too expensive	46	11.0
Other	30	7.2

* Among 533 households, 431 households did not vaccinate their dogs, and 12 households did not give the reasons.

TABLE 2. Dog-owning households rabies vaccination adoption (owning dog being vaccinated or not) in rural areas of Guangxi Zhuang Autonomous Region, China, 2021.

Variable	Households in which dogs were vaccinated n (%)	Households in which dogs were not vaccinated n (%)	Total number of observed n (%)	P
Gender				
Male	43 (42.2)	214 (49.7)	257 (48.2)	0.173
Female	59 (57.8)	217 (50.3)	276 (51.8)	
Total	102 (100.0)	431 (100.0)	533 (100.0)	
Age (years)				
18–30	39 (38.2)	76 (17.6)	115 (21.6)	0.000
31–50	39 (38.2)	164 (38.1)	203 (38.1)	
≥51	24 (23.5)	191 (44.3)	215 (40.3)	
Total	102 (100.0)	431 (100.0)	533 (100.0)	
Level of education				
Primary school and below	24 (23.5)	208 (48.3)	232 (43.5)	0.000
Junior high school	36 (35.3)	142 (32.9)	178 (33.4)	
Senior high school and above	42 (41.2)	81 (18.8)	123 (23.1)	
Total	102 (100.0)	431 (100.0)	533 (100.0)	
Can rabies be cured?				
Yes	56 (54.9)	274 (63.6)	330 (61.9)	0.105
No	46 (45.1)	157 (36.4)	203 (38.1)	
Total	102 (100.0)	431 (100.0)	533 (100.0)	
Do you know that rabies can be prevented by vaccinations?				
No	13 (12.7)	147 (34.1)	160 (30.0)	0.000
Yes	89 (87.3)	284 (65.9)	373 (70.0)	
Total	102 (100.0)	431 (100.0)	533 (100.0)	
Whether there is an injury history of dog bites in the past year?				
No	80 (78.4)	379 (87.9)	459 (86.1)	0.013
Yes	22 (21.6)	52 (12.1)	74 (13.9)	
Total	102 (100.0)	431 (100.0)	533 (100.0)	
Do you know that dogs should be vaccinated against rabies?				
No	12 (12.1)	255 (60.4)	267 (51.2)	0.000
Yes	87 (87.9)	167 (39.6)	254 (48.8)	
Total	99 (100.0)	422 (100.0)	521 (100.0)	
Do you know where to vaccinate dogs against rabies?				
No	34 (33.7)	315 (73.4)	349 (65.8)	0.000
Yes	67 (66.3)	114 (26.6)	181 (34.2)	
Total	101 (100.0)	429 (100.0)	530 (100.0)	
Do you know the local policy of dog vaccination against rabies?				
Unknown	25 (24.5)	271 (62.9)	296 (55.5)	0.000
Charges	63 (61.8)	142 (32.9)	205 (38.5)	
Free	14 (13.7)	18 (4.2)	32 (6.0)	
Total	102 (100.0)	431 (100.0)	533 (100.0)	

TABLE 3. Impact factors of dog owner's adoption of vaccination in rural areas of Guangxi Zhuang Autonomous Region, China, based on a binary logistic regression model.

Variable	B	S.E.	Wald	P	Exp(B)	95% CI
Gender						
Male	Ref.					
Female	0.303	0.259	1.366	0.242	1.354	0.816−2.259
Age (in years)	−0.003	0.011	0.058	0.809	0.997	0.976−1.019
Level of education						
Primary school and below	Ref.					
Junior high school	0.212	0.361	0.344	0.558	1.236	0.608−2.522
High school and above	0.623	0.453	1.896	0.168	1.865	0.769−4.562
Can rabies be cured?						
Yes	Ref.					
No	0.005	0.262	0.000	0.984	1.005	0.599−1.678
Do you know that rabies can be prevented by vaccinations?						
No	Ref.					
Yes	0.168	0.384	0.191	0.662	1.183	0.565−2.575
Whether there is an injury history of dog bites in the past year?						
No	Ref.					
Yes	0.754	0.350	4.636	0.031	2.124	1.059−4.205
Do you know that dogs should be vaccinated against rabies?						
No	Ref.					
Yes	1.601	0.385	17.257	0.000	4.956	2.387−10.914
Do you know where to vaccinate dogs against rabies?						
No	Ref.					
Yes	0.519	0.301	2.973	0.085	1.681	0.934−3.051
Do you know the local policy of dog vaccination against rabies?						
Unknown	Ref.					
Charges	0.650	0.310	4.401	0.036	1.915	1.048−3.543
Free	1.191	0.473	6.342	0.012	3.290	1.285−8.296
Constant	−3.736	0.783	22.768	0.000	0.024	0.005−0.107

