

*Review Article***Seasonal Pattern of Brucellosis in Iran: A Systematic Review and Meta-Analysis**Mahmood Moosazadeh<sup>1</sup> Ghasem Abedi<sup>1</sup> Motahareh Kheradmand<sup>2</sup> Saeid Safiri<sup>3</sup> \*Roja Nikaeen<sup>2</sup>

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**Abstract**

**Background and Purpose:** Investigation of the seasonal pattern of brucellosis occurrence may help us to determine the etiology of disease. Seasonal pattern of brucellosis in different parts of Iran has been reported by several studies. Combining the results of these studies provide a reliable estimation of a total seasonal pattern of this zoonosis disease. This study aims to determine the overall pattern of brucellosis in Iran using meta-analysis method.

**Materials and Methods:** Relevant evidence was identified searching the national and international databanks. Eligible articles were entered into the final meta-analysis after comprehensive review of evidence as well as quality assessment. We also calculated the standard error of the incidence according to binomial distribution formula. Because of the significant heterogeneity observed between the results, random effects model was used to combine the results. All data analyses were conducted using Stata software.

**Results:** In total, 26 studies were entered into this systematic review including 17,311 subjects. Incidences (95% confidence intervals) of brucellosis in Iran during spring, summer, autumn and winter were estimated as of 34.4% (30.3-38.6), 33.2% (30.7-35.7), 16.4% (13.3-19.5) and 14.9% (12.7-17.1), respectively.

**Conclusion:** This meta-analysis showed that the highest incidences of brucellosis are occurred during spring and summer, while the lowest incidences are occurred during winter and autumn.

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**Key words:** Brucellosis, Season, Systematic Review, Meta-analysis, Iran

## 1. Introduction

Brucellosis is one of the most common zoonotic diseases worldwide which is occurred by infection with an agent belongs to the *Brucella* family. Some areas in Mediterranean region, Middle East, South and Central America, and Indian subcontinent are endemic areas for brucellosis (1,2). According to the WHO reports, annually more than 500,000 incident cases of brucellosis are notified worldwide especially from developing countries (3).

Among livestock, brucellosis causes adverse effects on reproductive systems leading to abortion, low birth weight and weak neonates which are considered as great losses (4). Dairy products, climatic situation, environmental hygiene, and socio-economic conditions are main factors of infectiousness and transmission of brucellosis. Human contact with infected animals is the most common mode of transmission (5). There is a considerable variation in the frequency of brucellosis in different parts of Iran. The incidence varied between 98 and 130 per 100,000 population. Southern parts of Iran have the lowest incidences of brucellosis (6).

According to the results of previous studies (7-9), the prevalence of brucellosis is higher during the first half of the year which is the livestock calving season. During spring and summer, direct contacts between ranchers and aborted fetuses as well as consuming contaminated dairy products, increase the rate of brucellosis. It also decreases in the second half of the year (10).

Primary searches of electronic evidence exhibited various studies regarding seasonal patterns of brucellosis in Iran. Combining these results using appropriate methods will provide reliable estimates of seasonal patterns in Iran (11). Such estimates are useful for policymaking and future researches. This study aims to determine the seasonal pattern of brucellosis in Iran using meta-analysis.

## 2. Materials and Methods

### 2.1. Search strategy

We searched all available national (Medlib, Magiran, Iranmedex and SID) and international (Google Scholar, Scopus, Science Direct and PubMed) databanks to find electronically published studies from 1990 to 14 April 2015. The search was performed using keywords such as seasonal, seasonality, Iran, human brucellosis, brucellosis, Malta fever, and their Farsi equivalents within titles and abstracts in combination with "OR" and "AND" operators. To increase the search sensitivity, all references were also investigated. One of the team researchers randomly evaluated the search results and reported that no relevant study was ignored. We also reviewed non-electronic evidence and interviewed with relevant experts and research centers to identify any gray literatures.

