Incidence Rates of Surgically Managed Cystic Echinococcosis in Kazakhstan, 2007–2016

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Abstract. Cystic echinococcosis (CE) is a zoonotic disease caused by the larval stage of the cestode *Echinococcus granulosus*. The parasite typically infects dogs and ungulates, with humans acting as dead-end hosts. Information on the epidemiology of CE is lacking from Central Asia, including from Kazakhstan where CE cases are reported centrally. This study presents data from the Kazakhstan Scientific and Practical Center for Sanitary and Epidemiological Evaluation and Monitoring on CE patients treated surgically, with a diagnosis confirmed by pathology. Evaluation of data from 2007 to 2016 indicated that the CE incidence rate decreased during this time period in most areas of Kazakhstan (country-level incidence rate of 5.6 versus 4.7 cases/100,000 population in 2007 and 2016, respectively). Cystic echinococcosis had a higher incidence in southern Kazakhstan, with an incidence rate between 7.0 and 10.5 cases per 100,000 population, whereas northern regions had rates less than 4.0 cases per 100,000 population. Moreover, despite the overall decrease, CE incidence continues to increase in the south. Cystic echinococcosis surveillance is needed, particularly in the south, to help inform policymakers and orient disease control efforts.

INTRODUCTION

Cystic echinococcosis is a disease caused by the larval stage of the cestode *Echinococcus granulosus*. Dogs act as definitive hosts, harboring the adult form of the tapeworm in their intestines, whereas ungulates act as intermediate hosts, developing metacestode cysts, which mainly affect the liver and lungs.¹ Humans act as “dead-end” or accidental intermediate hosts. According to the WHO, more than 1 million humans are affected worldwide with CE.² Cystic echinococcosis is more prevalent in sheep-raising areas and often affects marginalized sections of society. The disease has a considerable economic impact because of both animal- and human-related expenses.^{1–4} Although death is uncommon, morbidity can be significant if CE is not properly diagnosed and treated.² Currently, epidemiological data on the distribution of CE are scarce for some regions of the world.¹ This hinders efforts for CE control, as reliable data on the distribution of CE within a specific territory are crucial for evidence-based policy decisions and resource allocation. Central Asia is generally considered endemic for CE, but published data from many countries in this geographic area are scarce.^{5,6} Previous publications from Kazakhstan have shown a high number of reported cases since 1994.⁷ The annual mean country-level CE incidence rate rose from 0.9 cases per 100,000 population in 1974 to 5.9 cases per 100,000 population in 2000.^{8,9} Studies published in 2003 and 2004 reported a 30% CE prevalence in sheep and a 50% prevalence in cattle, whereas the *E. granulosus* infection prevalence in dogs ranged from 5% to 25%.^{8–10} In this study, we provide an overview of the trends in human CE incidence rates from Kazakhstan for the

years 2007–2016 using data on surgically treated cases from a national CE registry.

METHODS

Data source and study design. Cystic echinococcosis incidence rates were evaluated using data from the Kazakhstan Scientific and Practical Center for Sanitary and Epidemiological Evaluation and Monitoring (SPCSEEM) for the years 2007–2016. The SPCSEEM manages a disease surveillance system that collects data on the occurrence and spread of infectious diseases in Kazakhstan. Cystic echinococcosis is a notifiable disease in Kazakhstan, and physicians working in hospitals throughout the country are mandated to report identified cases. Hospital administrators provide case information to regional public health centers in Kazakhstan. The SPCSEEM regional hubs then transmit monthly and annual reports to the main data center located in Almaty (Figure 1). As such, the dataset includes data from the entire country. However, the SPCSEEM is only notified of a CE case when patients undergo surgery and have their diagnosis confirmed via pathology. Collected data include demographics (name, date of birth, region, village, and district of origin), clinical and laboratory findings (cyst location and number, symptoms at presentation, serology, preoperative diagnosis, and pathology), and length of hospital stay. The dataset distinguishes new cases from disease relapses. If a patient is treated surgically within five years of the initial operation, the case is considered a relapse.

