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The Association of Acute Watery Diarrhea in Iranian Pilgrims of Iraq with Cholera Cases in Iranians

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Abstract

Background: Despite the advances in the control of infectious diseases like cholera, they can potentially cause epidemics, especially in mass gathering events. One of the most important countries on the walking way of the *Arbaeen* religious event is Iran, which requires health system preparedness. The aim of this study was to predict the cholera epidemic in Iran by using the syndromic surveillance system of Iranian pilgrims in Iraq.

Methods: The data of the Iranian pilgrims with acute watery diarrhea in Iraq during the *Arbaeen* religious event and the confirmed cholera cases of pilgrims after returning to Iran were analyzed. We used the Poisson regression model of the relationship between the numbers of cases to evaluate acute watery diarrhea and cholera. Spatial statistics and hot spot analysis were used to identify the provinces with the highest incidence. SPSS software Version 24 was used for statistical analysis.

Results: The frequency of acute watery diarrhea cases was 2232 and the frequency of cholera in pilgrims after returning to Iran was 641. The results of spatial analysis for acute watery diarrhea cases showed a high number of acute watery diarrhea cases in the Khuzestan and Isfahan provinces, located in hot spots. Using Poisson regression, the relationship between the number of acute watery diarrhea reported in the syndromic surveillance system and the number of cholera cases was confirmed.

Conclusion: The syndromic surveillance system is useful to predict the outbreak of infectious diseases in large religious mass gatherings.

Keywords: Syndromic Surveillance System, Epidemic, Cholera, Early Warning, Early Detection of Epidemics, *Arbaeen*

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Introduction

According to the World Health Organization "WHO", any spontaneous or organizational event leading to a definite number of people gathering in a special place, for a specific purpose in a determined cycle, putting pressure on the responding resources and the social programs, is named "mass gathering" (1). One of the health problems of mass gatherings is the outbreak of infectious diseases like cholera (2). In the early 1800s, millions of people were affected with the cholera pandemics. Facilities for clean water and sanitization have decreased the spread of cholera. However, cholera can afflict people in less developed countries where sanitation infrastructures and improved water are not available (3). An estimated 1.3 billion people are at risk for cholera and every year 2.86 million cholera cases occur in endemic countries. Between these cases, there are an evaluated 95,000 deaths (4). The public health system can be under intense pressure, even with progressive equipment and

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↑What is "already known" in this topic:
The syndromic surveillance system is an efficient technique for the early detection of epidemics since it is quicker than ordinary patient care based on a diagnosis validated by a laboratory.

→What this article adds:
The findings of surveillance systems can be used as an early event detection tool during and after the *Arbaeen* event in Iran.

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suitable resources for the prevention and control of infectious diseases (2, 4). Studies on mass gatherings same as the Day of *Ashura* in Karbala (Iraq), *Hajj* (Saudi Arabia), Sabarimala and Kumbh mela in India showed the outbreak of infectious diseases in these ceremonies (5). The *Arbaeen* ceremony is one of the world's largest religious gatherings, which takes place on the 40th day after the anniversary of Imam Hossain's testimony, he is the third Shia Imam. In the *Ashura* days, people walk to the city of Karbala. As founded on the statistics of 2017, the number of Iranian people in the *Arbaeen* ceremony was 2,320,000 (6). Iran is next to Iraq and shares a common land border. People from other neighboring countries of Iran, like Pakistan and Afghanistan, cross Iran to Iraq in the *Arbaeen* ceremony. Thus, a strategy for dealing with infectious diseases at this ceremony is required (2). Mass gatherings are not the same as structured disasters, therefore, many people will be affected (7). Although there are various ways to inhibit the spread of cholera, outbreaks can occur, necessitating the need for prompt outbreak detection (8). Timely detection of an outbreak can decrease morbidity, mortality, the extent of the spread of disease, and the cost of an outbreak (9, 10). Traditional disease surveillance methods depend on clinical diagnoses reported from treatment providers (11). A syndromic surveillance system without a break, on the other hand, keeps track of syndromes or symptoms that serve as proxies for diseases and collects them from a vast area or population, like emergency department chief complaint records (12). Using continuing symptom monitoring as proof of an outbreak, instead of reported diagnoses, can enable a syndromic system to find a disease outbreak sooner than the other traditional methods of surveillance (13, 14).

This study aimed to determine whether using acute watery diarrhea symptom data in Iraq with syndromic surveillance analysis could be detected to increase cholera cases sooner in Iran.

Methods

This cross-sectional study had 2 essential data sources from the Ministry of Health and Medical Education. In December and January 2017, information on pilgrims who had acute watery diarrhea syndromes was gathered in clinics in Iraq for Iranian pilgrims as well as information on cholera cases reported by pilgrims who had already returned to Iran.

