

Population-Based Epidemiology of Sepsis in a Subdistrict of Beijing

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Objective: Information about the epidemiology of sepsis in community residents in China remains scarce and incomplete. The purpose of this study was to describe the occurrence rate and outcome of sepsis in Yuetan Subdistrict of Beijing and to estimate the occurrence rate of sepsis in China.

Design: Retrospective cohort study.

Setting: All public hospitals serving residents in Yuetan Subdistrict, Beijing.

Patients: All patients ($n = 1,716$) meeting criteria for sepsis based on American College of Chest Physicians/Society of Critical Care Medicine consensus definition.

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Interventions: None.

Measurement and Main Results: We screened all adult residents in Yuetan Subdistrict who were hospitalized from July 1, 2012, to June 30, 2014, and reviewed medical records. Patients with sepsis were included in the analysis. We enrolled 1,716 patients with sepsis out of 21,191 hospitalized adults screened, among whom severe sepsis developed in 256 patients, and septic shock developed in 233 patients. The crude annual occurrence rates of sepsis, severe sepsis, and septic shock in Yuetan Subdistrict were 667, 103, and 91 cases per 100,000 population, corresponding to standardized occurrence rates of 461, 68, and 52 cases per 100,000 population per year, respectively. Both occurrence rate and mortality increased significantly with age, although males had higher age-adjusted occurrence rate and mortality. The occurrence rate of sepsis also exhibited seasonal variation, peaking in winter season. The overall hospital mortality rate of sepsis was 20.6%, yielding a standardized mortality rate of 79 cases per 100,000 population per year.

Conclusions: Sepsis is a common and frequently fatal syndrome in Yuetan Subdistrict, Beijing. The occurrence rate and mortality of sepsis are significantly higher in males and elderly people. (*Crit Care Med* 2017; XX:00–00)

Key Words: occurrence rate; mortality; sepsis; septic shock; severe sepsis

Sepsis is the most common cause of death in noncoronary ICUs (1). In the past 2 decades, the world has witnessed a significant increase in the occurrence rate of sepsis (2, 3). Despite a better understanding of the pathophysiology and protocolized care that have improved outcome of sepsis (2, 4–6), in-hospital deaths related to sepsis have remarkably increased. Furthermore, many survivors of sepsis would suffer from poor quality of life, as suggested by more physical function impairment, more dementia and/or cognitive defects, and higher readmission rates, or even increased long-term mortality (7, 8). The resource utilization in providing care to septic patients is also on the rise (9).

Valid and comparable data on the population burden of diseases may be the essential resource for guiding health policy and

allocating healthcare resource. The epidemiology of sepsis in ICUs has been well described (10–14). However, data about the population occurrence rate of sepsis remained scarce (2, 15). There are even no population-level sepsis occurrence rate estimates from low- and middle-income countries, including China (16).

The unique healthcare system in China precludes the extrapolation of information from other countries. Chinese government has initiated a new healthcare reform since April 2009, aiming at providing safe, affordable, effective basic care to all citizens by 2020 (17). As a result, the total healthcare expenditure reached \$465.6 billion US dollars, or 5.57% of gross domestic product in 2013 (18, 19). About 33.9% of the expenditure was funded by individuals, or \$115.9 US dollars per capita. The urban basic healthcare insurance program covered 570.7 million people (78.1% of the urban population), whereas the new rural cooperative medical system provided healthcare insurance to 98.7% of the rural population in 2013 (18, 19). About 89.8% of healthcare in China is delivered by public hospitals, including 45.3% provided in 1,787 tertiary hospitals.

Although ICU- or hospital-based data have been used to postulate the national occurrence rate of sepsis (15, 20, 21), this approach might be invalid in China. Mobile population in China was 245 million in 2013, approximately one sixth of the national population (22), which might significantly bias both numerator (number of sepsis cases) and denominator (population) when calculating occurrence rate of sepsis.

The aim of this study was to describe sepsis epidemiology in Yuetan Subdistrict in Beijing, to provide more information about the disease burden of sepsis throughout China.

MATERIALS AND METHODS

Data Source

The hospital discharge database of Beijing Public Health Information System is composed of all discharge records for inpatients compulsorily submitted by all public hospitals in Beijing, except military and private hospitals. Patients meeting the following criteria were selected from the database: 1) age 18 years old or older; 2) hospitalization during the study period (from July 1, 2012, to June 30, 2014); and 3) resident in Yuetan Subdistrict based on home address. For each selected patient, we extracted following data from the hospital discharge database: name of the hospital, case number, and dates of hospital admission and discharge.

We selected Yuetan Subdistrict based on data quality and availability, as well as relatively few mobile population in this area. Being one of the 15 administrative areas of Xicheng District of Beijing, Yuetan Subdistrict is composed of 26 communities within an area of 4.11 km². According to the national census (23), the population in Yuetan Subdistrict in 2010 was 142,730, among whom there were 128,695 adults (age, ≥ 18 yr), including 62,724 males (48.7%) and 65,971 females (51.3%). Furthermore, mobile population accounted for 18.3% of the adult population in this region, similar to the national estimate of 18.0% (22), while significantly lower than that of 53.5% in Beijing (23).

