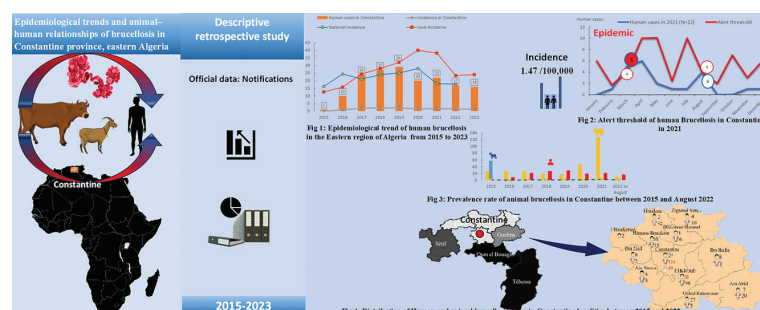




ORIGINAL ARTICLE

Epidemiological Trends and Animal–Human Relationships of Brucellosis in Constantine Province, Eastern Algeria from 2015 to 2023

Graphical abstract



Highlights

- Data from 2015 to 2023 (until August 2022 for animals) were analysed to explore brucellosis epidemiological characteristics and trends in the Algerian province of Constantine, identifying human–animal interactions.
- A total of 163 human cases were recorded.
- An annual average incidence of 1.47/100,000 was reported.
- The epidemic threshold exceeded in 2021 and 2022.
- A cattle prevalence of 1.32% and a screening rate below 7.5% were reported.
- A significant correlation was observed between humans and goats ($r = -0.747$, $p = 0.03$).
- The southern Constantine region was the most affected.

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Brief statement

This study describes the epidemiology of human and animal brucellosis in eastern Algeria. It confirms the persistence of this zoonosis as a significant public health threat with gaps in management, including inadequate screening of goats, insufficient vaccination coverage, and underreporting. This emphasises the need for comprehensive surveillance programmes to develop new strategies and better prevent this disease.

Epidemiological Trends and Animal–Human Relationships of Brucellosis in Constantine Province, Eastern Algeria from 2015 to 2023

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Abstract

Objective: The objectives of this study were to characterise the epidemiology of human and animal brucellosis in the eastern Algerian province of Constantine, and to identify the interactions between humans and animals, to establish strategies from a unique health perspective considering the context of endemicity and eradication challenges.

Methods: Data collected from official institutions regarding brucellosis in humans and animals in Constantine and seven other provinces from 2015 to 2023 (until August 2022 for animals) were analysed to estimate temporal trends, alert thresholds, and correlations between humans and animals.

Results: A total of 163 brucellosis cases in humans were recorded in Constantine between 2015 and 2023, and the annual average was 1.47/100,000. The epidemic threshold was exceeded in 2021 and 2022. Males and residents 20–44 years of age were the most affected groups. In cattle, the prevalence was 1.32%, and the screening rate was below 7.5%. The only significant correlation was observed between humans and goats ($r = -0.747$, $p = 0.03$). The southern Constantine region was the most affected.

Conclusion: Brucellosis is an underestimated public health threat in Algeria. Gaps in its management include inadequate screening of goats, insufficient vaccination coverage and underreporting. The implementation of more comprehensive surveillance programmes is imperative.

Key words: human brucellosis, incidence, animal brucellosis, zoonosis, epidemic threshold, One Health, Algeria

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INTRODUCTION

Brucellosis is a zoonotic disease affecting primarily livestock and wildlife. This infectious disease has serious public health and economic effects, particularly in regions with inadequate food safety measures, hygiene standards and veterinary care [1]. Brucellosis is caused by *Brucella abortus* or *Brucella melitensis* in cattle, buffalo and camels, and by *Brucella melitensis* in sheep and

goats. This notifiable disease is the most common zoonotic bacterial infection: recent estimates have indicated 2.1 million cases per year worldwide, a number much higher than previously believed [2]. The main clinical signs of disease in dairy cattle are abortion after mid-gestation and associated postpartum infections. In sheep and goats, abortion and mastitis are the most common signs of *Brucella* spp. infection. In males, the signs are epididymitis and

infertility [3]. The bacteria causing the infection are shed in vaginal secretions of infected females and peak immediately after abortion or parturition. Humans can become infected through consumption of raw milk and its derivatives, or through direct contact with infected animals, particularly after abortion. In endemic areas, brucellosis poses an occupational risk to veterinarians, farmers, and many other professionals with regular contact with animals or animal products [4,5].

