

# Recent Trends in Human Brucellosis in the West Bank, Palestine

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## Research Article

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# Abstract

## Background

Brucellosis in Palestine continues to be a significant public health problem due to its impact on the human health, as a result of the high prevalence level of infection in livestock especially in sheep and goats. The purpose of this research was to investigate the epidemiology of human brucellosis in the West Bank over the past 20 years with a focus on recent trends in disease incidence from 2010 through 2020.

## Methods

We conducted a long-term descriptive epidemiological study based on the Palestinian Ministry of Health records on human brucellosis from 2000-2020.

## Results

The total number of cases reported in this period was 7935 patients and the average annual incidence rate (AAIR) was 9.4 cases/10<sup>5</sup> population. Hebron was the most endemic among all studied governorates.

The AAIR ranged from 17.9 in 2000 to 15.7 cases/10<sup>5</sup> population in 2020. The AAIR markedly decreased from 17.9 in 2000, to 2.9 cases/ 10<sup>5</sup> populations in 2012. A dramatic increase in human cases started from 2013 onwards to mark a peak in 2016. Higher incidence was reported in male (57.1%) and among the age group 11-20 years (29%). A higher number of cases was reported during April, May and June with the highest peak recorded in May, and subsequently exhibiting a gradual decline during autumn and winter. 2850 (62.7%) patients reported contact with animals which included 1783 (62.6%) patients who had contact with sheep, 819 (28.7%) with goats, and 248 (8.7%) with cattle.

Moreover, (37.2%) of the patients reported raw milk consumption and (80.9%) reported white cheese consumption. Approximately (30%) had at least one infected household member. Diagnosis was based on the clinical picture and confirmed by laboratory tests. Patients were treated with a combination of Streptomycin and Tetracycline, or Tetracycline and Rifampicin.

## Conclusions

The incidence of human brucellosis in the West Bank has markedly increased in recent years. This dramatic increase is linked to the impaired control and surveillance of the disease. Mass vaccination, regular screenings of animals for brucellosis, continuous outreach campaigns on raising public health awareness, monitoring milk and homemade dairy products pose some recommended precautionary measures of coping with the epidemic.

## Background

Brucellosis, also known as Malta fever, undulant fever, and Mediterranean fever, is one of the most prevalent zoonotic diseases worldwide. It is caused by a group of gram-negative bacteria of the genus *Brucella* [1] and transmitted to humans by direct ingestion of raw animal products such as unpasteurized milk or contaminated dairy products, undercooked meat from infected animals, or contact with their secretions [1, 2].

The three most common species causing human brucellosis are *Brucella melitensis* (transmitted from sheep and goats), *B. abortus* (transmitted from cattle and other bovidae), and *B. suis* (transmitted to humans from pigs) [3]. The most endemic regions of brucellosis were detected in the Mediterranean basin, certain countries in Central and South America, India, Africa, and the Middle East [1, 4, 5]. According to the World Health Organization (WHO), 500,000 new human brucellosis cases are diagnosed every year on a global scale. Nevertheless, this might seem to reflect a potential underestimation given that many of the most endemic countries do not have adequate surveillance and many cases remain unreported [6, 7]. Moreover, conservative estimates of the global disease burden in livestock postulate that >300 of the 1400 million global cattle population is infected with *Brucella* [8].

In Palestine, brucellosis was recognized as a major health problem in the West Bank and the Gaza Strip [9, 10]. The incidence of human brucellosis in the Gaza strip in 1996 was  $8/10^5$  of the population with the highest incidence dominating the mid-zone district and Gaza City [10]. Higher risk was reported among animal breeders and people had consumed unpasteurized milk and milk products, particularly homemade cheese [10]. The seroprevalence of brucellosis in livestock in the West Bank in 1999 underlay 18% in sheep and goats and 80% in flocks with more than 800 human cases [11]. Several variables such as the consumption of unpasteurized milk and dairy products, as well as the herding and lambing were identified as significant risk factors [9].