Data Collection

All of the available medical records of enrolled patients were manually reviewed independently by any two of three investigators with more than 5 years of working experience in ICU. Any disagreement was resolved by discussion. In the event that consensus could not be reached, the steering committee consisting of three senior intensivists (X.X., Y.A., B.D.) helped in the final decision.

For all enrolled patients, the following data were retrieved: demographic data; admission category (medical, elective surgery, or emergency surgery); comorbidities, especially those included in Charlson comorbidity index (24); and hospital mortality. Based on the above retrieved data, severity of underlying illness was assessed by McCabe and Jackson (25) classification, whereas chronic organ dysfunction or immunosuppression was defined based on the criteria in Acute Physiology and Chronic Health Evaluation II score (26).

For patients with infection, we collected data about source of infection and relevant microbiologic information. For patients with sepsis, data about resource use (ICU admission, hospital length of stay, etc.) and Sequential Organ Failure Assessment (SOFA) score (27) were also collected.

Patients who developed sepsis before hospital admission or during hospital stay were both included in our cohort. Patients readmitted into hospitals during the study period were screened as new patients. Only the first episode of sepsis was counted during the same hospitalization.

Definitions

We identified cases with community-acquired infection based on clinical, imaging, and microbiologic parameters, whereas nosocomial infection was diagnosed according to the definitions of the Centers for Disease Control and Prevention (28). Microbiologically documented infection was the infection confirmed by positive cultures of blood or body fluid from a site of suspected infection; patients with the presence of gross purulence or an abscess (anatomical and/or by imaging and/or histologic evidence), but without a microbiologically documentation, were considered to be clinically documented infected.

We defined systemic inflammatory response syndrome (SIRS), sepsis, and septic shock according to the American College of Chest Physicians/Society of Critical Care Medicine consensus definition (1). Severe sepsis was diagnosed according to 2012 Surviving Sepsis Campaign guidelines (29). Patients with evidence of infection who fulfilled the definition for severe sepsis or septic shock but meeting fewer than two SIRS criteria were deemed as severe sepsis or septic shock, and analyzed as such (30).

Withholding life-sustaining therapy was defined as a predetermined decision not to implement therapies that would otherwise be deemed necessary, such as endotracheal intubation, mechanical ventilation, IV fluid expansion, transfusion, vasopressor infusion, cardiopulmonary resuscitation, and renal replacement therapy. Withdrawing life-sustaining therapy was defined as discontinuation of treatment that had previously been implemented (31).

Statistical Analysis

Data are presented as median and interquartile ranges (IQRs) for continuous variables due to nonnormal distribution, or as a percentage of the group from which they were derived for categorical variables. Continuous variables were compared using the Wilcoxon rank sum test, whereas categorical variables were compared using the chi-square test or Fisher exact test.

Occurrence rates and in-hospital mortality rates were normalized to the population distribution in the 2010 National Census (23). The differences of population occurrence rate and hospital mortality between genders and seasons were compared using z test as the data conformed to Poisson distribution. All comparisons were unpaired, and all tests of significance were two-tailed. A p value of less than 0.05 was considered statistically significant.

Ethics

This study was approved by the institutional review board of Peking Union Medical College Hospital, and the need for informed consent was waived. This study was registered at ClinicalTrials.gov, with registration number NCT02285257.

RESULTS

Patient Enrollment

During the 2-year study period, 22,552 adult patients in Yuetan Subdistrict were admitted into any of the 111 hospitals within the Beijing Public Health Information System. We were able to review medical records of 21,191 admissions (94.0%). The reasons for not reviewing the rest 1,361 cases included missing medical records ($n = 277$) and rejection of application by the hospital ($n = 1,084$).

Of the 21,191 hospitalizations investigated, median age was 66 years, 9,431 patients (44.5%) were male, 13,304 patients (62.8%) were medical admissions, and median Charlson comorbidity index was 1 (IQR, 0–2).

Characteristics of Patients With Sepsis

We identified 1,716 patients with sepsis. The median age was 80 years, and 57.6% were male, while more than 90% were medical admissions. Comorbidities were reported in 90% of patients with sepsis (Table 1).

One thousand ninety-one patients (63.6%) had community-acquired sepsis, whereas the remaining 625 patients (36.4%) developed hospital-acquired sepsis. Lower respiratory tract was the most common infection site, followed by genitourinary system and abdominal cavity (Table 2). A total of 988 pathogens were isolated from 646 patients (37.6%) with sepsis, including 765 Gram-negative bacilli and 178 Gram-positive cocci. *Pseudomonas aeruginosa* ($n = 237$) was the most common isolated pathogen, followed by *Acinetobacter baumannii* ($n = 183$), *Klebsiella pneumoniae* ($n = 91$), *Escherichia coli* ($n = 86$), and methicillin-resistant *Staphylococcus aureus* ($n = 70$) (Supplemental Table 1, Supplemental Digital Content 1, <http://links.lww.com/CCM/C542>).

Among patients, with sepsis, 265 (15.4%) were diagnosed as severe sepsis, whereas 233 patients (13.6%) met criteria for septic shock. The median SOFA score at the diagnosis of sepsis, severe sepsis, and septic shock was 2 (IQR, 0–3), 4 (IQR, 3–6), and 9 (IQR, 7–11), respectively. However, only 237 septic patients (13.8%) were admitted into ICU, compared with 20.0% ($n = 53$) in patients with severe sepsis and 59.2% ($n = 138$) in patients with septic shock.