Clinical manifestations of brucellosis in humans typically include a high, rolling fever; headache; and night sweats. However, the chronic form of the disease can potentially affect a wide range of organs in the host and consequently lead to diverse diseases including arthritis, orchitis, hepatitis, encephalomyelitis and endocarditis [6]. Human brucellosis is a highly endemic disease in the Mediterranean, Middle East and Africa [7]; these regions account for most human brucellosis cases and incidence [2]. However, brucellosis is often under-reported in both human and animal populations throughout the African continent [8]. The prevalence of this disease in the Maghreb remains underestimated, and the epidemiological status is largely unknown [9]. Unfortunately, human brucellosis remains endemic in Algeria [10]. Historically, the disease received increased attention after a major outbreak in Ghardaïa in 1984, which resulted in 600 recorded cases; the zoonosis has since been identified in several other locations in eastern and western Algeria, and its incidence remains high [11]. Brucellosis is among the major occupational diseases affecting veterinarians in Algeria [12]. Despite the implementation of a control programme in 1995 involving the mass vaccination of sheep and goats with Rev1 in high-risk areas, combined with screening and slaughter of cattle and goats, with compensation, brucellosis continues to pose a substantial financial burden on health authorities. For instance, between 2002 and 2004, 618,624 € was allocated to farmers after the slaughter of cattle and goats diagnosed with brucellosis [13]. Because the prevalence of human disease reflects the animal reservoir, accurate data on brucellosis hotspots would enable more targeted vaccination strategies in livestock and ultimately prevent human cases [8]. A comprehensive understanding of the epidemiological status and associated risk factors is also crucial to accurately document the true prevalence of human brucellosis, and to implement effective control strategies protecting both humans and animals under the One Health approach [14]. In this context, several studies on human and animal brucellosis have been performed in various geographical regions of Algeria, including studies on small ruminants [15–19], cattle [20,21] and humans [22–24]. However, few publications have described the status in animals and humans simultaneously; examples include [25, 26].

The aim of this study was to examine the epidemiological status of human and animal brucellosis, as reported by the competent authorities after official notification of cases. The selected study area covered eastern Algeria, comprising eight provinces, with a particular emphasis on Constantine, the third most populous city in the country.

This study examined the current evolution of brucellosis in animals and humans, and assessed control strategies' effectiveness and deficiencies in eradicating this zoonosis.

MATERIALS AND METHODS

Study region

This study focused on the eastern part of Algeria, covering the province of Constantine in addition to seven others: Guelma, Annaba, Tébessa, Jijel, Oum el Bouaghi, Sétif and Skikda. The study focused on Constantine, the official eastern capital. In 2022, A total of 8,260,050 inhabitants, representing approximately 20% of the national population, were estimated to live in these eight provinces [27]. Constantine is among the largest provinces in Algeria and is situated in the centre of the eastern region of the country. It covers an area of 2,187 km² and comprises 12 localities. Constantine is located at 36°17' N latitude, 7°23' E longitude and an altitude of 687 m above sea level. Its climate is semi-arid, characterised by a cold period with substantial rainfall (500–700 mm, average 370 mm/year) between October and March, and a warm, dry period between April and September, with temperatures of 25–45°C. The total estimated population is 1,146,684 inhabitants (2022), at an average density of approximately 510 inhabitants per square kilometre. A substantial proportion of the population (66%) resides in the principal localities, and approximately 56% are concentrated in the urban centre of Constantine (Fig 1) [28]. The most recent agricultural census (2021), which is not conducted on an annual basis indicated an official livestock population in Constantine of 230,940, including 41,874 cattle, 178,393 sheep and 10,673 goats. However, only 95,751 animals (33,681 cattle, 56,652 sheep and 5,418 goats) have been declared and are therefore subject to veterinary control (Table 1).