Using the syndromic surveillance system, patients with acute watery diarrhea who were referred to clinics in Iraq for visiting Iranian pilgrims were registered mentioning the name of the province. When the pilgrims returned to Iran, the confirmed cholera cases of the pilgrims were reported mentioning the name of the province. The number of cases of acute watery diarrhea reported by clinics located in Iraq for visiting Iranian pilgrims was considered a predictor of the addition of confirmed cholera cases in the provinces of Iran.

The syndromic analysis was completed using the Poisson regression model to evaluate the relationship between the number of cases of acute watery diarrhea as a predictor variable and the number of confirmed cases of cholera as a response variable.

In this study, we used a binomial test to compare the number of cases of acute watery diarrhea and cholera by gender and nationality.

Getis-ord G statistic was used to analyze hotspots (high risk) and to more accurately detect the spatial distribution of spatial clusters with large values.

Results

In 2017, the frequency of people who referred to the clinics located in Iraq for visiting Iranian pilgrims with symptoms of acute watery diarrhea was 2232 cases, and the frequency of confirmed cholera in pilgrims after returning to Iran was 641 cases. Among the cases of acute watery diarrhea, 519 (23%) patients were men, and 1713 (77%) were women. Among the cases of cholera, 486 (76%) patients were men, and 152 (24%) were women (Table 1). Among the cases of acute watery diarrhea, the number of acute watery diarrhea cases was significantly higher in women ($P < 0.001$). However, the number of cholera cases was much higher in men ($P < 0.001$). Both acute watery diarrhea and cholera cases were higher in Iranian pilgrims than non-Iranian pilgrims ($P < 0.001$) (Table 2). The 20–40 and 40–60 age groups saw the majority of cases of acute watery diarrhea and cholera, respectively (Table 3). Most cases of

Table 1. Frequency of Pilgrims' Acute Watery Diarrhea in Iraq and Cholera Cases After Returning to Iran by Gender in 2017

Gender	Frequency of Cholera (%)	Frequency of Acute Watery Diarrhea (%)
Female	152 (24)	1713 (77)
Male	486 (76)	519 (23)

Table 2. Frequency of Pilgrims' Acute Watery Diarrhea in Iraq and Cholera Cases After Returning to Iran in Both Iranian and non-Iranian Nationalities in 2017

Nationality	Frequency of Cholera (%)	Frequency of Acute Watery Diarrhea (%)
Iranian	612 (96)	2067 (93)
Non-Iranian	28 (4)	165 (7)

Table 3. Frequency of Pilgrims' Acute Watery Diarrhea in Iraq and Cholera Cases After Returning to Iran in Different Age Groups in 2017

Age Group (years) old)	Frequency of Cholera (%)	Frequency of Acute Watery Diarrhea (%)
<6	33 (5.4)	92 (4.1)
6-20	47 (7.7)	332 (14.9)
20-40	281 (45.8)	1095 (49.1)
40-60	192 (31.3)	581 (26)
>60	61 (9.9)	131 (5.9)
Total	641 (100)	2232 (100)

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Table 4. Frequency of Pilgrims' Acute Watery Diarrhea in Iraq and Cholera Cases After Returning to Iran by the Province of Residence in 2017

Province	Frequency of Cholera (%)	Frequency of Acute Watery Diarrhea (%)
East Azerbaijan	8 (1.2)	91 (4.1)
West Azerbaijan	4 (0.6)	39 (1.7)
Ardabil	1 (0.2)	25 (1.1)
Isfahan	118 (18.4)	383 (17.2)
Alborz	13 (2)	56 (2.5)
Ilam	4 (0.6)	7 (0.3)
Bushehr	7 (1.1)	12 (0.5)
Tehran	67 (10.5)	455 (20.4)
Chaharmahal and bakhtiari	22 (3.4)	17 (0.8)
South Khorasan	5 (0.8)	7 (0.3)
Razavi Khorasan	94 (14.7)	265 (11.9)
North Khorasan	5 (0.8)	7 (0.3)
Khozestan	110 (17.2)	94 (4.2)
Zanjan	2 (0.3)	26 (1.2)
Semnan	6 (0.9)	11 (0.5)
Sistan and baluchestan	7 (1.1)	9 (0.4)
Fars	38 (5.9)	94 (4.2)
Qazvin	3 (0.5)	38 (1.7)
Qom	37 (5.8)	120 (5.4)
Kurdistan	1 (0.2)	4 (0.2)
Kerman	3 (0.5)	35 (1.6)
Kermanshah	2 (0.3)	30 (1.3)
Kohgiluye and Boyer-Ahmad	2 (0.3)	6 (0.2)
Golestan	3 (0.5)	18 (0.8)
Gilan	2 (0.3)	19 (0.9)
Lorestan	7 (1.1)	19 (0.9)
Mazandaran	21 (3)	61 (2.7)
Markazi	13 (2)	49 (2.2)
Hormozgan	3 (0.5)	17 (0.8)
Hamedan	7 (1.1)	30 (1.3)
Yazd	26 (4.1)	23 (1)
Non-Iranian		165 (7.4)
Total	641 (100)	2232 (100)

acute watery diarrhea were related to pilgrims from Tehran province in Iraq, and most cases of cholera in Iran were reported in Isfahan province (Table 4).