### 2.2. Study selection

We extracted full texts or abstracts of all evidence identified during our advanced search. After excluding duplicates, we omitted irrelevant studies reviewing titles, abstracts and full texts of papers, respectively. To minimize the reprint bias, we tried to investigate all results in detail and remove any repeated studies.

### 2.3. Quality assessment

To assess the quality of the selected studies, we applied Strengthening the Reporting of Observational Studies in Epidemiology checklist (12) and also another checklist been used during a review literature (13). Our checklist included questions regarding different aspects of the study such as type of the study, sample size, study objectives, study population, inclusion/exclusion criteria, methods of matching, analysis techniques and methods of illustration of the results based on the study objectives. One score was assigned to each question and studies achieved at least eight quality scores were considered eligible for final meta-analysis.

#### 2.4. Data extraction

All required information such as title, first author name, publish date, sample size, place of study conduction, type of the study, minimum and maximum seasonal, and monthly incidence of brucellosis were extracted from the primary studies.

#### 2.5. Inclusion criteria

All articles written in Persian or English achieved enough quality scores and also reported sample size, seasonal and monthly incidence of brucellosis or at least minimum and maximum incidence of brucellosis were selected for systematic review and meta-analysis.

#### 2.6. Exclusion criteria

Studies did not report the seasonal or monthly incidence of brucellosis or its minimum/maximum incidence, those without an obvious sample size, abstracts presented in congresses without full text, case reports and finally studies did not achieved minimum quality scores were extracted from meta-analysis.

#### 2.7. Statistical analysis

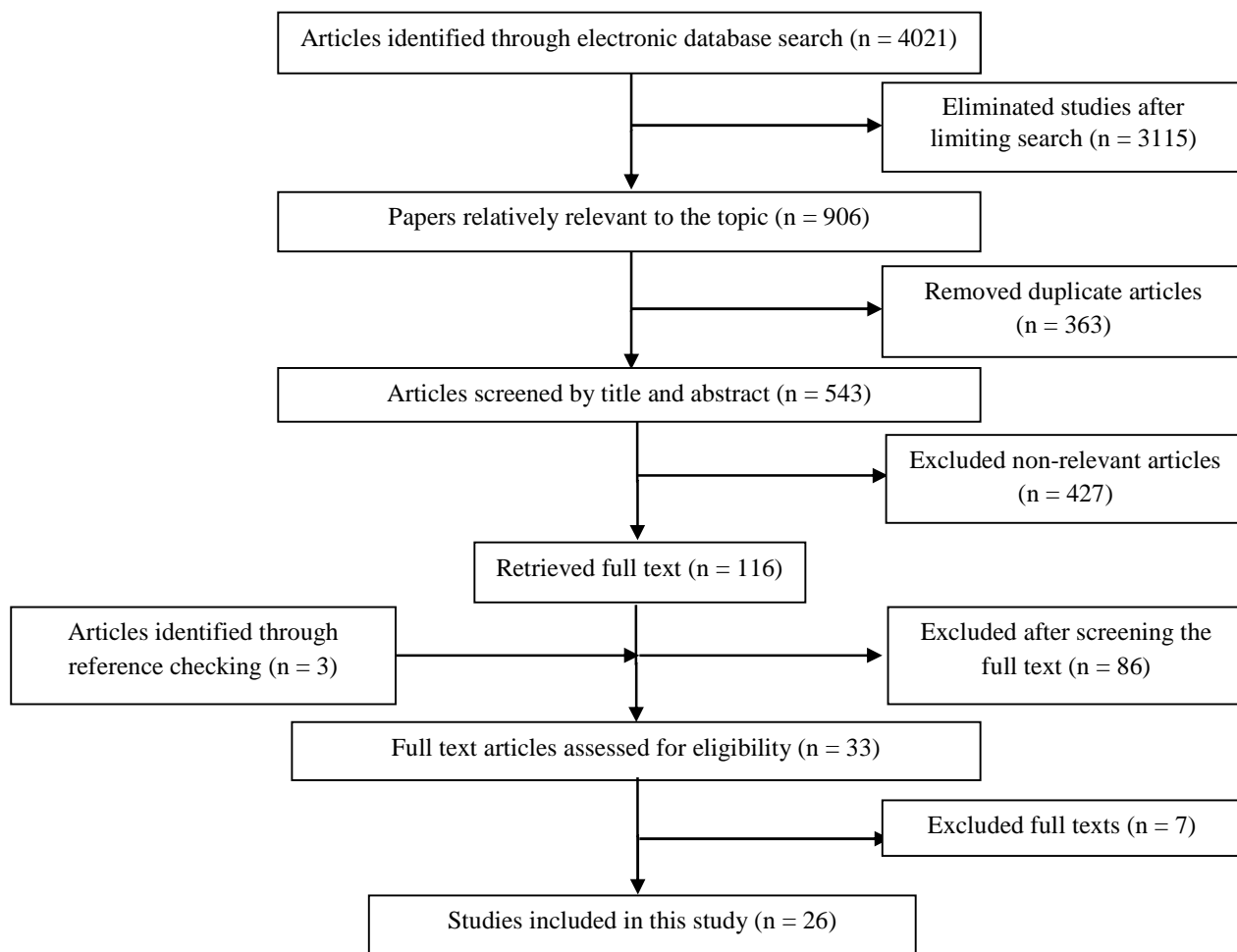
Stata V.11 (Stata Corporation, College Station, TX, USA) software was used for data analysis. The standard error of the incidence of brucellosis in each study was calculated based on binomial distribution formula. The heterogeneity between the results of the primary studies was detected using Cochran (Q) test and  $I^2$  index. According to the observed significant heterogeneity, random effects model was applied to combine the results. We also illustrated point estimates of incidence for each study with their 95% confidence intervals by forest plots. In this plot, size of each box indicated the study weight and crossed lines referred to 95% confidence intervals.