Notes: The Ref. were used as control groups, such as male, primary school, and below. Rabies awareness rate of single knowledge point = number of people answering correctly for single point /number of people answering this point; dogs are classified as immunized dog if it has been vaccinated once.

Abbreviations: B=partial regression coefficient; S.E.=standard error; Wald=wald test; Exp(B)=odds ratio; CI=confidence interval; Ref.=reference.

and people who knew the cost policy of dog vaccination may have access to acquire more knowledge about rabies. High understanding level about rabies prophylaxis knowledge and policy might drive people to vaccinate their dogs (5). In addition, local policies providing free canine rabies vaccines has reduced the economic burden on dog owners and further increased their willingness to vaccinate their dogs against rabies. This finding indicated that free mass vaccination program may help encourage dog owners in rural areas to have their dogs vaccinated.

In this study, among the dog owners who failed to vaccinate their dogs, 44.6% thought vaccinating dogs too troublesome and 31.5% did not know where to vaccinate dogs. Similarly, some previous studies also suggested other factors such as a limited number of vaccinating sites and veterinarians, long distance to the sites and veterinary clinic, and feeling difficulty confining the dogs for vaccination would prevent many dog owners from accessing rabies vaccinations (6–7). Therefore, supporting conditions for relevant policies, such as veterinary systems and a free policy, are also

important factors affecting dog vaccination against rabies. It is suggested to establish more rural vaccination sites, increase the number of mobile vaccination sites, even consider door-to-door vaccinations to raise the accessibility of dog vaccination service in rural areas, improve treatment and subsidies of veterinarians, increase the number of veterinarians in rural areas, increase the vaccine types provided by the free policy, and strengthen awareness campaign for dog rabies immunization strategies and measures.

The results of this study suggested that 23.7% of all households owned dogs in rural areas of Guangxi Zhuang Autonomous Region, higher than 18.0% of a rural district in Beijing (8) and higher than urban areas in Guangxi Zhuang Autonomous Region of China (9). This is related to the reason of keeping dogs for house guarding (10). This research also found that only about 19.1% of dog-owning households reported having their dogs vaccinated, much lower than the minimum requirement to achieve interruptions in dog-mediated rabies spread (1) and also lower than that in economically developed regions, such as 85.0%–100.0% in Shanghai (10), 80.0% in Beijing (11), and above 70% in the Pearl River Delta region in Guangdong Province (4). The findings illustrated that there will still be much room for improving rabies control when progress is achieved in the endemic area (12). This may also be due to a lack of an appropriate incentive system for veterinarians as insufficients veterinarians are at the grassroots level, which when coupled with the limited free vaccination policy coverage, may contribute to much lower vaccination rates in Guangxi Zhuang Autonomous Region when compared to megacities or more economically developed regions. The other reasons may be related to different measuring methods of coverage rate: some studies only include the registered dogs, while others also involve the unregistered dogs using a household survey. Veterinarians are only responsible to administer vaccines to registered dogs (11), but dogs in rural China are seldom registered and leashed, which are difficult to catch and inject with inactivated vaccines (13). Therefore, sub-par dog registration management in PLADs with poor economic development is also one of the reasons for the low vaccination coverage (13).