Data collection

Human brucellosis

Epidemiological data were extracted from confirmed cases of human brucellosis in the eastern region (Constantine and seven other provinces) occurring between 2015 and 2023. The data were reported by the Department of Health and Population (DSP) and the Regional Health Observatory (ORS East), which is responsible for epidemiological surveillance and monitoring of notifiable diseases. However, data regarding human brucellosis in eastern Algeria were available only between July and September 2019 and between July and December 2022. Epidemiological data were extracted for confirmed human brucellosis cases in the eastern region (Constantine and seven other provinces) in the period of 2015–2023.

Animal brucellosis

Data regarding animal brucellosis from 2015 to August 2022 came from the Department of Veterinary Services (DSA) of Constantine. The number of brucellosis cases in animals was based on the results of the annual cattle screening performed by the veterinary services on farms that were officially

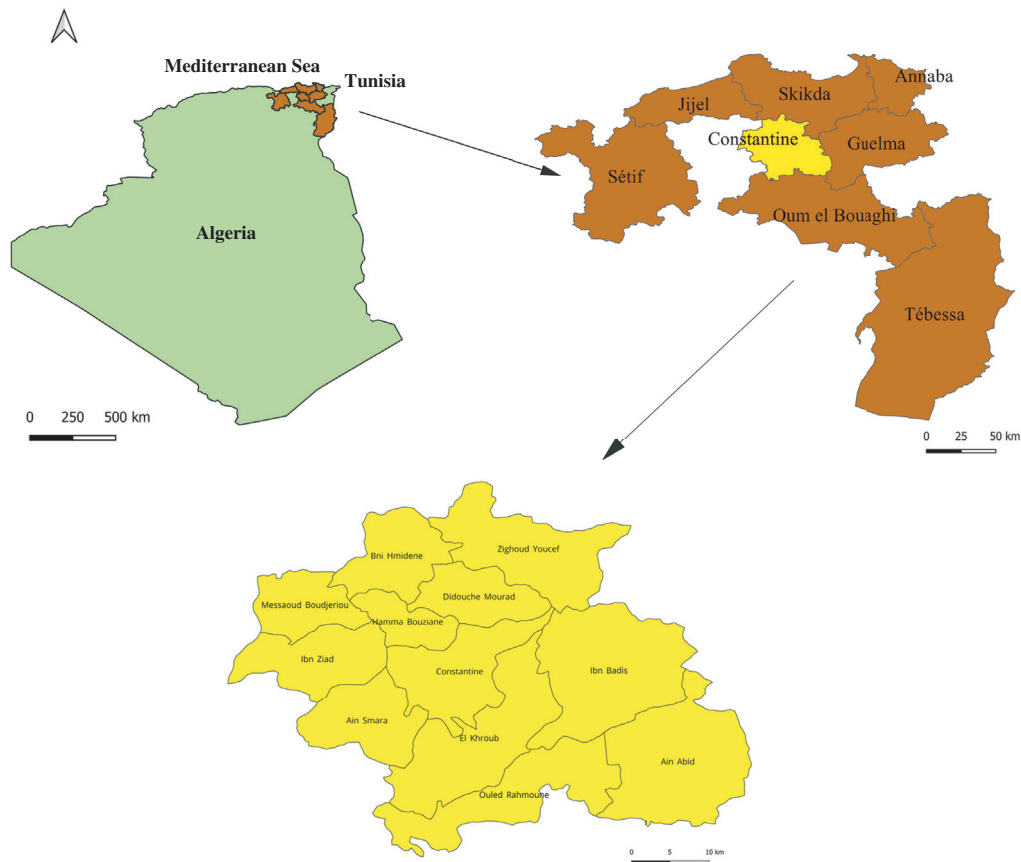


FIGURE 1 | Map of Algeria showing locations of Constantine and its localities [26].

TABLE 1 | Human and animal populations in Constantine localities in 2021 [29].