### 3. Results

During our primary search, 4021 studies were identified. Restricting the search strategy, 3115 articles were omitted. Reviewing the titles and abstracts and excluding duplicates, 116 papers were remained. Review of references added three relevant articles to this study. Moreover, three studies had been repeatedly published by different titles in several journals (3,10,14-17). After investigating full texts and quality assessment, 26 papers were identified eligible for systematic review and meta-analysis (Figure 1).

Of 26 studies entered into the current systematic review, 23 studies were cross-sectional (descriptive-analytic), while three studies had not determined the type of study. All studies were published from 2001 to 2013. According to the results of 13 studies, the least incidences of brucellosis were reported in winter and autumn; six of them reported that the lowest incidence was occurred in February and March. These studies found that the most incident cases of brucellosis were notified during April and June, five of which reported May as the month with the highest cases. Minimum incident cases were reported in winter (10 studies) and autumn (5 studies), while the highest incidences were reported in summer (8 studies), spring (7 studies) and spring + summer (5 studies) (Table 1).

Figure 2 illustrates the point incidence rates of brucellosis as well as the total estimate of brucellosis incidence in spring which varied between 22.6% in Hosseini study and 58.6% in Almasi study. According to the random effects model (Q = 134.6, P < 0.0001;  $I^2$ : 91.1%), the incidence (95% confidence interval) of brucellosis during spring was estimated as of 34.4% (30.3-38.6).



**Figure 1.** Literature search and review flowchart for selection of primary studies

As illustrated in figure 3, the incidence of brucellosis during summer varied from 26.9% in the study conducted by Almasi to 45.9% in the study carried out by Sasan. Based on the random effects model ( $Q = 48.4, P < 0.0001; I^2: 73.7%$ ), the total incidence (95% confidence interval) of brucellosis during summer was estimated as of 33.2% (30.7-35.7). Figure 4 indicates the incidence rate of brucellosis in autumn. The incidence rate was reported as of 6.7% in Almasi study to 22% in Hasanjani study. According to the random effects model ( $Q = 131.4, P < 0.0001; I^2: 90.9%$ ), the total incidence (95% confidence interval) of brucellosis during autumn was estimated as of 16.4% (13.3-19.5).