In conclusion, it is recommended to scale up free and more accessible mass dog vaccination campaign to reduce the rabies risk and even achieve "zero by 2030" in rural areas of China, as well as conduct an awareness campaign. The revised edition of China National Animal Epidemic Prevention Law endorsed in March 2021 required dog owners to vaccinate their dogs against rabies (14), which will promote China towards the elimination of dog-mediated rabies.

This study was subject to some limitations. The dog immunization status was reported by dog owners, and interviewers neither checked the vaccination certificate nor collected data on the number of dogs owned, and the number of dogs vaccinated in each household. Therefore, the reported rate may have some discrepancy with actual cases. The ratios of captive and free roaming dogs and of once immunized dogs and annually immunized dogs are also unclear. Additionally, this study only considered the influence of dog owners on dog vaccination against rabies and did not include the factors associated with the service providers, such as veterinarians, and thus follow-up requiring further qualitative research should be conducted to provide more details to form a better vaccination program.

Conflicts of interest: No conflicts of interest.

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Vital Surveillances

Characteristics of Settings and Etiologic Agents of Foodborne Disease Outbreaks — China, 2020

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ABSTRACT

Introduction: Foodborne diseases are a growing public health problem and have caused a large burden of disease in China. This study analyzed epidemiological characteristics of foodborne diseases in China in 2020 to provide a scientific basis for prevention and control measures.

Methods: Data were collected from 30 of 31 provincial-level administrative divisions (PLADs) in the mainland of China, excluding Xizang (Tibet) Autonomous Region, via the National Foodborne Disease Outbreaks Surveillance System. The number and proportion of outbreaks, illnesses, hospitalizations, deaths by setting, pathogen-food category pairs and etiology were calculated.

Results: In 2020, 7,073 foodborne disease outbreaks were reported, resulting in 37,454 illnesses and 143 deaths. Among the identified pathogens, microbial pathogens were the most common confirmed etiology, accounting for 41.7% of illnesses. Poisonous mushrooms caused the largest proportion of outbreaks (58.0%) and deaths (57.6%). For venues where foodborne disease outbreaks occur, household had the highest number of outbreaks (4,140) and deaths (128), and catering service locations caused the largest proportion of illnesses (59.9%). Outbreaks occurring between June and September accounted for 62.8% of total outbreaks.

Conclusions: Foodborne disease outbreaks mainly occurred in households. Microbial pathogens remained the top cause of outbreak-associated illnesses. Poisonous mushrooms were ranked the top cause of deaths in private homes in China. The supervision and management of food safety and health education should be strengthened to reduce the burden of foodborne diseases. Publicity should be increased to reduce the incidence of mushroom poisonings in families, and supervision and management of food should be strengthened to reduce microbial contamination.

INTRODUCTION

An outbreak of foodborne disease is defined as the occurrence of two or more cases of a similar illness resulting from ingestion of a common food (*1*). It is a global health problem that is harmful to humans. Foodborne diseases encompass a wide spectrum of illnesses, including infectious diseases caused by microorganisms and toxic diseases mainly caused by chemical and toxic agents. The World Health Organization estimated that 600 million foodborne diseases occurred globally in 2010, causing 420,000 deaths (*2*). The US CDC estimated that 48 million foodborne diseases (1 in 6 Americans) occur each year in the USA, resulting in 12,800 hospitalizations and 3,000 deaths (*3*). In the Western Pacific Region, including China, 125 million people get sick and more than 50,000 die every year due to foodborne diseases (*4*). Foodborne diseases bring huge economic burdens to human beings. According to the requirements of Food Safety Law of the People's Republic of China, the National Foodborne Disease Outbreaks Surveillance System was established to continuously and systematically collect data on foodborne disease outbreaks in 2010.

Therefore, the objectives of this study were to characterize the epidemiological status of foodborne diseases in China and to analyze the distribution of high-risk foods and pathogenic factors to provide technical support for food safety risk assessment, formulation and revision of standards, and risk management.