Human brucellosis was introduced to the West Bank and the Gaza Strip only recently with the first human case being reported in 1973 in the Hebron governate at the West Bank [9]. In 1998 the Palestinian Brucellosis Control Program (PBCP) was launched as a joint effort between the Palestinian Authority and the United Nations Development Program (UNDP). The implemented strategy of this program dictated mass vaccination of sheep and goats regardless of age and sex, except for mature pregnant females. The vaccination campaign started in 1999 and was repeated on a regular basis of two years until 2008, with coverage ranging between 25% – 95% depending on the year. As a result, the sheep and goat prevalence were reduced to 4.8%, whereas the flock prevalence was reduced to 46.3% as of 2005. Moreover, a significant decrease in human infections (< 200 cases) was reported over the same period [12].

Due to its zoonotic nature, brucellosis in humans and animals is recognized as a significant public health challenge in Palestine, with a major economic impact and financial burden which ought not to be underestimated. This study has investigated the epidemiology of human brucellosis in the West Bank over the past 20 years with a focus on recent trends in disease incidence from 2010 through 2020.

# Methods

## Design and Data Source

A long-term descriptive epidemiological study on human brucellosis was conducted in the West Bank, Palestine. The study covered a twenty-year period from 2000 – 2020, and was based on the Palestinian Ministry of Health (PMoH) records. The collected data included age, gender, geographical origin, contact with animals, consumption of milk and dairy products, date and methods of diagnosis, clinical picture, and treatment regime and response.

Human brucellosis is a reportable disease in Palestine - the PMoH provide diagnosis and treatment for patients through primary health care units distributed within all governorates.

There were no changes in the reporting system of human brucellosis in Palestine over the time period, hence all human cases were included in our study.

## Area and Population

We investigated all human brucellosis cases reported by the PMoH in all areas of the West Bank, Palestine. This included eleven governorates; Hebron, Beithlahem, Jerusalem, Ramallah, Jericho, Salfit, Tubas, Nablus, Tulkarem, Qalqilya and Jenin (Fig1). The West Bank is located in the Levant region of Western Asia, west of the Hashemite Kingdom of Jordan (Geographic coordinates: 32 00 N, 35 15 E). It has an estimated population of 3,053,183 Palestinian inhabitants, as published by the Palestinian Central Bureau of Statistics (PCBS) in mid-2020 [13]. The population is distributed across 11 governorates and ranges from 52,355 in Jericho to 762,541 in Hebron (Fig1).

## Data Analysis

We calculated the average annual incidence rate per  $10^5$  population for each governorate between 2000 - 2020 based on mid-year population size estimated for each governorate in the year of infection. Distribution and frequency tables, figures and maps were plotted for each governorate mapping the relevant year and month of infection, and the average number of cases. Cases were distributed by gender, age and season of infection.

## Results

The Palestinian Ministry of Health reports on human brucellosis were investigated for the period between 2000–2020. The total number of cases reported in this period was 7935 patients and the average annual incidence rate for the years 2000–2020 was 9.4 cases/ $10^5$  population.

Hebron was the most endemic governorate with a total number of cases of 6106 (77%) and an average annual incidence rate (AAIR) of 45.6 cases/ $10^5$ . The average number of patients per year in Hebron was 290.8 patients/year. Figure 1 and Table 1 demonstrate the respective distribution of human brucellosis

cases in all governorates within the West Bank represented by the total and the average number of cases per year, and the AAIR /10<sup>5</sup> population for the study period from 2000–2020.