Figure 5 shows the incidence rate of brucellosis during winter for each of the primary studies. The incidence of brucellosis

varied between 6.8% in the study carried out by Sasan to 19.6% in the study conducted by Hamzavi. Using random effects model ( $Q = 69.9, P < 0.0001; I^2: 81.4%$ ), the total incidence (95% confidence interval) of brucellosis during winter was estimated as of 14.9% (12.7-17.1).

#### 4. Discussion

In this study, we entered 26 papers investigating the seasonal pattern of brucellosis among 17,311 Iranian population. The incidence rates of brucellosis in Iran during spring, summer, autumn and winter were estimated as of 34.4%, 33.2%, 16.4% and 14.9%, respectively. Moreover, the most incidence rates were reported for spring and summer and the lowest rates were reported for winter and autumn.

**Table 1.** Baseline characteristics of included studies in meta-analysis of seasonal pattern of brucellosis incidence in Iran

ID	First author	Publication year	Sample size	Incidence (%)				Minimum of incidences		Maximum of incidence	
				Spring	Summer	Autumn	Winter	Monthly	Seasonality	Monthly	Seasonality
1	Soleimani et al. (29)	2012	5732	-	-	-	-	February	-	May	-
2	Mamishi et al. (30)	2005	44	-	-	-	-	-	-	-	Spring and Summer
3	Karami et al. (31)	2009	194	-	-	-	-	-	Fall	-	Summer
4	Beheshti et al. (32)	2001	130	-	-	-	-	-	-	-	Spring and Summer
5	Hasanzadeh et al. (33)	2013	139	-	-	-	-	-	-	-	Spring and Summer
6	Ettehad et al. (34)	2007	51	-	-	-	-	-	-	-	Spring and Summer
7	Hamzavi et al. (35)	2014	777	33.5	30.2	15.7	19.6	October	Fall	May	Spring
8	Ghasemi et al. (36)	2003	1591	-	-	-	-	November	-	April	-
9	Esmailnasab et al. (37)	2007	1059	30.5	33.3	18.99	17.2	March	Winter	June	Summer
10	Shoraka et al. (6)	2010	64	32.8	28.1	20.3	18.8	-	Winter	-	Spring
11	Haddadi et al. (38)	2006	415	30.36	31.8	21.01	16.83	-	Winter	-	Summer
12	Eini et al. (3)	2012	230	33.6	29.6	18.8	17.9	-	Winter	-	Spring
13	Ayazi et al. (15)	2012	175	30	43	13	14	-	Fall	-	Summer
14	Bahador et al. (39)	2012	40	-	-	-	-	November, February, March	-	July	-
15	Sasan et al. (40)	2012	82	-	45.9	-	6.8	-	Winter	-	Summer
16	Kassiri et al. (10)	2013	43	25.5	34.8	20.9	18.7	December	Winter	May	Summer
17	Almasi et al. (41)	2012	210	58.6	26.9	6.7	7.2	-	Fall	-	Spring
18	Mohammadian and Mohammadian-Hafshejani (42)	2014	554	45.85	30.32	6.86	16.97	November	Fall	May	Spring
19	Zeinalian et al. (43)	2012	1996	-	-	-	-	March	-	June	-
20	Sahargahi et al. (44)	2014	458	-	-	-	-	November	-	April	-
21	Almasi-Hashiani et al. (45)	2011	907	36.7	28	19.1	16.2	March	Winter	May	Spring
22	Hasanjani Roushan et al. (46)	2004	469	25.2	40.1	22	12.8	-	Winter	-	Summer
23	Maleki et al. (47)	2015	492	-	-	-	-	December	-	April	-
24	Hosseini et al. (48)	2009	115	22.6	37.4	20.9	19.1	-	Winter	July	Summer
25	Rajabzadeh et al. (49)	2014	1310	38.2	35.6	15.1	11.1	March	Winter	June	Spring
26	Fanni et al. (50)	2013	34	-	-	-	-	-	-	-	Spring and Summer