METHODS

The study obtained data on foodborne disease cases reported through the National Foodborne Disease Outbreaks Surveillance System from January 1, 2020 to December 31, 2020. Data were collected from 30 of 31provincial-level administrative divisions (PLADs) in the mainland of China, excluding Xizang (Tibet) Autonomous Region. Data requested for each outbreak

report included the individual CDC reporting the outbreak, date of occurrence, number of illnesses, hospitalizations, and deaths, etiology, implicated food(s) and setting. All variable values were reported as counts or proportions (%). The number and proportion of outbreaks, illnesses, and deaths by etiology, setting, and food categories were calculated. The statistical analysis was performed using SPSS (version 21.0, IBM Corp, Chicago, USA).

RESULTS

Most outbreaks (97.5%), illnesses (98.0%), and deaths (99.1%) were linked to households and catering service locations. Households and catering service locations were the most common settings of reported outbreaks. In 2020, the highest number of outbreaks occurred in households (4,140), followed by catering service locations (2,719), and school campuses (27). Most illnesses (59.9%) were reported in catering service locations, followed by households (37.6%), and 0.5% in campuses. Within catering service locations, street stalls accounted for the largest proportion (26.2%) of outbreaks, and school canteens accounted for the largest proportion (13.6%) of illnesses. However, households had the most deaths, accounting for 89.5% of all deaths (Table 1); poisonous mushrooms (79 deaths), aconite (10 deaths), bongkrek acid (11 deaths), and methanol (8 deaths) were the most common causes of deaths, accounting for 84.4%

of total deaths in private home settings.

In 2020, there were 4,662 outbreaks with confirmed etiology. Poisonous mushrooms were the most common cause of outbreaks and deaths, accounting for 58.0% of outbreaks and 57.6% of deaths; bacterial pathogens were the most common cause of illnesses (41.7%); in poisonous animals and plants and their toxins, undercooked *Phaseolus* was the most common cause leading to the largest proportion of outbreaks (31.2%) and illnesses (33.3%); aconite had the most deaths, accounting for 57.1%. Within microbial pathogens, *Salmonella* (286 outbreaks and 3,446 illnesses) was the most common bacterial pathogen associated with outbreaks and illnesses, followed by *Vibrio parahaemolyticus* (128 outbreaks and 1,848 illnesses), and *Staphylococcus aureus* (75 outbreaks and 954 illnesses). Bongkrek acid accounted for the largest proportions (75.0%) of deaths and the largest fatality rate (52.2%). Among the chemical agents, nitrite was the most common pathogenic factor associated with outbreaks (49.1%) and illnesses (49.6%), followed by pesticide (32.5% outbreaks and 27.7% illnesses); methanol had the highest death and fatality rates at 63.6% and 25.0%, respectively, followed by nitrite at 22.7% and 1.1%, respectively (Table 2).

In 2020, outbreaks that occurred at households (7,073) had surpassed those of catering service units (5,652), and outbreaks (485) and outbreak-associated illnesses (6,661) caused by *Salmonella* surpassed those

TABLE 1. Number and proportion of foodborne disease outbreaks, illnesses, and deaths by setting in China, 2020.

Setting	Outbreaks		Illnesses		Deaths		Fatality rate* (%)
	Number	Proportion (%)	Number	Proportion (%)	Number	Proportion (%)	
Household	4,140	58.5	14,066	37.6	128	89.5	0.9
Catering Service Places	2,719	38.4	22,432	59.9	15	10.5	0.1
Street stall	712	10.1	2,659	7.1	3	2.1	0.1
Hotel restaurant	508	7.2	4,184	11.2	5	3.5	0.1
Staff canteen	371	5.3	3,607	9.6	1	0.7	0.0
School canteen	310	4.4	5,081	13.6	0	0.0	0.0
Bistro	291	4.1	1,473	3.9	3	2.1	0.2
Fast food restaurant	240	3.4	1,171	3.1	0	0.0	0.0
Rural banquet	130	1.8	2,165	5.8	3	2.1	0.1
Home delivery of meal	110	1.6	1,807	4.8	0	0.0	0.0
Other	47	0.7	285	0.8	0	0.0	0.0
Campus	27	0.4	196	0.5	0	0.0	0.0
Other location	187	2.6	760	2.0	0	0.0	0.0
Total	7,073	100.0	37,454	100.0	143	100.0	0.4

* Fatality rate=number of deaths / number of illnesses.