The overall hospital mortality rate was 20.6% (353/1,716), including withdrawing and withholding life-sustaining therapy in 109 and 83 patients, respectively. In comparison, hospital mortality for severe sepsis and septic shock was 26.0% and 84.5%, respectively.

Occurrence Rate of Sepsis

The crude occurrence rate of sepsis, severe sepsis, and septic shock was 667, 103, and 91 cases per 100,000 population per year, respectively (Table 3), corresponding to 8.1 (95% CI, 7.7–8.5), 1.3 (95% CI, 1.1–1.4), and 1.1 (95% CI, 1.0–1.2) cases per 100 hospital admissions, respectively.

After we adjusted for age and gender, the standardized occurrence rate was 461, 68, and 52 cases per 100,000 population for sepsis, severe sepsis, and septic shock, respectively. Assuming that the above standardized occurrence rates were representative of those of China, this produced a national estimate of 4,856,532 cases of sepsis, 713,553 cases of severe sepsis, and 551,454 cases of septic shock per year.

The occurrence rate of sepsis and its complications (i.e., severe sepsis and septic shock) in men was significantly higher than that in women (Fig. 1 and Table 3). Women were more likely to have genitourinary infections (11.4% vs 7.1%; $p = 0.002$) and less likely to have lower respiratory tract infections (70.1% vs 72.7%; $p = 0.032$) but otherwise had a similar distribution of infection sites. In comparison, distribution of infection sites did not show seasonal variations.

The occurrence rate exhibited a slow but steady increase since adolescence (98 per 100,000 population < 50 yr old), and increased sharply through most of the adulthood (1,330.8 per 100,000 population 71–75 yr old), and peaked in the elderly (15,200 per 100,000 population > 90 yr old).

The occurrence rate of sepsis exhibited significant seasonal variation, being highest in winter (December, January, and February) and lowest in autumn (September, October, and November) (Supplemental Table 2, Supplemental Digital Content 2, <http://links.lww.com/CCM/C543>). The occurrence rate of severe sepsis and septic shock demonstrated similar seasonal variation.

The crude population mortality rates of sepsis, severe sepsis, and septic shock were 137, 27, and 77 cases per 100,000 population per year, respectively. This represented 831,674 deaths with sepsis, 156,057 deaths with severe sepsis, and 447,219 deaths with septic shock nationally, although this extrapolation was only speculative. Mortality was significantly higher in men than women for sepsis and septic shock, but not severe sepsis (Table 3). Mortality for sepsis increased with age from 2.4% in adults less than 50 years old to 30.7% in those more than 90 years old (Fig. 2).

TABLE 1. Characteristics of Patients Without Infection, Patients With Nonseptic Infection, and Patients With Sepsis

Characteristics	No Infection (n = 17,742)	Infection		
		Total (n = 3,449)	No Sepsis (n = 1,733)	Sepsis (n = 1,716)
Age, yr, median (IQR)	63 (49–78)	79 (64–85)	79 (62–84)	80 (66–85)
Male sex, n (%)	7,545 (42.5)	1,886 (54.7)	898 (51.8)	988 (57.6)
Smoking, n (%)	3,270 (18.4)	940 (27.3)	440 (25.4)	500 (29.1)
Alcoholism, n (%)	1,334 (7.5)	268 (7.8)	122 (7.0)	146 (8.5)
Type of hospital admission, n (%)				
Medical	10,235 (57.7)	3,069 (89.0)	1,516 (87.5)	1,553 (90.5)
Elective surgery	7,269 (41.0)	314 (9.1)	186 (10.7)	128 (7.5)
Emergency surgery	238 (1.3)	66 (1.9)	31 (1.8)	35 (2.0)
Comorbidities, n (%)				
None	4,581 (25.8)	371 (10.8)	199 (11.5)	172 (10.0)
Hypertension	7,891 (44.5)	1,979 (57.4)	1,029 (59.4)	950 (55.3)
Diabetes	3,995 (22.5)	936 (27.1)	482 (27.8)	454 (26.5)
Malignancy	3,311 (18.7)	529 (15.3)	255 (14.7)	274 (16.0)
Cerebrovascular disease	2,720 (15.3)	1,173 (34.0)	540 (31.2)	631 (36.8)
Coronary heart disease	3,347 (18.9)	1,099 (31.9)	549 (31.7)	550 (32.1)
Chronic lung disease	1,165 (6.6)	784 (22.7)	400 (23.1)	385 (22.4)
Peptic ulcer	597 (3.4)	254 (7.4)	106 (6.1)	148 (8.6)
Rheumatic disease	375 (2.1)	118 (3.4)	52 (3.0)	66 (3.8)
Hematologic malignancy	170 (1.0)	48 (1.4)	16 (0.9)	32 (1.9)
McCabe and Jackson (25) classification, n (%)				
Nonfatal	9,572 (54.0)	2,475 (71.8)	1,265 (73.0)	1,210 (70.5)
Ultimately fatal	3,040 (17.1)	514 (14.9)	225 (13.0)	289 (16.8)
Rapidly fatal	549 (3.1)	89 (2.6)	44 (2.5)	45 (2.6)
Charlson comorbidity index, median (IQR)	1 (0–2)	2 (1–3)	1 (0–3)	2 (1–3)
Chronic organ dysfunction, n (%)				
None	14,872 (83.8)	2,850 (82.6)	1,484 (85.6)	1,366 (79.6)
Cardiovascular	186 (1.0)	75 (2.2)	38 (2.2)	37 (2.2)
Liver	253 (1.4)	81 (2.3)	49 (2.8)	32 (1.9)
Respiratory	64 (0.4)	144 (4.2)	37 (2.1)	107 (6.2)
Renal	240 (1.4)	98 (2.8)	43 (2.5)	55 (3.2)
Immunosuppression	2,214 (12.5)	266 (7.7)	115 (6.6)	151 (8.9)
Hospital length of stay, median (IQR)	8 (4–14)	15 (9–27)	14 (9–22)	18 (10–34)
In-hospital mortality, n (%)	132 (0.7)	397 (11.5)	44 (2.5)	353 (20.6)