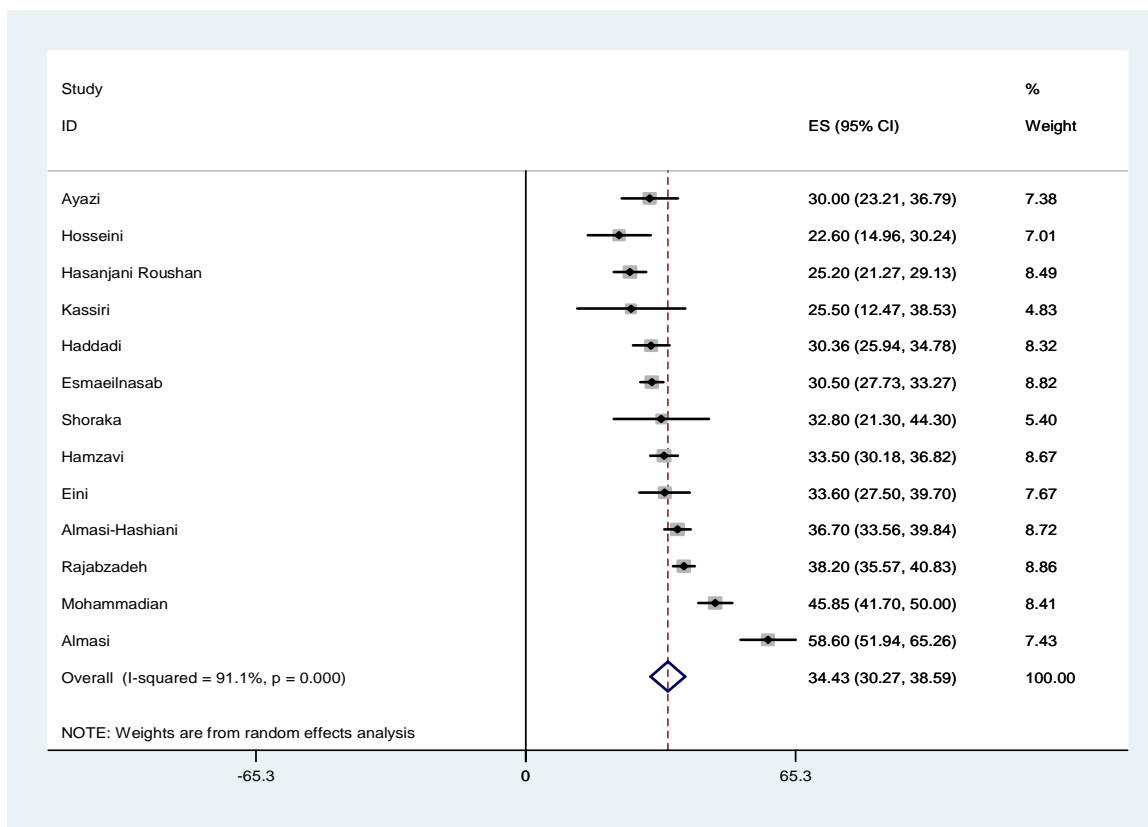


Figure 2. The prevalence of brucellosis in spring seasonal in per study and pooled estimate