Statistical analysis. Age- and gender-specific incidence rates (per 100,000 population) as well as age-standardized incidence rates were calculated for CE cases reported from each region (oblast) of Kazakhstan, as well as from the cities of Nur-Sultan and Almaty, from 2007 to 2016. The mean standardized incidence rate for the years 2007–2016 was also calculated. A direct standardization method was used to compare oblasts.¹¹ Regional comparisons were based on the WHO world standard population to adjust for age structure

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FIGURE 1. Flowchart detailing disease notification and data gathering in the Sanitary and Epidemiological Evaluation and Monitoring database.

differences in each oblast over time.¹¹ Oblast- and city-level population numbers were obtained from the annual Kazakhstan population datasheet from the Kazakhstan Agency of Statistics.¹² The least squares method was used to assess trends across time, and the geometric mean was used to calculate the average annual percent change in the incidence rate. Two-way analysis of variance was used to assess differences in gender and age-groups. A *P*-value of < 0.05 was deemed significant. Data analysis was carried out using SPSS ver.17.0 (SPSS Inc., Chicago, IL).

RESULTS

A total of 8,443 CE cases were reported from January 1, 2007, to December 31, 2016. Of these cases, 46.0% were male and the age of diagnosis ranged from 11 months to 80 years. Newly diagnosed patients accounted for 97.4% (*n* = 8,224) of cases, while 2.6% (*n* = 219) of cases were considered relapses. Cysts were found primarily in the liver and lungs, with 6,106 cases (72.3%) with liver cysts, 1,836

cases (21.7%) with lung cysts, and 501 cases (5.9%) with cysts in other organs. Figure 2 shows the total number of cases and the number of cases by organ location. Data on cases with concurrent lung and liver involvement are not presented because of the low number of cases per year registered in the dataset (total 52, range 3–8, and median 5).

The overall CE incidence rate decreased from 5.6 to 4.7 cases per 100,000 population from 2007 to 2016 ($R^2 = 0.6686$, $P = 0.004$), which is indicative of a downward trend during the period under review as shown in Figure 3.

The 30- to 39-year age-group had the highest overall incidence rate. There was a statistically significant difference among age classes ($P = 0.001$), with the lowest rate for children younger than 5 years (Figure 4). Women had a higher overall incidence rate than men ($P = 0.017$), and this appears to be largely driven by the high incidence rate in women in the 30- to 39-year age-group (Figure 4) ($P = 0.017$). Men had higher rates in the 15- to 19- and 20- to 29-year age-groups, as well as in older than 49 years age classes, although the difference was not significant except for the 70-year or older age-group ($P = 0.189$).

Figure 5 shows the geographic distribution of CE incidence rates in Kazakhstan. The mean nationwide incidence rate was 5.19 cases per 100,000 population (95% CI: 4.91–5.47). Three oblasts in the southern part of the country (south Kazakhstan, Zhambyl, and Almaty) had the highest incidence rates, with 10.76, 8.73, and 7.43 cases per 100,000 population, respectively. The northern part of Kazakhstan, including the city of Nur-Sultan (formerly Astana city) and the oblasts of Kostanai and Pavlodar, had the lowest incidence rates, with 1.32, 1.29, and 0.51 cases per 100,000 population, respectively (Figure 5). The decrease in incidence rate between 2007 and 2016 ranged from 4.0% to 98.0% for all regions, except for Almaty, Aktobe, and East Kazakhstan (Table 1).