Locality	Area (km ²)	Human population	Cattle	Sheep	Goats	Overall animal
Constantine	232	262.816	4.040	4.240	180	8.460
El Khroub	240	460.212	3.320	8.592	355	12.267
Ain Smara	125	104.735	1.072	2.244	111	3.427
Ouled Rahmoune	255	30.122	1.826	11.987	969	14.782
Ain Abid	116	41.913	2.748	5.308	687	8.743
Ibn Badis	240	25.565	4.710	6.719	289	11.718
Zighoud Youcef	310	40.896	2.912	2.138	209	5.259
Bni Hmidene	131	11.152	3.690	6.389	1.597	11.676
Hamma Bouziane	71	82.778	1.839	1.680	-	3.519
Didouche Mourad	209	53.720	739	1.911	66	2.716
Ibn Ziad	151	21.531	6.585	5.144	955	12.684
Messaoud Boudjeriou	107	11.244	200	300	-	500
Overall*	2187	1.146.684	33.681	56.652	5.418	95.751
Number of heads of animals registered			41.874	178.393	12.196	232.463

*Total number of animals officially declared to veterinary services.

declared to the competent authorities and had participated in national prophylaxis programmes or the screening of animals in contact with humans after a declared outbreak. The

data presented herein were collected at the end of 2022, because the results for 2023 had not yet been reported at the time of this study.

Importantly, only cattle are subjected to annual screening. This procedure was previously conducted on small ruminants in several provinces in Algeria until 2009. Since then, sheep and goats have been vaccinated with the *Brucella melitensis* strain Rev.1. In Constantine, this vaccination program was terminated in 2016 in favour of addressing other emerging diseases. Screening is conducted only on a case-by-case basis in the event of a health department alert after human cases with sheep or goat contact are reported.

Therefore, the data availability was as follows:

- Human brucellosis: data available from 2015 to 2023 (all months included).
- Data on characteristics of human brucellosis: available between only July and September 2019 and between July and December 2022.
- Animal brucellosis: data available from 2015 to August 2022.

Diagnostic tests

Human brucellosis

All reported cases were diagnosed and confirmed in medical or hospital settings, after which a report was submitted to the relevant authorities and disseminated as part of the normal disease notification procedure. Three authorities were alerted: the Epidemiology and Preventive Medicine Service (SEMEP), DSP and Ministry of Health. The approved tests, the Rose Bengal test (RBT) and the Wright test (in which a serological Ac titre of 1/80 or greater was considered positive), were used for patients in various disease stages. For focal and chronic forms, the recommended tests were indirect immunofluorescence tests or enzyme-linked immunosorbent assay (ELISA). In some cases, bacteriological diagnosis by blood culture was performed only in equipped hospital facilities, with identification by genus rather than biovar; however, these procedures were not standard for the diagnosis of human brucellosis in Algeria.

Animal brucellosis

A positive brucellosis result in an animal was indicated by the presence of antibodies in the animal's serum after RBT screening. This result was then confirmed with a complement fixation test or the indirect ELISA. Diagnostic procedures were performed at the Eastern Regional Veterinary Laboratory in El Baaraouia (Constantine). Culture and biotyping of *Brucella* isolates by PCR were not routinely conducted for brucellosis diagnosis in Algeria, because of the high cost of diagnostics.

Statistical analyses

Incidence, defined as the number of cases recorded each year, or the mean annual incidence, was used for statistical purposes. Incidence was estimated by sex, age and location. Monthly incidence and seasonal variations were also calculated.

Pearson's r correlation coefficient was determined in SPSS 23 for Windows software (IBM, USA) [30], to assess the influence of season on brucellosis incidence rates and the relationship between human and animal incidence.

The statistical significance threshold was set at the 95% confidence interval (CI) and a p -value $<5\%$.