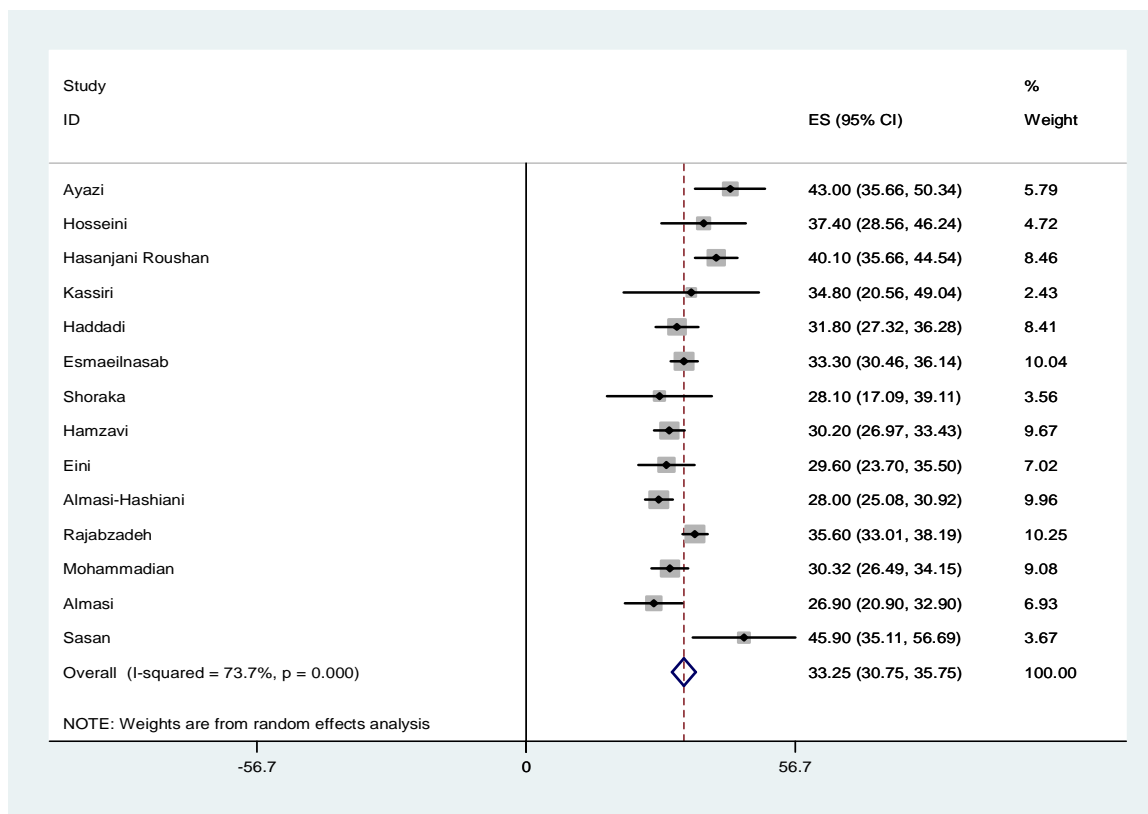


Figure 3. The prevalence of brucellosis in summer seasonal in per study and pooled estimate