DISCUSSION

To our knowledge, this is the first report on the trends in age-standardized CE incidence rates for the different regions in Kazakhstan. Our findings indicate that the overall CE incidence rate gradually declined in Kazakhstan from 2007 to 2016. It should be noted that although the overall country-level incidence significantly decreased, the age-standardized CE incidence rate in Aktobe oblast significantly increased in this time period, indicating that in some regions, control measures may need to be reinforced. Moreover, a clear north–south gradient in disease distribution appears to exist.^{10,13} The reported country-level CE incidence rate of 4.7 cases per 100,000 population for 2016 is higher than the rate of 1.4 cases per 100,000 population reported in 1990.¹⁴ Overall, the higher incidence rate may partially be explained by an improved diagnostic capability for CE, in addition to an increased awareness of the disease in the local population and by the medical community. This is also supported by the fact that the majority of cases in the dataset were new, although relapses accounted for 2.6% of the total number.

Information on surgical procedures used is not available in the current version of the database. Therefore, some of the relapsed cases may represent the reactivation of a treated cyst (e.g., the appearance of daughter vesicles in a treated CE

FIGURE 2. Total number of reported surgically managed cystic echinococcosis cases in Kazakhstan and the number of cases by organ location, for the years 2007–2016. Data for cases with multiple organ localizations are not shown because of the low number of cases (52 overall, range 3–8, median 5).

cyst that reached inactivation) instead of a true relapse (e.g., the appearance of a CE cyst in the same or proximal anatomical location from the original cyst). Moreover, cases of secondary CE (e.g., the appearance of new cysts due to the spillage of scoleces during a surgical procedure or consequent to cyst rupture) might be misclassified as relapses. Secondary CE most commonly presents in the peritoneum as scoleces are dispersed following the spontaneous, accidental, or iatrogenic rupture of cysts, which are mainly located in the liver. Other rarer locations of secondary CE include other organs that can be reached by hematogenous spreading of scoleces.^{14–16}

In the current study, people in the 30- to 39-year age-group had the highest CE incidence rate. This is expected as CE is most often diagnosed in this decade of adult life as cysts take a long time to develop and become symptomatic. Moreover, patients in this age range often undergo medical examinations for other reasons.¹⁷ However, the incidence rate in children younger than 15 years was also considerable, suggesting ongoing local transmission.^{6,10,13} Ongoing transmission in the younger age-groups can be explained by the continuation of traditional livestock-rearing practices that put young Kazakhs in contact with infected shepherd dogs.^{6,10,13} A study published

in 2003 found that rural dogs had an *E. granulosus* infection prevalence of between 5% and 10%, with some populations of shepherd dogs having a prevalence greater than 20%.¹³

In the current study, women had an overall higher CE incidence rate than men, which concurs with the findings of previous studies. This finding may be explained by women having the main role in domestic activities, including food preparation and caring for the family dog.¹⁸ However, despite the fact that some surveys report a higher prevalence of dog contact among CE-affected individuals, these studies are often based on serosurveys and not on cases diagnosed by diagnostic imaging or other methods with greater accuracy.¹⁵ Moreover, a recent analysis of risk factors from a prevalence survey in three endemic countries (Romania, Bulgaria, and Turkey) conducted by members of the HERACLES consortium found no statistically significant difference between cases and controls in terms of contact with dogs.¹⁸ Recently, the government of Kazakhstan has launched programs for the improvement of food quality, including actions targeting zoonotic diseases. Hopefully, these programs will contribute to decreasing disease transmission in the coming years.¹⁹

This study shows that southern Kazakhstan has a higher CE incidence rate than the rest of the country, which is in

FIGURE 3. Sex- and age-specific CE incidence rates (per 100,000 pop.) in Kazakhstan, 2007–2016. This figure appears in color at www.ajtmh.org.