TABLE 2. Number and proportion of foodborne disease outbreaks, illnesses, and deaths by etiology in China, 2020.

Etiology	Outbreaks		Illnesses		Deaths		Fatality rate* (%)
	Number	Proportion (%)	Number	Proportion(%)	Number	Proportion(%)	
Poisonous mushrooms	2,705	38.2	9,111	24.3	80	55.9	0.9
Plant and animal toxicants	1,020	14.4	4,584	12.2	21	14.7	0.5
Undercooked Phaseolus*	318	4.5	1,526	4.1	0	0.0	0.0
Coriaria sinica	111	1.6	354	1.0	0	0.0	0.0
Potherb	93	1.3	355	1.0	1	0.7	0.3
Aconite	84	1.2	337	1.0	12	8.4	3.6
Bitter bottle gourd	48	0.7	381	1.0	0	0.0	0.0
Tungoil or seed	46	0.7	238	0.6	0	0.0	0.0
Hyoscyamine	33	0.5	183	0.5	1	0.7	0.6
Herb-medicine	27	0.4	110	0.3	0	0.0	0.0
Elephant's-ear	24	0.3	86	0.2	0	0.0	0.0
Sproutedpotato/solanine	17	0.2	97	0.3	2	1.4	2.1
Colchicin	12	0.2	78	0.2	0	0.0	0.0
Gelsemine	11	0.2	64	0.2	3	2.1	4.7
Castor bean	10	0.1	58	0.2	0	0.0	0.0
Pokeberry root	10	0.1	42	0.1	1	0.7	2.4
Sago seed	10	0.1	36	0.1	0	0.0	0.0
Barbados nut	9	0.1	41	0.1	0	0.0	0.0
Undercooked soymilk/Trypsin inhibitor [†]	3	0.0	18	0.1	0	0.0	0.0
Other plants toxicants[§]	83	1.2	285	0.8	0	0.0	0.0
Fish roe	19	0.3	51	0.1	0	0.0	0.0
Tetrodotoxin	15	0.2	53	0.1	1	0.7	1.9
Pupae	13	0.2	60	0.2	0	0.0	0.0
langoustine	10	0.1	25	0.1	0	0.0	0.0
Other animal toxicants[**]	14	0.2	106	0.3	0	0.0	0.0
Bacterial	766	10.8	10,483	28.0	16	11.2	0.2
Salmonella	286	4.0	3,446	9.2	4	2.8	0.1
Vibrio parahaemolyticus	128	1.8	1,848	4.9	0	0.0	0.0
Staphylococcus aureus	75	1.1	954	2.6	0	0.0	0.0
Escherichia coli	54	0.8	1,520	4.1	0	0.0	0.0
Bacillus cereus	50	0.7	620	1.7	0	0.0	0.0
Bacillus proteus	10	0.1	149	0.4	0	0.0	0.0
Clostridium perfringens	5	0.1	287	0.8	0	0.0	0.0
Bongkrek acid[††]	5	0.1	23	0.1	12	8.4	52.2
Campylobacter jejuni	3	0.0	133	0.4	0	0.0	0.0
Clostridium botulinum	3	0.0	10	0.0	0	0.0	0.0
Listeria monocytogenes	1	0.0	28	0.1	0	0.0	0.0
Others	108	1.5	807	2.2	0	0.0	0.0
2 or more pathogens	12	0.2	224	0.6	0	0.0	0.0
Norovirus	26	0.4	434	1.2	0	0.0	0.0
Chemical agents	163	2.3	922	2.5	22	15.4	2.4
Nitrite	80	1.1	457	1.2	5	3.5	1.1

TABLE 2. (Continued)