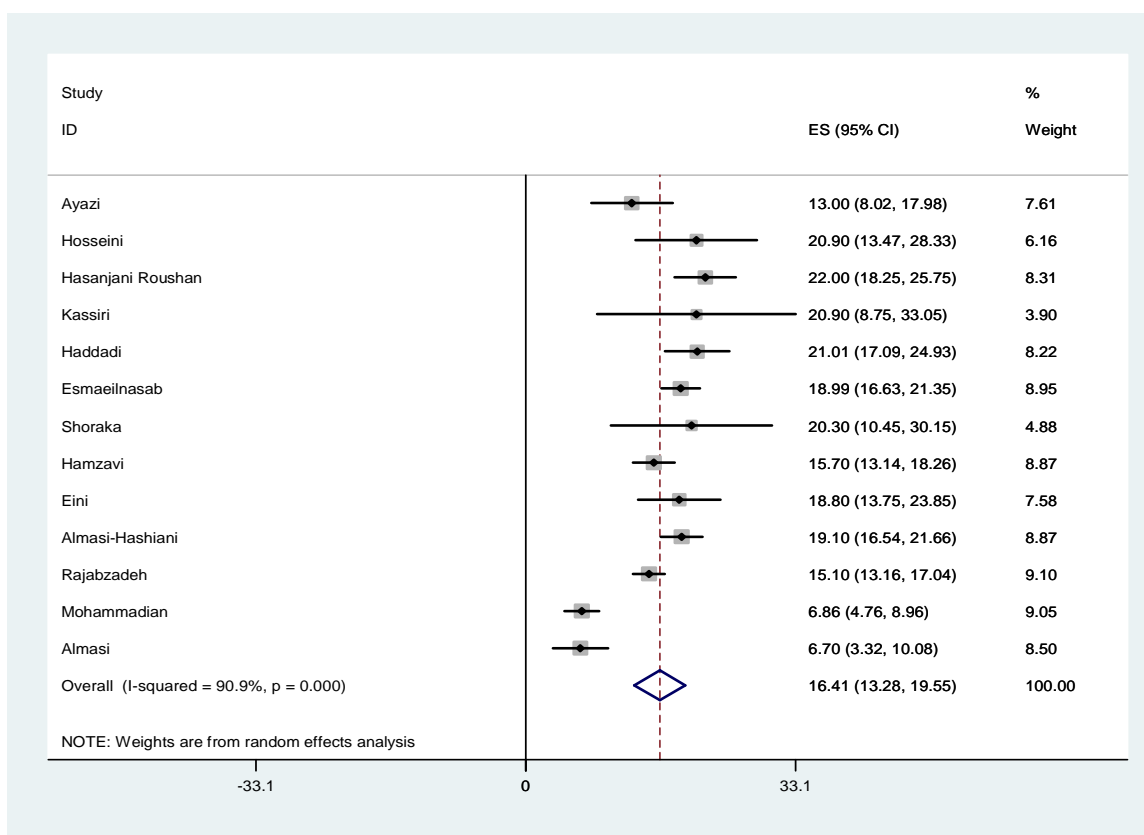


Figure 4. The prevalence of brucellosis in autumn seasonal in per study and pooled estimate

