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Brief Report

# Levels of Alarm Thresholds of Meningitis Outbreaks in Hamadan Province, west of Iran

**Mohammad Faryadres (BSc)[a], Manoochehr Karami (PhD)[b*], Abbas Moghimbeigi (PhD)[c], Nader Esmailnasab (PhD)[d], Khabat Pazhouhi (MSc)[a]**

[a] *Department of Biostatistics and Epidemiology, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran*

[b] *Modeling of Non-communicable Diseases Research Center and Department of Biostatistics & Epidemiology, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran*

[c] *Brucellosis Research Center, Department of Biostatistics and Epidemiology, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran*

[d] *Kurdistan Research Center for Social Determinants of Health, School of Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran*

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**** Correspondence***
*Manoochehr Karami (PhD)*
***Tel:*** *+98 81 38380090*
***Fax:*** *+98 81 38380509*
***E-mail:*** *ma.karami@umsha.ac.ir*

## ABSTRACT

**Background:** Few studies have focused on syndromic data to determine levels of alarm thresholds to detection of meningitis outbreaks. The purpose of this study was to determine threshold levels of meningitis outbreak in Hamadan Province, *west of Iran*.

**Methods:** Data on both confirmed and suspected cases of meningitis (fever and neurological symptom) from 21 March 2010 to 20 March 2012 were used in Hamadan Province, Iran. Alarm threshold levels of meningitis outbreak were determined using four different methods including absolute values or standard method, relative increase, statistical cutoff points and upper control limit of exponentially weighted moving average (EWMA) algorithm.

**Results:** Among 723 reported cases, 41 were diagnosed to have meningitis. Standard level of alarm thresholds for meningitis outbreak was determined as incidence of 5/100000 persons. Increasing 1.5 to two times in reported cases of suspected meningitis per week was known as the threshold levels according to relative increase method. An occurrence four cases of suspected meningitis per week that equals to 90$^{th}$ percentile was chosen as alarm thresholds by statistical cut off point method. The corresponding value according to EWMA algorithm was 2.57 i.e. three cases.

**Conclusions:** Policy makers and staff of syndromic surveillance systems are highly recommended to apply the above different methods to determine the levels of alarm threshold.

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## Introduction

Meningitis is an inflammation of the membranes surrounding the brain and spinal cord that can cause severe brain damage. Bacterial meningitis is a global threat, which annually causes 17,000 deaths of people in the world[1]. Bacterial, viral, fungal factors, trauma and bleeding are the known causes of meningitis. Neck stiffness, sudden high fever, sensitivity to light, confusion, headaches indicate suspected meningitis.

Diagnosis of meningococcal disease by history, and puncture Cerebral Spinal Fluid (CSF) are performed for absolute diagnosis[2]. Timely response to health events such as occurrence emerging diseases and outbreaks are considered as a major public health priority. Syndromic surveillance uses different detection methods to detect increase in the number/rate of health events beyond an expected level. Such systems routinely monitor the trend of syndromes and other pre-diagnostic data to detect increase/decrease in the health events. In dealing with such changes in the trend of syndromes, two questions should be considered. The first one is “Is it real?” and the second is “Is it significant?”[3] The importance such increase and whether this event could be considered as outbreak is the main interest of this work.

Knowledge on the levels of alarm threshold especially at national and local levels is limited. In remainder of this introduction, methods to determining such thresholds, which are responses to the second question, are stated. Generally, methods to define the threshold levels are under the umbrella of four methods as follow[4]:

- Absolute values/ standard thresholds[1,4,5].
- Relative increase
- Statistical cut off points
- Upper control limits of outbreak detection methods

Given that few studies have been carried out related to detect multiple simultaneous threshold, the aim of this study was to determine the outbreak threshold of fever and neurological symptoms syndrome as suspected cases of meningitis in Hamadan Province, west of Iran.

## Methods

### *Data source for applying alarm thresholds*

Data on both confirmed and suspected cases of meningitis (Fever and neurological symptoms) from 21 March 2010 to 20 March 2012, at daily basis in Hamadan Province, reported through meningitis surveillance to detect alarm threshold levels of meningitis outbreak, was used. Meningitis is considered as notifiable diseases and by definition when a suspected case of meningitis is detected by a health care provider, it must be reported as a clinical case; at which point the surveillance process will begin. Suspected cases of meningitis is defined as individuals who have clinical findings including an illness with sudden onset of fever (> 38.5 °C rectal or 38.0 °C axillary) and one of the following signs: neck stiffness, sudden loss of consciousness or other meningeal sign (neurologic sign). Such cases are reported to upper levels of the surveillance system daily. During the study period, 721 suspected cases of meningitis were reported to the national surveillance system in Hamadan Province.