IQR = interquartile range.

TABLE 2. Site of Infection in Patients With Infection, Including Nonseptic Infection and Sepsis

Infection Site	Patients With Infection	Patients With Nonseptic Infection	Patients With Sepsis
Total, <i>n</i> (%)	3,449	1,733	1,716
Lower respiratory tract infection	2,218 (64.3)	970 (56.0)	1,248 (72.7)
Urogenital tract infection	421 (12.2)	268 (15.5)	153 (8.9)
Intra-abdominal infection	205 (5.9)	70 (4.0)	135 (7.9)
Upper respiratory infection	197 (5.7)	141 (8.1)	56 (3.3)
Gastroenteritis	170 (4.9)	102 (5.9)	68 (4.0)
Skin and soft tissue infection	145 (4.2)	113 (6.5)	32 (1.9)
Bacteremia	95 (2.8)	11 (0.6)	84 (4.9)
Other	169 (4.9)	105 (6.1)	64 (3.7)
Community-acquired, <i>n</i> (%)	2,474	1,383	1,091
Lower respiratory tract infection	1,593 (64.4)	795 (57.5)	798 (73.1)
Urogenital tract infection	280 (11.3)	193 (14.0)	87 (8.0)
Intra-abdominal infection	150 (6.1)	59 (4.3)	91 (8.3)
Upper respiratory infection	120 (4.9)	86 (6.2)	34 (3.1)
Gastroenteritis	140 (5.7)	90 (6.5)	50 (4.6)
Skin and soft tissue infection	118 (4.8)	98 (7.1)	20 (1.8)
Bacteremia	40 (1.6)	2 (0.1)	38 (3.5)
Other	122 (4.9)	89 (6.4)	33 (3.0)
Hospital-acquired, <i>n</i> (%)	975	350	625
Lower respiratory tract infection	625 (64.1)	175 (50.0)	450 (72.0)
Urogenital tract infection	141 (14.5)	75 (21.4)	66 (10.6)
Intra-abdominal infection	55 (5.6)	11 (3.1)	44 (7.0)
Upper respiratory infection	77 (7.9)	55 (15.7)	22 (3.5)
Gastroenteritis	30 (3.1)	12 (3.4)	18 (2.9)
Skin and soft tissue infection	27 (2.8)	15 (4.3)	12 (1.9)
Bacteremia	55 (5.6)	9 (2.6)	46 (7.4)
Other	47 (4.8)	16 (4.6)	31 (5.0)

DISCUSSION

Systemic review of available literature called for urgent action to measure sepsis morbidity and mortality in low- and middle-income countries (16). To the best of our knowledge, this is the first study to report population-based epidemiology of sepsis in China. We found that sepsis is very common and is associated with a high mortality rate, especially in males and elderly people. The estimated 4.86 million cases of sepsis, as well as 831,674 deaths, in adult population indicate significant disease burden in China, which underscores the importance of sepsis as a major health problem.

Both the crude and standardized occurrence rates of sepsis in our study were significantly higher than those reported in the literature. Similar to Wang et al (32), we identified cases of

sepsis by manual review of medical records, including progress notes, nursing charts, and laboratory tests. In comparison, by using *International Classification of Diseases* (ICD) codes, lower occurrence rates of sepsis were reported, such as 240.4 (2), 149 (21), and 166 cases (33) per 100,000 population in the United States, Norway, and Australia, respectively. However, both sensitivity and specificity of ICD-based algorithms had been questioned (34, 35), although a minor modification of administrative data capture and diagnostic criteria might result in substantial variability in occurrence rate and mortality of sepsis and severe sepsis up to 3.5-fold (36–38). Furthermore, the burden of sepsis measured by the use of administrative data was vulnerable to multiple confounding factors, such as changes in coding practice, introduction of new diagnosis codes over time,

TABLE 3. Crude and Standardized Occurrence Rate and Mortality Rates of Sepsis, Severe Sepsis, and Septic Shock

Sepsis and Complications	Occurrence Rate			Mortality		
	Crude (95% CI) ^a	Standardized ^b	National Estimate ^c	Crude (95% CI) ^a	Standardized ^b	National Estimate ^c
Sepsis	667 (622–711)	461	4,856,532	137 (117–157)	79	831,674
Men	788 (718–857) ^d	527	2,808,343	168 (136–200) ^d	91	482,861
Women	552 (495–608)	393	2,048,189	108 (83–133)	67	348,813
Severe sepsis	103 (85–120)	68	713,553	27 (18–36)	15	156,057
Men	130 (102–158) ^d	84	447,197	29 (15–42)	14	76,541
Women	77 (56–99)	51	266,356	25 (13–37)	15	79,516
Septic shock	91 (74–107)	52	551,454	77 (61–92)	42	447,219
Men	118 (91–145) ^d	63	336,130	102 (77–127) ^d	52	278,749
Women	64 (45–84)	41	215,324	52 (35–70)	32	168,470

^aThe occurrence and mortality rates of sepsis, severe sepsis, and septic shock in Yuetan Subdistrict of Beijing (per 100,000 population per year).