Etiology	Outbreaks		Illnesses		Deaths		Fatality rate* (%)
	Number	Proportion (%)	Number	Proportion(%)	Number	Proportion(%)	
Pesticide[§§]	53	0.8	255	0.7	2	1.4	0.8
Prohibited drugs	10	0.1	115	0.3	1	0.7	0.9
Methanol	9	0.1	56	0.2	14	9.8	25.0
Other chemical pollutants[***]	11	0.2	39	0.1	0	0.0	0.0
Fungi	7	0.1	27	0.1	0	0.0	0.0
Parasitic	1	0.0	4	0.0	0	0.0	0.0
Unknown etiology	2,411	34.1	12,323	32.9	4	2.8	0.0
Total	7,073	100.0	37,454	100.0	143	100.0	0.4

* Refers to uncooked *Phaseolus* beans.
[†] Contained in uncooked soy milk.
[§] Including wild flowers, hellebore, wild ginseng, pollen, daffodils, and wild fruits, etc. Including bee pupae and silkworm pupae.
[**] Including dog liver, insects, fish gall, toads and ants, etc.
[††] Including Shigella, Aeromonas, Enterobacter cloacae, Citrobacter flaudus, Schneider, and Enterococcus, etc.
[§§] Including Carbamates, organophosphates, pyrethroids, paraquat, bromfamethamine and bromadiolone, etc. Including clenbuterol hydrochloride, xylazine, and tetramine.
[***] Including lead, engine oil, desiccant, chlorine dioxide, and detergent, etc.

of *Vibrio parahaemolyticus*. Foodborne disease illnesses occurred in school canteens (5,081).

The top 10 pathogen-food category pairs resulting in outbreaks, outbreak-associated illnesses, and deaths were analyzed. *Salmonella* in eggs had the highest occurrence, accounting for 32.8% (75/229) of outbreaks, followed by *Salmonella* in sauce-marinated meat (Table 3). *Salmonella* in sauce-marinated meat had the highest proportion (21.7%) of illnesses and 23.2% of hospitalizations, followed by *Salmonella* in eggs.

CONCLUSION AND COMMENT

Influenced by the coronavirus disease 2019 (COVID-19) pandemic, epidemiological characteristics of foodborne diseases in China had changed greatly in 2020.

For the first time in the past 5 years, outbreaks that occurred in private homes had surpassed that of catering service units in 2020 (5). The local residents in mountainous areas of southwest and central China tended to pick mushrooms and poisonous plants frequently in the wild (6). Continued and targeted health education programs should caution against picking wild mushrooms and toxic wild fruits. Eating habits with regional characteristics should be further emphasized and intervention measures should be taken to reduce the occurrence of poisonings.

The study showed that poisonous mushrooms caused the most deaths, the same as previous studies

TABLE 3. Top 10 number and proportion of most common confirmed pathogen-food category pairs resulting in outbreak in China, 2020.

Etiology	Food category	No. outbreaks	Proportion (%)
Salmonella	Egg	75	32.8
Salmonella	Sauce-marinated meat	44	19.2
Salmonella	Pastry	28	12.2
Bacillus cereus	Rice flour	22	9.6
Vibrio prahaemolyticus	Sauce-marinated meat	17	7.4
Salmonella	Livestock meat	13	5.7
Vibrio parahaemolyticus	Crustaceans	11	4.8
Escherichia coli	Sauce-marinated meat	10	4.4
Staphylococcalaureus enterotoxins	Pastry	9	3.9
Salmonella	Poultry	6	100.0
Total		229	32.8

(5). They were mainly caused by wild mushrooms collected by households (97.5%). This was consistent with the research results of Ren et al. (6). Residents picking and eating mushrooms could not distinguish between poisonous mushrooms from non-toxic mushrooms, and the rate of timely treatment after poisoning was low and increased the risk of death. Health education targeted for specific groups in rural areas is also essential to reduce mushroom poisonings.

Outbreaks and illnesses caused by *Salmonella* surpassed that of *Vibrio parahaemolyticus*, becoming the first pathogenic bacteria of bacterial foodborne diseases. This analysis on pathogen and food pairs in China showed that *Salmonella* outbreaks were most often linked to eggs, sauce-marinated meat products. Data showed that *Salmonella* was responsible for the largest number of outbreaks, hospitalizations, and deaths among meats and eggs; this was consistent with the result from the EU: *Salmonella* accounted for 36.8% of deaths in "eggs and egg products" (7). For *Salmonella* outbreaks, most outbreak-associated cases in the US were associated with seeded vegetables, eggs, poultry, beef, and pork, which differed from China (8). Pathogenic microbial contamination was still the main pathogenic factor of foodborne diseases in China and an important food safety issue that should not be ignored. Hygiene guidance and education should be done to reduce the burden of foodborne diseases caused by microbial factors.