Table 1  
Distribution of human brucellosis cases in the West Bank from 2000 to 2020

Governorate	Number of patients <sup>a</sup>	Percentage	AAIR/10 <sup>5</sup> population <sup>b</sup>	Average number of patients/years
Hebron	6106	77.0%	45.6	290.8
Bethlehem	697	8.8%	16.6	33.2
Ramallah	274	3.5%	4.3	13.0
Jerusalem	169	2.1%	2.4	8.5
Nablus	158	2.0%	2.2	7.5
Jenin	124	1.6%	2.2	5.9
Salfit	117	1.5%	9.2	5.6
Qalqilya	105	1.3%	4.9	5.0
Jericho	81	1.0%	10.3	3.9
Tulkarem	68	0.9%	2.0	3.2
Tubas	36	0.5%	2.8	3.0
<b>Total</b>	<b>7935</b>	<b>100.0%</b>	<b>9.4</b>	<b>377.9</b>
<sup>a</sup> Total number of human brucellosis cases from 2000 to 2020 in each governorate in the West Bank				
<sup>b</sup> Average Annual Incidence Rate per 100.000 population calculated for each governorate				

The geographical location of the West Bank, Palestine (top left). Distribution of human brucellosis from 2000 to 2020 in each Palestinian governorate. Cases are represented on the map by the average number of patients per year, and the average annual incidence rate per 100.000 population in each governorate (in parenthesis). The table below shows the mid-year population for 2020 in each governorate as estimated by the Palestinian Central Bureau of Statistics PCBS. Maps were created, adapted and edited by Adobe® Photoshop® CC 2015 and Microsoft Paint (MSPaint) 2017.

The annual incidence rate per 10<sup>5</sup> population (AAIR) ranged from 17.9 in 2000 to 15.7 in 2020. The number of cases per year and the (AAIR) markedly decreased from 17.9 to 2.9 per 10<sup>5</sup> population in 2000 and 2012, respectively. A dramatic increase in the AAIR started to show beginning 2013 and has peaked in 2016. The corresponding AAIR were 6.2 and 20.8 per 10<sup>5</sup> population, respectively (Fig. 2A).

The full patient's investigation forms, which included sociodemographic data, clinical manifestation, diagnostic methods and risk factors, were thoroughly analysed for the period 2010–2020. A total of 5890 patients were reported and investigated from this period. There were 3361 (57.1%) males and 2529 (42.9%) females - with a male to female ratio of (1.3:1).

The age of the patients at onset of illness ranged from 1 month to 95 years - with a mean age of  $25.9 \pm 16.9$  years and a median of 22 years. Of the total patients, 1707 (29%), 1123 (19.1%) and 809 (13.7%) cases were reported in those between 11–20, 21–30 and 31–40 years of age, respectively. Children less than 10 years of age and patients older than 41 years constituted 17.3% and 20.4% of all the patients, respectively (Fig. 2B).

Trends of seasonality of human brucellosis were investigated. Higher numbers of cases were reported throughout April, May and June - with the highest peak recorded in May. The total number and percentage of cases in those months corresponded to 2514 (42.7%). Nevertheless, the incidence was shown to decrease gradually during the autumn and winter seasons - with the lowest number reported in December 157 (2.7%) and January 211 (3.6%) (Fig. 2C).

The number of patients reported to have had contact with animals corresponded to 2085 (62.7%). This included 1783 patients (62.6%), 819 (28.7%) and 248 (8.7%) catering for sheep, goats and cattle, respectively.

A detailed history of milk and dairy products consumption was obtained for patients from 2010 to 2020. 1692 (37.2%) patients reported raw milk consumption and 3679 (80.9%) patients reported white cheese consumption, whereas the rest of patients reported other products, such as butter and Jameed mostly produced from sheep milk.

Among the total number of patients reported from 2010–2020, approximately (30%) had at least one household member who was previously or currently infected with *Brucella*.

Diagnosis of human brucellosis was based on clinical analyses and laboratory tests. The most common symptoms were fever (97.2%), sweating (92.2%), chills (92.7%), and fatigue and body ache (70.8%). Other symptoms, such as arthralgia, headache, backache, myalgia and lethargy, loss of weight and appetite, were also reported (25.1%). Cases were confirmed by laboratory tests, which included the Rose Bengal Plate Test (RBT) where positive results were reported in (90.9%) of the patients. The Serum Agglutination Test (SAT) (titer 1: 160 and more) (88.5%), the ELISA test (7.6%), and blood cultures (1%) were further used to confirm the results.