By including the cholera frequency as a response variable and the number of instances of acute watery diarrhea as a predictor variable in the model, Poisson regression was used to predict the number of cholera cases. Relative rate was determined to be 1.006 after this model's analysis (95% CI, 1.00585-1.00627), indicating the relationship between the number of acute watery diarrhea reported in the syndromic surveillance system and the number of reported cases of cholera.

Figure 1 shows the results of spatial autocorrelation analysis for acute watery diarrhea cases, which shows Isfahan province with the symbol HH (high hot), showing the high number of acute watery diarrhea cases reported in this province and adjacent areas.

Figure 2 shows the mapping of cholera cases across the country using GIS software, and shows the country map of high and low-incidence areas. Using GIS statistics, Khuzestan and Isfahan provinces were located in hot spots, both with 95% CI ($P < 0.001$).

Discussion

The study's major findings were that in 2017, there were 2232 cases of Iranian pilgrims attending clinics in Iraq with symptoms of acute watery diarrhea, and there were 641 cases of confirmed cholera in pilgrims who returned to Iran. Also, the number of cholera cases was predicted using Poisson regression, when the number of cholera cases as a response variable and the number of acute watery diarrhea cases as a predictor variable were entered into the model. The study of this model yielded the following results: relative rate = 1.006 (95% CI, 1.005-1.006), which indicates the relationship between the number of acute watery diarrhea reported in the syndromic surveillance system and the frequency of reported cholera cases. In fact, per the number of Iranian pilgrims with diarrhea in each province, the risk of cholera increases by 0.006 in the same province.

In the current study, it was demonstrated that the health system may be ready for a potential outbreak by adopting a syndromic surveillance system, which depends on gathering and recording essential symptoms and does not require special equipment for a conclusive diagnosis of cholera. The health system can be prepared for a possible outbreak. Previous studies showed that the 4 main problems of the health system copping with infectious diseases in the *Arbaeen* ceremony were as follows: lack of health infrastructure

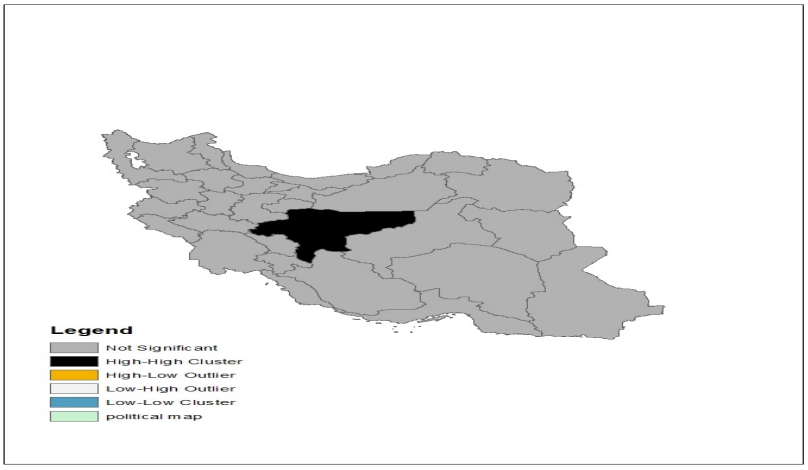

Figure 1. Nationwide distribution of acute watery diarrhea among Iranian pilgrims in 2017 using muran I analysis

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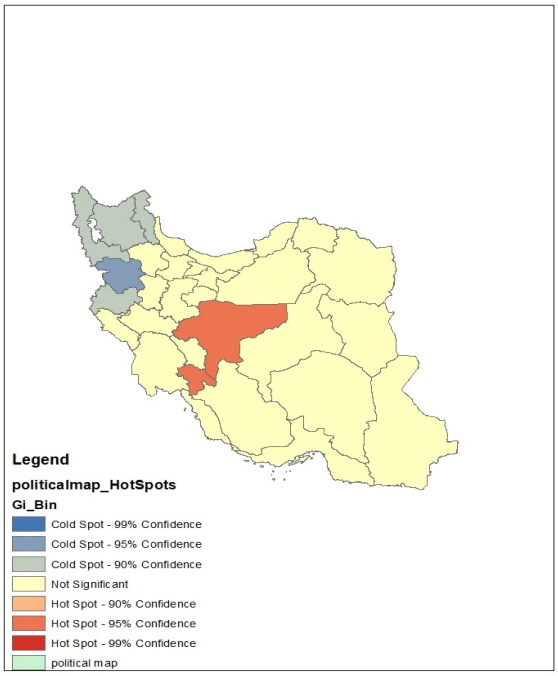