^bThe national-estimated occurrence and mortality rates of sepsis, severe sepsis, and septic shock, which were calculated by adjusting the corresponding data of Yuetan Subdistrict for age and gender (per 100,000 population per year).

^cThe estimated number of cases and deaths of sepsis, severe sepsis, and septic shock.

^d*p* < 0.001 versus women.

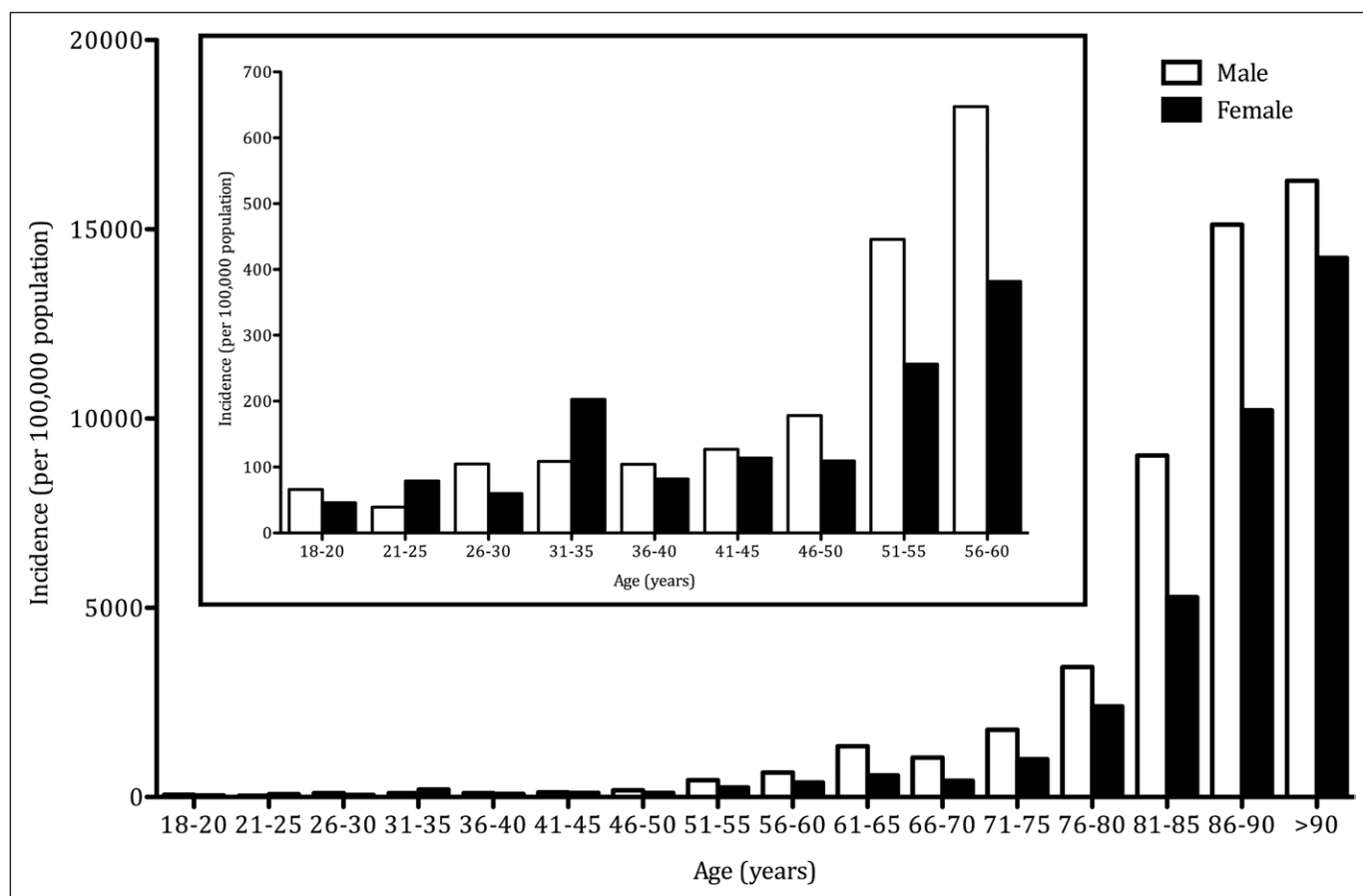


Figure 1. Age-specific occurrence rate of sepsis by gender.