Therefore, continued surveillance for foodborne disease outbreaks is important to understand changes in the foods, settings, and pathogens associated with illness (9). In order to reduce public health risks, more measures were adopted to enhance awareness of reporting, improve trace-back technology to achieve early detection, early warning, and early control of food safety risks.

This study was subject to at least two limitations. First of all, for many reported outbreaks, information on certain aspects of the outbreaks was missing or incomplete, so the conclusions might not be representative of unknown aetiologies or food categories. Second, reported foodborne disease outbreaks can't represent all actual occurred outbreaks, since underreporting existed for various reasons, such as administrative intervention, insufficient ability of outbreak investigation, etc.

Not all the National Foodborne Disease Outbreaks Surveillance System recorded with the epidemiological information in 2020. Like most countries, there are also cases of under-report, and incomplete information.

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Notifiable Infectious Diseases Reports

Reported Cases and Deaths of National Notifiable Infectious Diseases — China, August, 2021

Diseases	Cases	Deaths
Plague	1	0
Cholera	0	0
SARS-CoV	0	0
Acquired immune deficiency syndrome*	4,710	1,874
Hepatitis	126,075	62
Hepatitis A	1,057	0
Hepatitis B	102,061	51
Hepatitis C	20,001	9
Hepatitis D	23	0
Hepatitis E	2,109	2
Other hepatitis	824	0
Poliomyelitis	0	0
Human infection with H5N1 virus	0	0
Measles	66	0
Epidemic hemorrhagic fever	255	2
Rabies	14	8
Japanese encephalitis	72	1
Dengue	3	0
Anthrax	115	1
Dysentery	5,326	0
Tuberculosis	67,966	120
Typhoid fever and paratyphoid fever	913	1
Meningococcal meningitis	0	0
Pertussis	1227	0
Diphtheria	0	0
Neonatal tetanus	3	0
Scarlet fever	1,152	0
Brucellosis	6,867	0
Gonorrhea	12,019	1
Syphilis	46,091	7
Leptospirosis	81	0
Schistosomiasis	9	0
Malaria	60	0
Human infection with H7N9 virus	0	0
COVID-19[†]	1,893	0
Influenza	21,375	0
Mumps	8,353	0

Continued

Diseases	Cases	Deaths
Rubella	68	0
Acute hemorrhagic conjunctivitis	2,016	0
Leprosy	36	0
Typhus	143	0
Kala azar	28	0
Echinococcosis	241	0
Filariasis[†]	1	0
Infectious diarrhea[¶]	103,609	0
Hand, foot and mouth disease	71,283	0
Total	**482,071**	**2,077**

* The number of deaths of Acquired immune deficiency syndrome are the number of all-cause deaths reported in the month by cumulative reported AIDS patients.
[†] The data were from the website of the National Health Commission of the People's Republic of China.
[§] The one filariasis case was imported case.
[¶] Infectious diarrhea excludes cholera, dysentery, typhoid fever and paratyphoid fever.
The number of cases and cause-specific deaths refer to data recorded in National Notifiable Disease Reporting System in China, which includes both clinically-diagnosed cases and laboratory-confirmed cases. Only reported cases of the 31 provincial-level administrative divisions in the mainland of China are included in the table, whereas data of Hong Kong Special Administrative Region, Macau Special Administrative Region, and Taiwan are not included. Monthly statistics are calculated without annual verification, which were usually conducted in February of the next year for de-duplication and verification of reported cases in annual statistics. Therefore, 12-month cases could not be added together directly to calculate the cumulative cases because the individual information might be verified via National Notifiable Disease Reporting System according to information verification or field investigations by local CDCs.

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