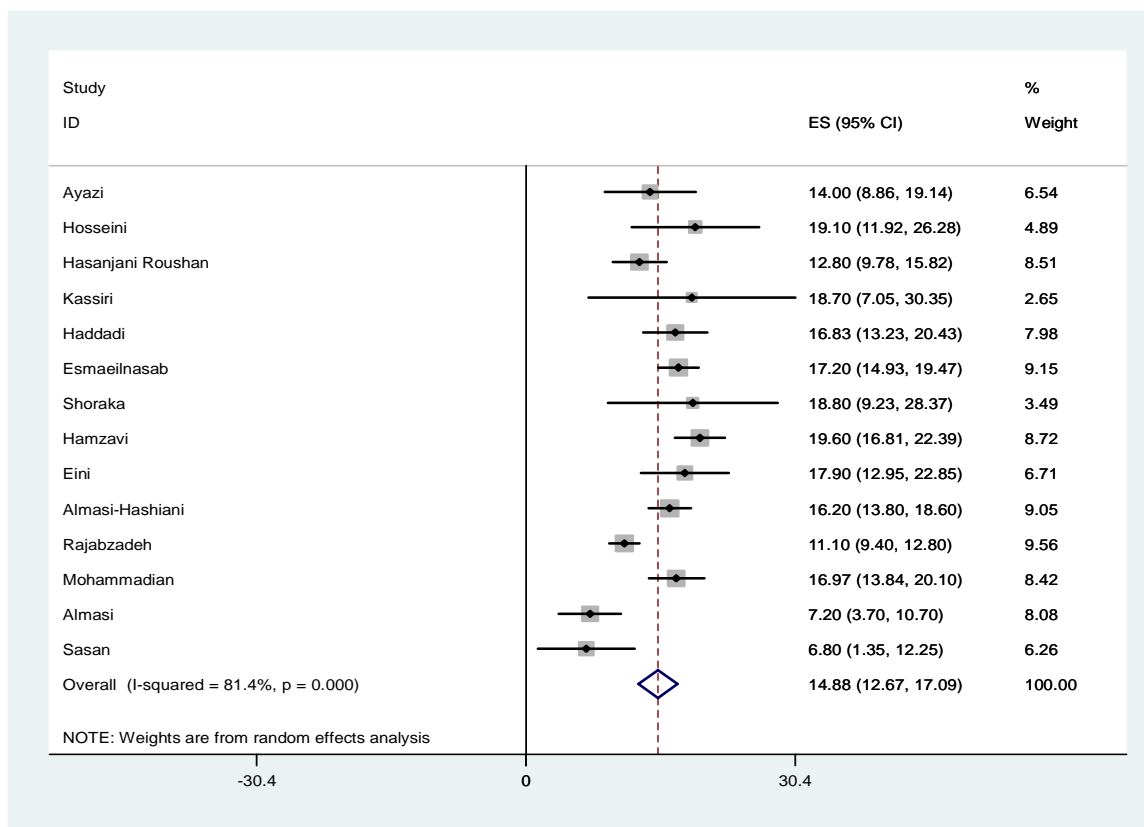


Figure 5. The prevalence of brucellosis in winter seasonal in per study and pooled estimate

In a study conducted in Central Greece, a significant association has been observed between season and brucellosis and the risk of developing disease was higher during April and May in spring, while the lowest incident cases were notified in September and October (7). In a study carried out by Buzgan (18) in Turkey, spring and winter seasons had the highest and lowest incident cases, respectively. In Germany (19), the peak of disease has been reported during July and August in summer, and the lowest cases were reported in January and February (winter). Another study conducted in The North-West of Greece (20) showed that the maximum and minimum rates of disease are in spring (March and April) and autumn (September and October). Among Turkish population aged 4-15 years, the highest cases were reported in spring and summer, while the lowest cases were reported during winter and autumn (21). Results of a study carried out in a province of Kingdom Saudi Arabia (22), showed that the incidence of brucellosis is the highest during spring and lowest during winter. According to a 24 years survey investigating the epidemiology of brucellosis in the eastern part of Kingdom Saudi Arabia (23), April and May had the most incident cases while December and January were reported as months with lowest cases. Donev et al. (24) in Macedonia observed the highest incidence of brucellosis in the last month of the spring. They also found that the lowest cases were occurred in the first month of winter. Obradovic and Velic (9) in Bosnia and Herzegovina reported the highest occurrence of disease during the first month of spring and the lowest rates of disease during December and January. An investigation in Serbia was conducted to assess the epidemiological characteristics of brucellosis during 1980-2008, showed a significant influence of season on the occurrence of disease so that the most cases were occurred during summer (August and September) and the minimum incidence rate

were report during December and January (8). In Italy, during 1997-2002 (25), the most incident cases were reported in spring (April and May). The seasonal patterns shown in approximately all of the above regions are similar to that of Iran.

Predominant occurrence of brucellosis during a specific season is due to multiple factors. Alavi et al. (26) showed significant associations between the occurrence of brucellosis and factors such as exposure to animals and their waste and consumption of unpasteurized dairy products. According to the results of a study carried out by John et al. (27) in Tanzanian rural, participation in livestock abortion was significantly associated with developing brucellosis. Since the livestock calving season is during spring and summer, more incident cases are reported in these seasons. The rate of disease among those with high-risk jobs and those having direct contact with livestock and its products particularly during animal deliver is more than that among other persons (28).

The considerable heterogeneity observed between the results of the primary studies is one of the limitations of our meta-analysis. However, we tried to combine the results using random effects model. The variation in the representation of seasonal patterns among primary studies is another limitation in the current systematic review/meta-analysis. This pattern has not comprehensively been investigated in all of the above studies as shown in table 1.

The current systematic review/meta-analysis provided reliable evidence regarding the seasonal pattern of brucellosis occurrence. These evidence can be useful resources for health policymakers within Ministry of Health and Medical Education as well as Veterinary Organization. According to the results of this systematic review, there is no need to design studies investigating the seasonal pattern of brucellosis.

In conclusion, our study showed that the



highest incidence rate of brucellosis in Iran is during spring and summer, while the lowest cases occur during winter and autumn.

### **Conflict of Interests**

The Authors have no conflict of interest.

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