### *Methods of alarm thresholds*

*Absolute values:* To obtain the levels of alarm thresholds for fever and neurological symptoms syndrome, the absolute values method (also called standard thresholds) was used. The values recommended by WHO are 5 or 7 cases per 100000 inhabitants per week and for populations under 30000, 3 to 5 cases in one or two weeks [4,5].

*Relative increase:* Levels of alarm thresholds for fever and neurological symptoms syndrome in relative increase method were set as percentage of increases over a specific period.

*Statistical cut off points:* Among different methods, for cut off point's method, weekly counts or percent of reported syndromes greater than 90th percentile of historical data is set as alarm thresholds for fever, neurological symptoms and meningitis syndromes.

*Upper control limits of exponentially weighted moving average:* Exponentially weighted moving average (EWMA) algorithm as an outbreak detection method was introduced in 1959 by Robert, the aim of which was to monitor mean of products in industrial environments. The EWMA control chart is very effective against small process shifts. In this algorithm, new data take more weights than old data. EWMA statistics is defined by the following recursive equation [6](1).

$$EWMA_t = \lambda Y_t + (1 - \lambda)\, EWMA_{t-1} \qquad (1)$$

Where, $Y_t$ equals the number of suspected cases of meningitis in day, λ is the smoothing parameter for which $0 < \lambda \leq 1$ is typically considered. A good rule of thumb is to use smaller values of λ to detect smaller shifts; $EWMA_{t-1}$ parameters are estimated at time t-1, a day before the desired time. In this algorithm, the upper limit threshold control, as follows, is intended to be and if that amount is greater than its $EWMA_t$ alarm outbreak are announced.

Upper limit control or the threshold level of this statistics is calculated using the following equation (2):

$$\text{Upper Control Limit} = EWMA_0 + k \times \sigma_{EWMA} \qquad (2)$$

Where k is the desired confidence interval, in this study we considered the 95% confidence interval. $\sigma_{EWMA}$ is standard deviation of the estimated statistics of EWMA at times t to $t_n$ and $EWMA_0$ is the mean of historical data at non outbreak times.

### *Statistical Analyses*

All of applied statistical methods to detection and removing of explainable patterns were computed using the Microsoft Excel Add In software entitled XLSTAT (XLSTAT [computer program]. New York: Addinsoft; 2011).

## Results

During the study period, 721 suspected cases of fever and neurological syndrome were reported to the national surveillance system in Hamadan Province. Mean of daily reported cases ranged from daily zero report to 8 cases. Descriptive statistics for fever and neurological symptom syndrome is shown in Table 1.

**Table1:** Descriptive statistics of suspected cases of meningitis from 21 March 2010 to 20 March 2012

| Indices | Suspected cases of meningitis (Fever and neurological symptom syndrome) |
|---|---|
| Mean(SD) | 1.37 (1.43) |
| Minimum | 0.00 |
| Maximum | 8.00 |
| Median | 1.00 |
| 3rd Quartile | 2.00 |

### *Absolute values*

To detect outbreaks in a population less than 30,000 people, occurrence 3 cases of suspected meningitis per week is considered as the threshold. In a population more than 100,000 five cases per week was considered. During the three-year of study, outbreaks of fever and neurological symptoms were not specified. According to the latest census, the population of the province in 2012 was 1,758,268 people.

### *Relative increase*

Considering the three years of study period from 2010 to 2012, increasing one and a half or two times of cases in a week could be determined as levels of alarm threshold. According to it, there was not seen any outbreak of the disease.

### *Statistical cut off points*

Levels of alarm thresholds for syndrome of fever and neurological symptoms and meningitis in this method with 90th percentile being equal to 4 was taken as weekly threshold of meningitis without considering the days we did not have a case. The corresponding values for 50th and 75th percentile were 2 and 3 cases per week.

### *Exponentially weighted moving average (EWMA)*

By using XLSTAT software, Upper control limit equaled to 2.57 and 2.56. In other word, the level of alarm threshold according to the EWMA algorithm was defined as occurrence of 3 cases of suspected meningitis during study period. Line plot of reported cases of suspected meningitis from 21 March 2010 to 20 March 2012 and corresponding levels of alarm threshold according to EWMA algorithm is shown in Figure1.