FIGURE 4. Overall mean annual standardized cystic echinococcosis incidence rates (per 100,000 population) for Kazakhstan. This figure appears in color at www.ajtmh.org.

line with previous reports.¹⁰ Environmental differences may play a role, as southern Kazakhstan has a high humidity index, mild temperatures, and a long vegetative period, all of which are favorable conditions for maintaining *E. granulosus* eggs in the soil.^{19,20} Second, sociocultural practices in pastoral communities include routine contact with dogs that are allowed to consume raw offal from infected livestock.^{5,6,8,10,14} Furthermore, southern Kazakhstan borders Uzbekistan and Kyrgyzstan, which are both considered to be hyperendemic for CE.¹ Commerce and movement of livestock have been increasing in Kazakhstan as a result of new plans to boost economic activities connected to animal husbandry. This could have increased the circulation of infected intermediate hosts, contributing to maintaining active disease transmission.¹⁹ Individuals who reside along the border often travel between these countries, and CE-infected migrants could have contributed to part of the disease burden detected in Kazakhstan.

A limitation of this study is that, in Kazakhstan, CE cases are reported to the SPCSEEM only after a patient undergoes surgery with the diagnosis confirmed by pathology. Because CE is asymptomatic in up to 70% of cases,¹⁷ many patients stay asymptomatic until an accidental diagnosis is made. In Kazakhstan, surgery has traditionally been the primary treatment for CE cases, which has led to the surgical treatment of inactive cysts. This practice is not restricted to Kazakhstan and has been reported from other countries.^{22,23} However, some CE patients were likely treated medically or followed using a watch-and-wait approach, excluding them from inclusion in the centralized database. As our study is based on surgical data, our findings likely report an underestimated frequency of disease by not including medically treated outpatients and asymptomatic cases.²⁴ Moreover, cases of false positive diagnosis of CE have been reported even when pathology was used as a diagnostic mean. Therefore, due to the limitations of the current surveillance system. The disease

FIGURE 5. Mean annual standardized cystic echinococcosis incidence rates by region (per 100,000 population) in Kazakhstan, 2007–2016. This figure appears in color at www.ajtmh.org.

TABLE 1
Evaluation of age-standardized cystic echinococcosis incidence rates by region

Region	2007 incidence	2016 incidence	Mean incidence	Incidence difference, %	95% CI for mean incidence value	Pearson correlation coefficient	R ²	P-value
Kazakhstan	5.60	4.74	5.19	-15.40	4.91-5.47	-0.82	0.67	0.004
Akmola oblast	2.71	2.14	2.83	21.00	2.45-3.20	-0.11	0.01	0.76
Aktobe oblast	1.80	2.55	2.08	+41.70	1.29-2.87	+0.71	0.50	0.02
Almaty city	3.32	2.24	2.53	-32.50	2.20-2.87	-0.67	0.44	0.04
Almaty oblast	7.09	7.65	7.43	+7.90	7.11-7.76	-0.38	0.14	0.28
Astana city (Nur-Sultan)	5.34	0.10	1.32	-98.10	0.13-2.76	-0.74	0.54	0.022
Atyrau oblast	4.99	1.14	3.20	-77.20	2.30-4.11	-0.79	0.63	0.01
East Kazakhstan oblast	2.16	2.48	1.64	+14.80	1.34-1.95	+0.20	0.04	0.58
Karagandy oblast	3.26	2.49	2.72	-23.60	2.39-3.05	-0.37	0.14	0.29
Kostanai oblast	1.19	0.82	1.29	-31.10	0.88-1.69	+0.21	0.04	0.57
Kyzylorda oblast	4.55	3.11	5.00	-31.70	4.06-5.94	-0.56	0.32	0.09
Mangistau oblast	5.10	2.59	4.70	-49.20	3.55-5.85	-0.67	0.44	0.04
North Kazakhstan oblast	2.63	1.80	2.23	-31.60	1.69-2.77	-0.71	0.50	0.02
Pavlodar oblast	0.59	0.23	0.51	61.00	0.33-0.69	-0.36	0.13	0.31
South Kazakhstan oblast	10.37	9.93	10.76	-4.30	10.17-12.05	-0.27	0.07	0.45
West Kazakhstan oblast	7.01	3.11	4.89	-55.60	3.38-6.40	-0.87	0.755	< 0.01
Zhambyl oblast	12.08	8.00	8.73	-33.80	7.50-9.96	-0.89	0.789	< 0.01