According to the PMoH reports and protocols, (8.4%) of brucellosis patients were hospitalized. Patients were treated with a combination of Streptomycin (1 gm/day) and Tetracycline (2 gm/day) for 4–6 weeks, or Tetracycline (2 gm/day) and Rifampicin (600–900 mg/day) And for 6 weeks. Rifampicin (600–900 mg/day) for 6 weeks and a combination of Trimethoprim (160 mg) and Sulfamethoxazole (800 mg) for 6 weeks were particularly used for pregnant women and infants, respectively.

## Discussion

Brucellosis continued to be endemic in most Middle Eastern countries with considerable burden on human health and livestock productivity [14, 15]. Herein, we investigated the epidemiology and recent trends in human brucellosis over the past 20 years in the West Bank, Palestine.

The total number of cases reported in the West Bank over the past 20 years was 7935 and the overall AAIR was 9.4 cases/10<sup>5</sup> population. The highest number of cases and corresponding AAIR were reported in the Hebron governate, which represented 77% of the total human brucellosis cases in the West Bank (Fig. 1 and Table 1). Hebron is considered the historical endemic district for brucellosis where the first Palestinian case was reported in 1973. Moreover, the area is known to endow the highest percentage of sheep and goats in the West Bank. [16].

The incidence of human brucellosis was higher among the age group 11–20 years and among males with a male to female ratio of (1.3:1). Similar results showed male predominance in Saudi Arabia [17, 18], Israel [19] and Greece [20]. This is probably related to a higher occupational exposure of these groups in contrary compared to exposure acquired through ingestion of milk or dairy products.

The AAIR markedly decreased and reached the lowest peak in 2005 after launching the Palestinian Brucellosis Control Program (PBCP) in 1998, which implemented a mass vaccination strategy of sheep and goats on a two-year basis until 2008. The number of human cases decreased from 837 to < 200 in 1998. The rate of reported animal cases decreased from 25 to < 10 cases/ year since the implementation of the PBCP guidelines [11]. The dramatic increase in AAIR from 2013 onward is markedly linked to impaired control and surveillance of the disease after the closure of the PBCP. Apparently, mass vaccination of the entire population of animals in our area is the only efficient method for brucellosis control. This would require a sustainable and a well-supported surveillance program by means of an efficient collaboration among the PMoh, PMoA and the Palestinian farmers at the national level.

The seasonal distribution of human brucellosis in the West Bank was explored. The highest incidence was reported during the spring season having peaked in May and subsequently gradually decreased until the end of summer (Fig. 2C). This is explained by the parturition season of sheep and goats in Palestine, which extends mainly from December through March, followed by the lactation period extending from March through September. The production and consumption of milk and dairy products have increased during this period, and have, further, coincided with the incidence of brucellosis, which continued until the end of the lactation season in August and September. This trend of seasonality is similar in other Mediterranean countries, such as Jordan [21], Greece [20], and Israel [19], where parturition and lactation commonly determine the seasonality of human brucellosis inclined to peak in spring and decline through summer [22]. However, animal breeding in tropical and subtropical areas tend to exhibiting an ongoing trend throughout the year and rather has no seasonal influence over the incidence of human brucellosis [22].

The major sources of infection in our study correspond to the direct contact with animals (mainly sheep and goats), and the consumption of their raw milk and dairy products. Previous studies have shown that the consumption of contaminated milk, dairy products and raw meat, and the direct contact with animals within a variety of frames, such as milking, herding, and slaughtering, were the main risks factors pertaining to human brucellosis in the West Bank [9] and other countries [20, 21, 23]. The practices followed in marketing and distributing milk and dairy products in and to our endemic areas make the enforcement of hygienic measures very difficult [22]. Family-owned flocks of sheep and goats are the source of unpasteurized milk and homemade dairy products, which mark the source of most human infection. However, such factors are changeable and could be adjusted accordingly. Vaccination and regular screening of sheep and goats for brucellosis should be mandatory and supervised by the Ministry of Health and the Ministry of Agriculture. Marketing and the distribution of milk and dairy product should be licenced and monitored. Moreover, the continuous outreach campaigns on raising awareness of the health risks of buying and consuming unlicenced dairy products ought to be significantly considered.