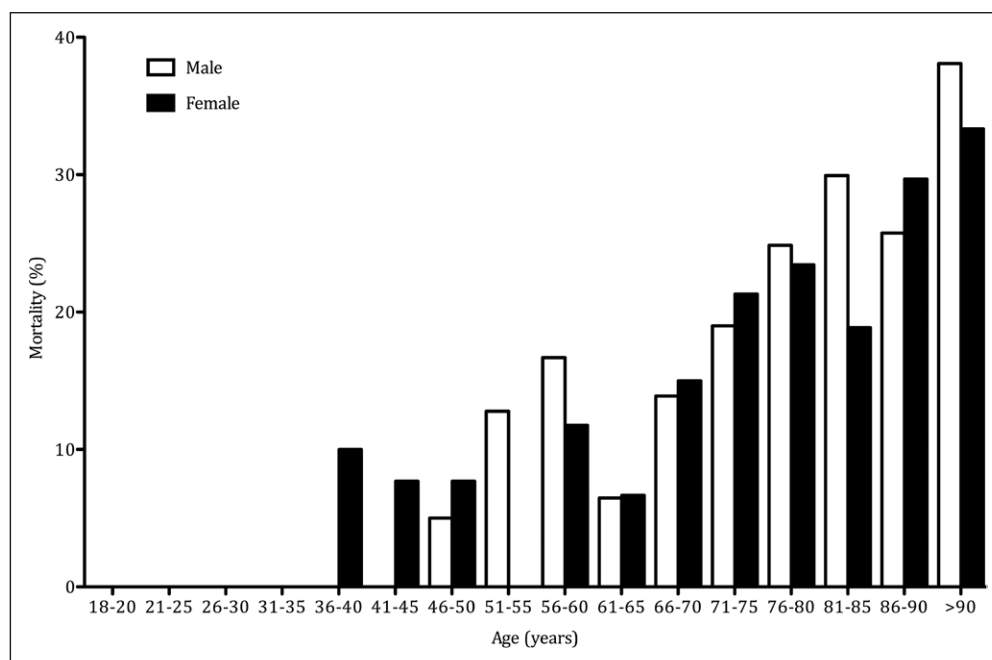


Figure 2. Age-specific mortality rate of sepsis by gender.

lack of important prognostic indicators, and no access to real-time information (34, 35). Another potential reason was that the hospitalized patients in our study were older. Our findings that the occurrence rate of sepsis and its complications significantly increased with age were consistent with Angus et al (39), and the elderly septic patients with comorbidities were more likely to be hospitalized (40). In fact, the extremely high occurrence rate of sepsis (15,200 cases per 100,000 population) in elderly people more than 90 years old has never been reported.

The high mortality rate of sepsis, severe sepsis, and septic shock in our cohort might be explained by several reasons. Septic patients in our study had a median age of 80 years, whereas increased age had been shown to be associated with higher hospital mortality rate (39). The 90% prevalence of comorbidities in our cohort of sepsis might also contribute to the observed mortality rate. Furthermore, the high rate of withdrawing and withholding life-sustaining therapy among nonsurvivors (54%, 192/353) was unexpected (41), possibly due to poor preexisting functional status associated with aging, moribund status secondary to acute illness, and monetary issues.

Previous studies showed that fewer than half of patients with severe sepsis ever received ICU treatment during hospitalization (39, 42). The ICU admission rate among septic patients in our study was even lower, which might also explain, at least in part, the observed high mortality rate. The population-adjusted ICU beds in China was estimated as only one fifth of that of the United States (43), which inevitably resulted in less tendency to admit some critically ill patients into the ICU. Robert et al (44) found that delayed ICU admission due to a full unit after first referral was associated with increased mortality. Interestingly, Esteban et al (42) reported that patients with septic shock

who were not admitted to the ICU had a higher mortality rate than those admitted to the ICU with the diagnosis of septic shock. The fact that majority of patients with sepsis were not admitted to the ICU also questioned the common approach that extrapolated ICU data to estimate population occurrence rate.

National projections of epidemiology of sepsis in our study were only estimates and merited meticulous interpretation. Although we had adjusted the occurrence rate by age and sex, the population we studied was more likely representative of an aging population, while young population was more common nationwide. However, preliminary results of an ongoing study, based on the national

mortality surveillance system that covered 24.3% of the total population of China with 605 surveillance points (including Yuetan Subdistrict) (45), reported sepsis-related mortality of 84.5 cases per 100,000 population in 2015 (L. Weng and B. Du, unpublished data, 2017). This is consistent with the standardized mortality rate of 79 cases per 100,000 population reported in the present study, suggesting the robustness of our findings.

Attempts to understand accurate national estimates of sepsis epidemiology are not simple, because the gross disparity between the data available in our study and the rest of China has to be closed if the global effort to improve sepsis care is to succeed. However, these efforts are important for understanding the national burden of the clinical syndrome, allocating limited healthcare resources, benchmarking the quality of healthcare delivery, and prioritizing research budgets (1). In addition, given the high occurrence rate and mortality of sepsis reported in our study, potential strategies for the prevention of sepsis should be proactively investigated, which might include, but not limited to, vaccination in vulnerable population, implementation of infection prevention programs mainly targeting nosocomial infections, promotion of increased awareness of sepsis among healthcare providers as well as general public, and development of real-time sepsis screening system as a priority.