Figure 2. Nationwide distribution of cholera among Iranian pilgrims after returning to Iran in 2017 using GIS software

in Iraq (such as health system issues); inadequate control measures of infection diseases; low risk perception among pilgrims; and problems in health education and communication (15).

A 2016 study by Saulnier et al found that data from the syndromic surveillance system could show a rise in cases of cholera before a rise in hospitalizations. In the current study, using acute watery diarrhea syndrome in pilgrims, cholera cases could be predicted before laboratory confirmation and epidemic (16).

In a 2009 study by Malik et al in Manitoba, the trend of Google search about flu and emergency department data for real-time detection of H_1N_1 pandemics was measured. The time series curves for H_1N_1 cases during the 2009 pandemic were plotted relying on 3 syndromic indicators— Google search trend about influenza; the frequency of influenza-like illnesses in all emergency departments every week; and percentage of the frequency of influenza-like illnesses in all emergency departments.

Our findings are in line with these reports, and all cases escalated to be 2 weeks sooner than laboratory-confirmed cases (17).

In a 2017 study in Republic of Korea by Dong Woo Seo et al, data analysis showed a significant temporal correlation between search engine data and influenza and MERS data. As a result, the digital syndrome monitoring system can be useful to prevent the outbreak of infectious diseases (18). According to our study, the syndromic surveillance system, which is based on continuous monitoring of disease symptoms, can detect outbreaks earlier than traditional methods of disease monitoring.

In order to support the 8th Micronesian Games in 2014, the main health care division of Pohnpei state set up an improved monitoring system for the early detection of infectious disease epidemics. The threshold level was determined for each syndrome and when the number of syndromes reached to the threshold, the public health system responded. During the games, no infectious disease outbreaks were reported. Technology is very helpful in strengthening the surveillance system (19).

Using a syndrome-based monitoring system, a study was conducted in Australia by Khatib et al to look into the emergence and transmission of infectious illnesses among asylum seekers. This study showed that the use of the Infectious Diseases Syndromic Care System among asylum seekers is beneficial and no identified alarms lead to disease outbreaks (20).

Strengths and limitations

This study is one of the first to predict and prevent the cholera outbreak by a syndromic surveillance system in religious gatherings and can be used as a baseline study to predict the outbreak of infectious diseases after religious ceremonies. One of the study's limitations is that no cases of acute watery diarrhea from other clinics, particularly those associated with charitable processions, have been documented. These clinics are solely in Iraq and serve Iranian pilgrims who are on pilgrimage. On the other hand, in the case of cholera patients in Iran, only cases related to the public sector have been reported. These problems lead to selection bias that should be considered in future studies.

Conclusion

In this study, using Poisson regression, a formula for predicting cholera cases in Iranian provinces was obtained using acute watery diarrhea cases in pilgrims in Iraq. The use of spatial analysis showed that Isfahan province was worse than other provinces in terms of acute watery diarrhea and cholera. The province of Isfahan is one of the busiest in terms of travel and transportation, as well as other economic, political, and structural circumstances. A lot of people live in this province and travel frequently. Therefore, the syndrome surveillance system can be used to predict the possible provinces involved in the country for the cholera outbreak during the *Arbaeen* event. This technique can be applied in comparable and significant occasions, such as the assembly of pilgrims at the Hajj. This strategy is often applicable to avoiding other infectious diseases because it is crucial to stop infectious disease epidemics in religious settings.

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Author's Contribution

Initial idea and conceptualization: Babak Eshrati, Mohammad-Reza Sohrabi; analysis and interpretation of the results: Mohammad-Reza Sohrabi, Babak Shruti, Mahbobeh Taheri; original draft preparation: Mahbobeh Taheri, Mohammad-Reza Sohrabi; Babak Shruti; revising draft and supervision: Mohammad-Reza Sohrabi, Babak

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Ethical Considerations

The study was approved by the ethics committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1398.269). In this study, the principle of confidentiality and protection of information of the participants has been considered. Any use of the data of the Ministry of Health was done with the written permission of that center.

Conflict of Interests

The authors declare that they have no competing interests.

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