Approximately one-third of our patients reported positive family history of brucellosis. The latter was identified as a risk factor significantly associated with disease incidence [9, 24, 25]. The risk of transmission among household members can be exceedingly high, especially following the point-source exposure exuding contaminated raw milk and dairy products. Hence, the screening of family members with respect might prove to be crucial [22].

The diagnosis of human brucellosis in Palestine was based on the patient history and background, and the clinical analysis. Nevertheless, the latter has rather proven unspecific and variable, thus paving the need for bacteriological and serological tests to assess a patient's proper diagnoses and treatment. The RBT, which is useful in small clinics and laboratories, can be used as an initial rapid screening test especially in countries with limited resources [26]. Diagnosis should, however, be confirmed by bacteriological and other serological tests, such as SAT and ELISA both of which are free offered by the Palestinian Ministry of health at no charge. Moreover, the treatment of *Brucella* infections with antibiotics has also proven to be challenging and rather requires the prolonged administration of antimicrobial combinations that are not routinely prescribed for other infectious diseases, thus requiring significant medical supervision and hospitalization for severely ill patients. Hence, the correct diagnosis of human brucellosis not only proves crucial for a healthier society, but also serves to offset serious epidemiological, economical, and public health consequences markedly posing a grave rubicon in the absence of proper and timely management.

## Conclusion

Brucellosis continues to portray a public health challenge in Palestine. The major sources of infection correspond to the direct contact with animals (mainly sheep and goats), and the consumption of their raw milk and dairy products. The incidence of human brucellosis in the West Bank has markedly increased in recent years. This dramatic increase is linked to the impaired control and surveillance after the closure of the PBCP. Mass vaccination, regular screening of sheep and goats for brucellosis,

continuous outreach campaigns on raising awareness, monitoring milk and homemade dairy products constitute viable precautionary measures that ought to be supervised by public policy lawmakers, namely the Palestinian Ministry of Health and the Ministry of Agriculture. Moreover, the intersectoral cooperation with the different governmental and nongovernmental organizations should prove key to further empowering the fight against brucellosis.

## **Abbreviations**

AAIR: average annual incidence rate, ELISA: Enzyme Linked Immunosorbent Assay, PBCP: Palestinian Brucellosis Control Program, PMoH: Palestinian Ministry of Health, PCBS: Palestinian Central Bureau of Statistics, RBT: Rose Bengal Plate Test, SAT: Serum Agglutination Test, UNDP: Palestinian Authority and the United Nations Development Program, WHO: World Health Organization

## **Declarations**

### **Ethics approval and consent to participate**

The study methods, procedures and protocols were thoroughly revised and approved by the Research Ethics Committee at Al-Quds University (REC.AQU). All patients' private data were anonymized and confidentially handled.

### **Consent for publication**

All authors consent for publication of the manuscript.

### **Availability of data and materials**

All data during this study are included in this published article

### **Competing interests**

The authors declare no competing interests.

### **Funding**

No funding was disclosed.

### **Authors' contributions**

AA designed the study and drafted the manuscript. BM and DH provided the data from the PMoH, BM, DH, OH and AA did the data analysis and validation. AA supervision and drafting and editing. All authors read and approved the final manuscript.