Our study is subject to other limitations. First, the retrospective nature of our study might compromise the credibility of our results. However, we tried to capture every septic case by reviewing medical records of all hospitalized patients during the study period, which might be more reliable than using administrative data (32). Second, the occurrence rate of sepsis might be underestimated in our study, because some patients might seek for medical care in military or private hospitals,

which were not included in our database. Nevertheless, the number of these patients was presumed to be very small due to reimbursement policy. Third, the reported mortality rate was all-cause estimate rather than attributable mortality rate. In fact, without a case-control design, it would be impossible to estimate the contributable mortality in a cohort study. Fourth, the microbiologic data reported in this retrospective cohort study might be biased in favor of nosocomial bacterial pathogens, due to lack of consistent sepsis workup across all hospitals, and perception of well-established microbiology in most community-acquired infections. Furthermore, in contrast to the most recent study of microbiologic causes of community-acquired pneumonia (46), the importance of viral etiology was under recognized due to limited access to the more sensitive diagnostic techniques (e.g., polymerase chain reaction). Finally, as a retrospective cohort study, it would be very difficult to define the effect of financial issue and/or lack of health-care insurance coverage on patient outcome.

CONCLUSIONS

We found that sepsis is associated with high occurrence rate and poor prognosis, especially in males and elderly population, in Yuetan Subdistrict, Beijing. Considering the fact that China is stepping into an aging society, the disease burden of sepsis is expected to increase in the future. Given the importance of sepsis as a public health problem, prospective studies should be performed to confirm our findings, as well as to delineate the associated cost of care and long-term outcome.

REFERENCES

- Bone RC, Balk RA, Cerra FB, et al: Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. *Chest* 1992; 101:1644–1655
- Martin GS, Mannino DM, Eaton S, et al: The epidemiology of sepsis in the United States from 1979 through 2000. *N Engl J Med* 2003; 348:1546–1554
- Walkey AJ, Lagu T, Lindenauer PK: Trends in sepsis and infection sources in the United States. A population-based study. *Ann Am Thorac Soc* 2015; 12:216–220
- Harrison DA, Welch CA, Eddleston JM: The epidemiology of severe sepsis in England, Wales and Northern Ireland, 1996 to 2004: Secondary analysis of a high quality clinical database, the ICNARC Case Mix Programme Database. *Crit Care* 2006; 10:R42
- Kaukonen KM, Bailey M, Suzuki S, et al: Mortality related to severe sepsis and septic shock among critically ill patients in Australia and New Zealand, 2000–2012. *JAMA* 2014; 311:1308–1316
- Rivers E, Nguyen B, Havstad S, et al; Early Goal-Directed Therapy Collaborative Group: Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 2001; 345:1368–1377
- Iwashyna TJ, Ely EW, Smith DM, et al: Long-term cognitive impairment and functional disability among survivors of severe sepsis. *JAMA* 2010; 304:1787–1794
- Cuthbertson BH, Elders A, Hall S, et al; Scottish Critical Care Trials Group; Scottish Intensive Care Society Audit Group: Mortality and quality of life in the five years after severe sepsis. *Crit Care* 2013; 17:R70
- Lagu T, Rothberg MB, Shieh MS, et al: Hospitalizations, costs, and outcomes of severe sepsis in the United States 2003 to 2007. *Crit Care Med* 2012; 40:754–761
- Alberti C, Brun-Buisson C, Burchardi H, et al: Epidemiology of sepsis and infection in ICU patients from an international multicentre cohort study. *Intensive Care Med* 2002; 28:108–121
- Pittet D, Rangel-Frausto S, Li N, et al: Systemic inflammatory response syndrome, sepsis, severe sepsis and septic shock: Incidence, morbidities and outcomes in surgical ICU patients. *Intensive Care Med* 1995; 21:302–309
- Sakr Y, Elia C, Mascia L, et al: Epidemiology and outcome of sepsis syndromes in Italian ICUs: A multicentre, observational cohort study in the region of Piedmont. *Minerva Anestesiol* 2013; 79:993–1002
- Vincent JL, Sakr Y, Sprung CL, et al; Sepsis Occurrence in Acutely Ill Patients Investigators: Sepsis in European intensive care units: Results of the SOAP study. *Crit Care Med* 2006; 34:344–353
- Zhou J, Qian C, Zhao M, et al; China Critical Care Clinical Trials Group: Epidemiology and outcome of severe sepsis and septic shock in intensive care units in mainland China. *PLoS One* 2014; 9:e107181
- Andreu Ballester JC, Ballester F, González Sánchez A, et al: Epidemiology of sepsis in the Valencian Community (Spain), 1995–2004. *Infect Control Hosp Epidemiol* 2008; 29:630–634
- Fleischmann C, Scherag A, Adhikari NK, et al; International Forum of Acute Care Trialists: Assessment of global incidence and mortality of hospital-treated sepsis. Current estimates and limitations. *Am J Respir Crit Care Med* 2016; 193:259–272
- Chen Z: Launch of the health-care reform plan in China. *Lancet* 2009; 373:1322–1324
- Information CoSa, China NHaFPCotPsPo: Statistical communiqué of People's Republic of China on the 2013 National Healthcare Development. 2014. Available at: <http://www.nhfpc.gov.cn/guihuaxxs/s10742/201405/886f82dafa344c3097f1d16581a1bea2.shtml>. Accessed November 28, 2016
- China NBoSo: China Statistical Yearbook 2014. 2014. Available at: <http://www.stats.gov.cn/tjsj/ndsj/2014/indexch.htm>. Accessed November 28, 2016
- Engel C, Brunkhorst FM, Bone HG, et al: Epidemiology of sepsis in Germany: Results from a national prospective multicenter study. *Intensive Care Med* 2007; 33:606–618
- Flaatten H: Epidemiology of sepsis in Norway in 1999. *Crit Care* 2004; 8:R180–R184
- China NBoSo: Statistical Communiqué of the People's Republic of China on the 2013 National Economic and Social Development. 2015. Available at: http://www.stats.gov.cn/english/PressRelease/201502/t20150228_687439.html. Accessed July 10, 2015
- Population Census Office Under the State Council and Department of Population and Employment Statistics NBoS: Tabulation on the 2010 Population Census of People's Republic of China. Beijing, China Statistics Press, 2012
- Charlson ME, Pompei P, Ales KL, et al: A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *J Chronic Dis* 1987; 40:373–383
- McCabe WR, Jackson G: Gram-negative bacteremia. I: Etiology and ecology. *Arch Intern Med* 1962; 110:847–855
- Knaus WA, Draper EA, Wagner DP, et al: APACHE II: A severity of disease classification system. *Crit Care Med* 1985; 13:818–829
- Vincent JL, de Mendonça A, Cantraine F, et al: Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: Results of a multicenter, prospective study. Working group on “sepsis-related problems” of the European Society of Intensive Care Medicine. *Crit Care Med* 1998; 26:1793–1800
- Garner JS, Jarvis WR, Emori TG, et al: CDC definitions for nosocomial infections, 1988. *Am J Infect Control* 1988; 16:128–140
- Dellinger RP, Levy MM, Rhodes A, et al; Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup: Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med* 2013; 41:580–637
- Kaukonen KM, Bailey M, Pilcher D, et al: Systemic inflammatory response syndrome criteria in defining severe sepsis. *N Engl J Med* 2015; 372:1629–1638
- Le Conte P, Riochet D, Batard E, et al: Death in emergency departments: A multicenter cross-sectional survey with analysis of withholding and withdrawing life support. *Intensive Care Med* 2010; 36:765–772