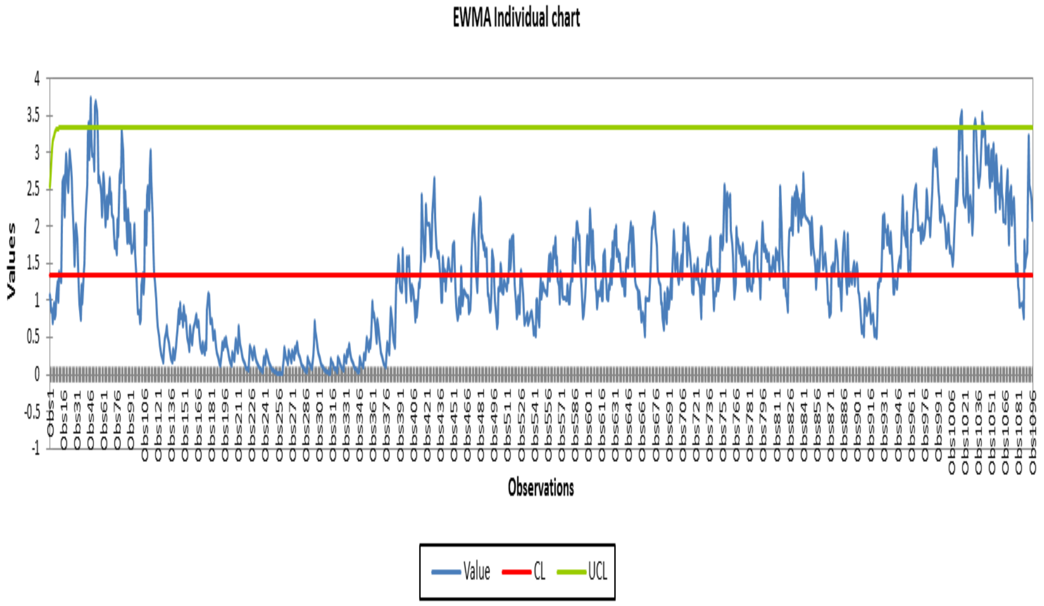


**Figure 1:** Line plot of reported cases of suspected meningitis (Value) from 21 March 2010 to 20 March 2012 and corresponding levels of alarm threshold according to EWMA algorithm (Green Line). The abscissa (horizontal) axis represents the study period and the ordinate (vertical) one shows the frequency of suspected cases of meningitis

## Discussion

This study aimed to define level of thresholds for those syndromes with available data source on daily manner. Although, there are some published studies in literature, which determined the thresholds levels of alarms/epidemics [7-11], the results of this project are not comparable with other published studies because of principles of determining alarm thresholds such as considering the epidemiology of interested diseases, priority for early detection and historical/baseline data and history of outbreak occurrence during recent years.

Generally, the methodology of defining the levels of alarm thresholds for syndromic data with available data source on baseline data include the application of absolute values, relative increases in the recent trend of data, statistical cut off points or upper control limits of some outbreak detection methods like EWMA are comply with the above mentioned studies in literature. Usually, monitoring data related to a specific syndrome or suspected cases of a specific disease uses various methods of detection algorithms such as cumulative sum (CUSUM) algorithm and exponentially weighted moving average [12].

Our study finding to determine the threshold level of meningitis outbreaks corresponded with the study of Han et al., however the differences between the CUSUM, and EWMA was not found[13]**.** The study of Kaninda et al. showed the threshold level as seven to ten for 100,000 people per week. Although, because of non- endemic meningitis in our country, the threshold was 5 cases per 100,000 people per week [5,14].

Regarding EWMA algorithms, since we are looking to discover outbreaks, upper control limits are most important for us. If the upper limit threshold is considered, the likelihood of discovering the outbreaks is reduced. Instead, the probability of false alarm is reduced. If we consider the lower control limit, the detection of outbreaks is easier but the chances of false alarm are greater.

The main limitations of present study are two general issues as follows:

- There are no single methods of alarm definition with a specific threshold level that can cover different syndromes under different circumstances.
- There is no reliable historical/baseline data on our interested syndromes.

Besides these limitations, the application of four different methods to define the levels of alarm thresholds including absolute values, relative increases in the recent trend of data, statistical cut off points, and upper control limits of EWMA.The limited baseline is the strengths of present work. Finally, the methodology of this study can also be used in other surveillance programs for the rapid detection of other diseases.

## Conclusions

There is no single algorithm with a specific threshold level can cover a wide range of meningitis outbreaks under different circumstances. Thus, the levels of alarm thresholds should be defined periodically with consideration to the epidemiology of interested diseases, priority for early detection, costs for investigating false alarms using different methods as stated in present study.

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## Conflict of interest statement

Authors have no conflict of interests.

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