### **Acknowledgement**

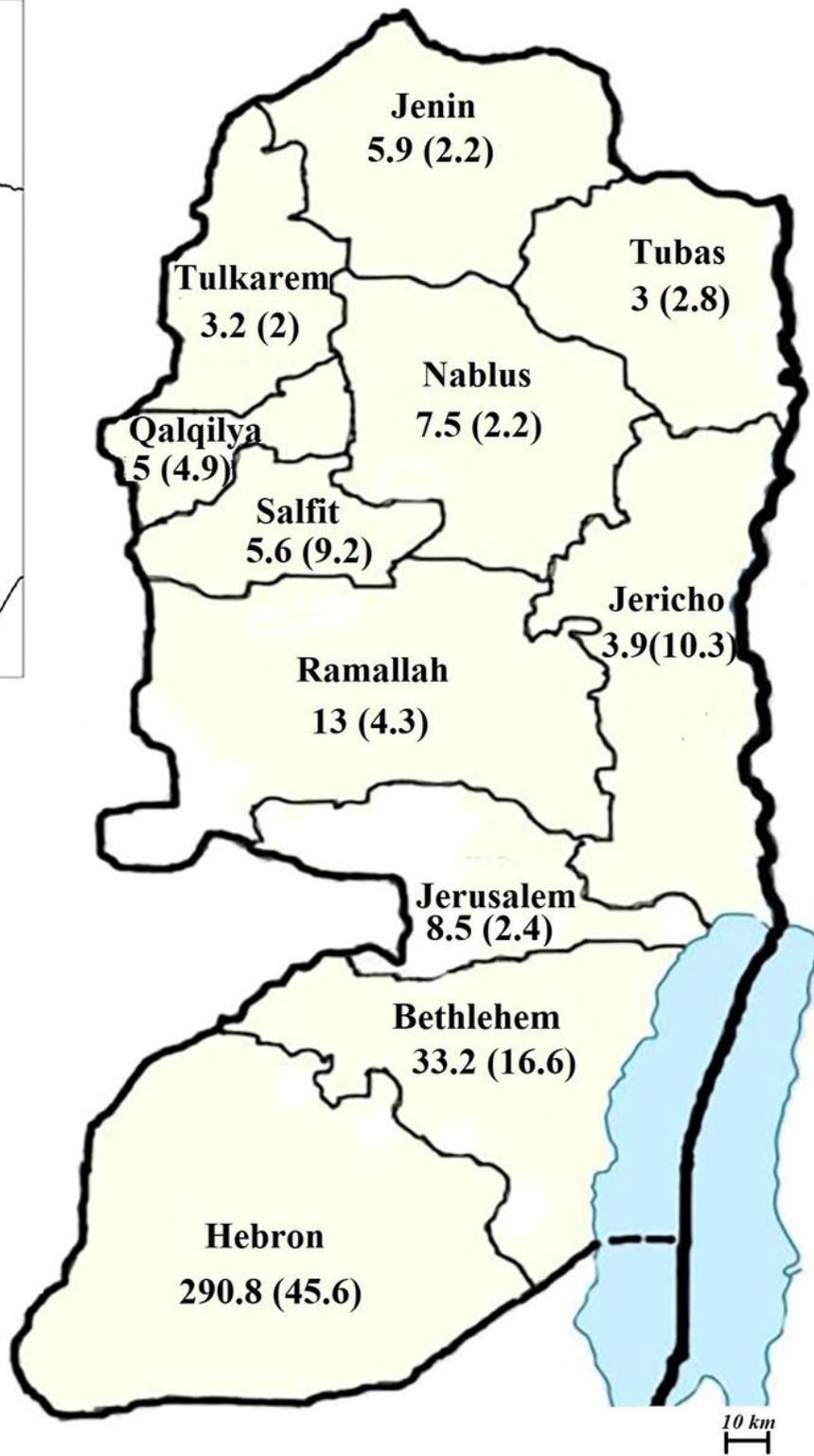
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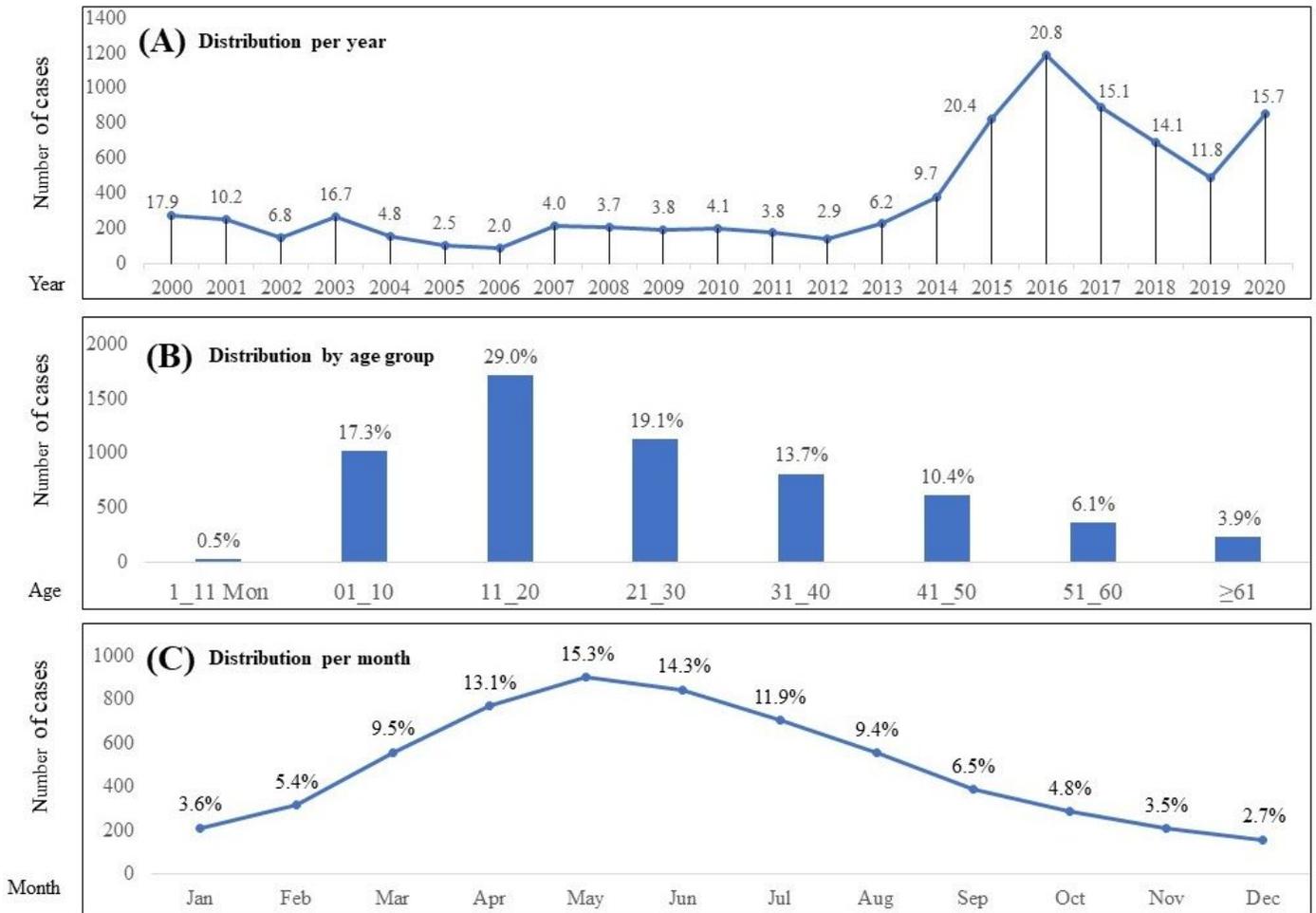
## Figures



Governorate	Population
Hebron	762,541
Bethlehem	229,884
Ramallah	347,818
Jerusalem	461,666
Jericho	52,355
Nablus	407,754
Tulkarem	195,341
Salfit	80,225
Qalqilya	119,042
Jenin	332,050
Tubas	64,507
<b>Total</b>	<b>3,053,183</b>

**Figure 1**

Map of the West Bank, Palestine show the distribution of human brucellosis from 2000 to 2020. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.



**Figure 2**

Annual, seasonal and age distributions of human brucellosis in Palestine (A): Distribution of human brucellosis per year for the period 2000-2020. Data labels show the annual incidence rate/100.000 population calculated for each year. (B): Patients-age distribution of human brucellosis at onset of illness. (C): Total numbers and percentages of human brucellosis per month in the West Bank for the whole study period 2010-2020.