32. Wang HE, Addis DR, Donnelly JP, et al: Discharge diagnoses versus medical record review in the identification of community-acquired sepsis. *Crit Care* 2015; 19:42
33. Sundararajan V, Macisaac CM, Presneill JJ, et al: Epidemiology of sepsis in Victoria, Australia. *Crit Care Med* 2005; 33:71–80
34. Cremer OL: Can administrative data be used to consistently measure the burden of sepsis? *Crit Care Med* 2014; 42:747–749
35. Sarrazin MS, Rosenthal GE: Finding pure and simple truths with administrative data. *JAMA* 2012; 307:1433–1435
36. Klein Klouwenberg PM, Ong DS, Bonten MJ, et al: Classification of sepsis, severe sepsis and septic shock: The impact of minor variations in data capture and definition of SIRS criteria. *Intensive Care Med* 2012; 38:811–819
37. Gaieski DF, Edwards JM, Kallan MJ, et al: Benchmarking the incidence and mortality of severe sepsis in the United States. *Crit Care Med* 2013; 41:1167–1174
38. Søgaard KK, Thomsen RW, Schönheyder HC, et al: Positive predictive values of the International Classification of Diseases, 10th revision diagnoses of Gram-negative septicemia/sepsis and urosepsis for presence of Gram-negative bacteremia. *Clin Epidemiol* 2015; 7:195–199
39. Angus DC, Linde-Zwirble WT, Lidicker J, et al: Epidemiology of severe sepsis in the United States: Analysis of incidence, outcome, and associated costs of care. *Crit Care Med* 2001; 29:1303–1310
40. Henriksen DP, Pottegård A, Laursen CB, et al: Risk factors for hospitalization due to community-acquired sepsis - a population-based case-control study. *PLoS One* 2015; 10:e0124838
41. Weng L, Joynt GM, Lee A, et al: Chinese Critical Care Ethics Group: Attitudes towards ethical problems in critical care medicine: The Chinese perspective. *Intensive Care Med* 2011; 37: 655–664
42. Esteban A, Frutos-Vivar F, Ferguson ND, et al: Sepsis incidence and outcome: Contrasting the intensive care unit with the hospital ward. *Crit Care Med* 2007; 35:1284–1289
43. Du B, Xi X, Chen D, et al; China Critical Care Clinical Trial Group (CCCCTG): Clinical review: Critical care medicine in mainland China. *Crit Care* 2010; 14:206
44. Robert R, Reignier J, Tournoux-Facon C, et al; Association des Réanimateurs du Centre Ouest Group: Refusal of intensive care unit admission due to a full unit: Impact on mortality. *Am J Respir Crit Care Med* 2012; 185:1081–1087
45. Liu S, Wu X, Lopez AD, et al: An integrated national mortality surveillance system for death registration and mortality surveillance, China. *Bull World Health Organ* 2016; 94:46–57
46. Jain S, Self WH, Wunderink RG, et al; CDC EPIC Study Team: Community-acquired pneumonia requiring hospitalization among U.S. adults. *N Engl J Med* 2015; 373:415–427