For each region, 2007 and 2016 incidence rates are provided, along with the difference in these two values. Pearson correlation coefficients, R² values, and the relative P-values are also provided for the trend line associated with the years between 2007 and 2016. Significant P-values are presented in bold.

frequency could be more precisely reported by including these groups in future surveillance programs. To this end, the recently launched European Register for Cystic Echinococcosis (ERCE) could serve as a platform for centers in Kazakhstan, as it allows for the collection of clinical and epidemiological data. The registry has recently accepted its first member centers outside of the European Union.²⁵ The ERCE also allows for the collection of data from cases identified during ultrasound-based screenings. This information is needed to assess the prevalence of CE in a given geographical area, which is a crucial piece of information needed to inform policymakers on control measures.²⁶ Recently, an international collaboration between researchers from Kazakhstan and Italy implemented a standardized approach to the diagnosis of CE and a stage-specific approach to the treatment of these patients. The program started in 2016 in the Almaty oblast, and efforts are underway to extend the program to other parts of the country.

In conclusion, this is the first study to evaluate trends in the age-standardized CE incidence rates for the different regions in Kazakhstan. Overall, the CE incidence rate has declined over the past decade. However, the incidence rate continues to be high, especially in the southern part of the country, and new cases in children are troubling. Increasing incidence rates in Aktobe oblast suggest that transmission is on the rise in some parts of the country. This trend calls for the early detection of disease using ultrasound screening and preventive actions among high-risk groups to lower the burden of CE in all regions of the country.

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REFERENCES

1. Deplazes P et al., 2017. Global distribution of alveolar and cystic echinococcosis. *Adv Parasitol* 95: 315-493.
2. Budke CM, Deplazes P, Torgerson PR, 2006. Global socioeconomic impact of cystic echinococcosis. *Emerg Infect Dis* 12: 296-303.
3. Romig T, Deplazes P, Jenkins D, Giraudoux P, Massolo A, Craig PS, Wassermann M, Takahashi K, de la Rue M, 2017. *Ecology and Life Cycle Patterns of Echinococcus Species*. Vol 95. Elsevier Ltd. Available at: <https://doi.org/10.1016/bs.apar.2016.11.002>.
4. Craig PS, Budke CM, Schantz PM, Li T, Qiu J, Yang Y, Zeyhle E, Rogan MT, Ito A, 2007. Human echinococcosis: a neglected disease? *Trop Med Health* 35: 283-292.
5. Zhang W, Zhang Z, Wu W, Shi B, Li J, Zhou X, Wen H, McManus DP, 2015. Epidemiology and control of echinococcosis in central Asia, with particular reference to the People's Republic of China. *Acta Trop* 141: 235-243.
6. Torgerson PR, 2013. The emergence of echinococcosis in central Asia. *Parasitology* 140: 1667-1673.
7. Torgerson PR, Burtisumov KK, Shaikenov BS, Rysmukhambetova AT, Abdybekova AM, Ussenbayev AE, 2003. Modelling the transmission dynamics of *Echinococcus granulosus* in sheep and cattle in Kazakhstan. *Vet Parasitol* 114: 143-153.
8. Shaikenov BS, Torgerson PR, Usenbayev AE, Baitursynov KK, Rysmukhambetova AT, Abdybekova AM, Karamendin KO,

2003. The changing epidemiology of echinococcosis in Kazakhstan due to transformation of farming practices. *Acta Trop* 85: 287–293.
9. Abdybekova A, Sultanov A, Karatayev B, Zhumabayeva A, Shapiyeva Z, Yeshmuratov T, Toksanbayev D, Shalkeev R, Torgerson PR, 2015. Epidemiology of echinococcosis in Kazakhstan: an update. *J Helminthol* 89: 647–650.
10. Torgerson PR, Oguljahan B, Muminov AE, Karaeva RR, Kuttubaev OT, Aminjanov M, Shaikenov B, 2004. Present situation of cystic echinococcosis in central Asia. *Parasitol Int* 55 (Suppl): S207–S212. Available at: <https://doi.org/10.1016/j.parint.2005.11.032>.
11. Ahmad OB, Boschi-Pinto C, Lopez AD, Murray CJ, Lozano R, Meade I, 2001. *Age Standardization of Rates: A New Who Standard*, Vol. 65. Geneva, Switzerland: WHO. Available at: <https://doi.org/10.1161/hypertensionaha.114.04394>.
12. Shaikenov BS, Torgerson PR, Usenbayev AE, Baitursynov KK, Rysmukhambetov AT, Abdybekov AM, Karamendin KO, 2003. The changing epidemiology of echinococcosis in Kazakhstan due to transformation of farming practices. *Acta Trop* 85: 287–293.
13. Torgerson PR, Shaikenov BS, Baitursynov KK, Abdybekova AM, 2002. The emerging epidemic of echinococcosis in Kazakhstan. *Trans R Soc Trop Med Hyg* 96: 124–128.
14. Polat P, Kantarci M, Alper F, Suma S, Koruyucu MB, Okur A, 2003. Hydatid disease from head to toe. *Radiographics* 23: 475–494; quiz 536–537.
15. Cattaneo L et al., 2019. Cystic echinococcosis of the bone: a European multicenter study. *Am J Trop Med Hyg* 100: 617–621.
16. Ramia JM, 2015. Severe vascular complications due to liver hydatid cyst relapse: a case report and review of the literature. *J Surg Surgical Res* 1: 1–3.
17. Agudelo Higuera NI, Brunetti E, McCloskey C, 2016. Cystic echinococcosis. *J Clin Microbiol* 54: 518–523.
18. Tamarozzi F et al., 2019. Epidemiological factors associated with human cystic echinococcosis: a semi-structured questionnaire from a large population-based ultrasound study in Eastern Europe and Turkey. *Parasit Vectors* 12: 371.
19. FAO, 2017. Human Development Index. *Country Fact Sheet on Food and Agriculture Policy Trends–Kazakhstan*.
20. World Bank, 2013. *Kazakhstan–Overview of Climate Change Activities*, Vol. 48. Washington, DC: World Bank.
21. Possenti A, Manzano-Román R, Sánchez-Ovejero C, Boufana B, La Torre G, Siles-Lucas M, Casulli A, 2016. Potential risk factors associated with human cystic echinococcosis: systematic review and meta-analysis. *PLoS Negl Trop Dis* 10: e0005114.
22. Escolà-Vergé L et al., 2019. Retrospective study of cystic echinococcosis in a recent cohort of a referral center for liver surgery. *J Gastrointest Surg* 23: 1148–1156.
23. Patkowski W, Krasnodębski M, Grąt M, Masior Ł, Krawczyk M, 2017. Surgical treatment of hepatic *Echinococcus granulosus*. *Prz Gastroenterol* 12: 199–202.
24. Tamarozzi F, Mariconti M, Casulli A, Magnino S, Brunetti E, 2015. Comment on: retrospective study of human cystic echinococcosis in Italy based on the analysis of hospital discharge records between 2001 and 2012. *Acta Trop* 144: 50–51.
25. Rossi P, Tamarozzi F, Galati F, Pozio E, Akhan O, Cretu CM, Vutova K, Siles-Lucas M, Brunetti E, Casulli A; HERACLES Extended Network, 2016. The first meeting of the European Register of Cystic Echinococcosis (ERCE). *Parasit Vectors* 9: 243.
26. Tamarozzi F et al., 2018. Prevalence of abdominal cystic echinococcosis in rural Bulgaria, Romania, and Turkey: a cross-sectional, ultrasound-based, population study from the HERACLES project. *Lancet Infect Dis* 18: 769–778.