The epidemic/alert threshold (ET), also known as the basic reproduction number (R_0), is an epidemiological parameter indicating whether an infectious disease can spread throughout the population. An outbreak is characterised by an increase in case counts above the threshold for the normal seasonal pattern of that disease in an area. The threshold is calculated with only counts from comparable periods in previous years. This threshold is usually calculated on the basis of historical routine data at the district level for at least 3–5 years [31]. The ET is the monthly incidence (expected number of cases) of disease at which an epidemic process can be considered underway. Herein, ET was determined with the recommended mean + 2SD method, on the basis of monthly data for the past 3 to 5 years. The ET for human brucellosis was calculated for the past 3 years: 2021, 2022 and 2023.

The geographical maps were produced in QGIS software [32].

Ethics statement

Blood and serum samples were collected from animals during screening programs by the Algerian Veterinary Services, which followed standard procedures avoiding suffering according to:

- Law No. 88–08 of 26 January 1988 relating to veterinary activities and the protection of animal health, (No. official Journal: 004 du 27-01-1988)
- Interministerial Decree of 26 December 1995 establishing specific measures for the prevention and control of bovine brucellosis (Official Journal N 65 of 30/10/1996)
- Wilaya Order No. 1679 of 18.04.2021, creating a Wilaya Committee for the Prevention and Control of Zoonoses

Human case declarations were performed in accordance with Order No. 79/MS/CAB, 17 November 1990, which established the list of notifiable diseases and the notification procedures. This order was sourced from the DSP (Health and Population Department) and the ORS (Regional Health Observatory) archives anonymously and did not contain patients' personal information.

RESULTS

Status of human brucellosis in Constantine Incidence

Between 2015 and 2023, a total of 163 cases of human brucellosis were recorded, and the average incidence was 1.47 per 100,000 (Fig 2). The highest annual incidence was observed in 2019 (29 cases), whereas the lowest was recorded in 2015 (one case). This incidence was relatively low relative to the national and regional incidence rates in the same period. Constantine had among the lowest average annual incidences among the seven provinces in eastern Algeria in 2023 (0.6–2.5), whereas Oum El Bouaghi, Sétif and Tébessa had among the highest (14.5–21.1) (Fig 2).

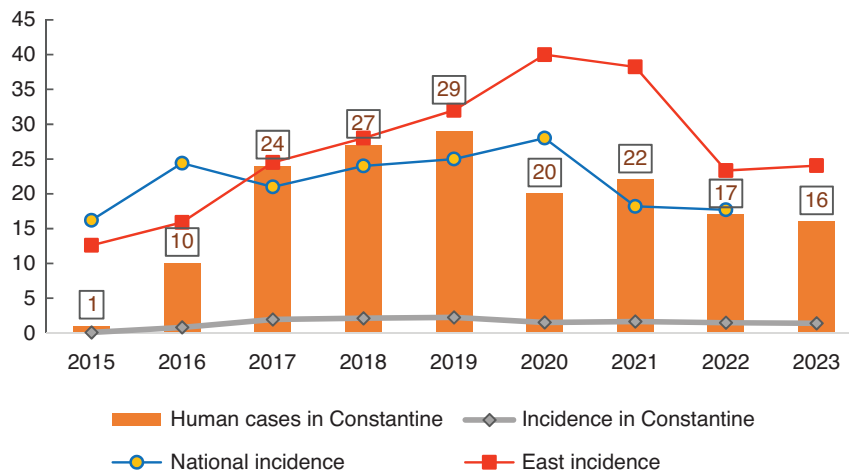


FIGURE 2 | Epidemiological trends in human brucellosis in the eastern region of Algeria from 2015 to 2023.

Epidemic/alert threshold

A comparison of the ETs for the past 3 years revealed that the number of cases exceeded the threshold twice: in March 2021 (four expected and five recorded cases) and in November 2022 (three expected and nine recorded cases). Therefore, brucellosis transitioned from enzootic to epizootic mode with the emergence of an outbreak (Fig 3).

Regional incidence

In 2023, the eight provinces of eastern Algeria were classified into four classes according to the range of human

incidence. Constantine was among the provinces with the lowest incidence (0.6–2.5/100000 inhabitants), whereas Tébessa and Oum el Bouaghi (21.1–117.4), followed by Sétif (14.5–21.1), were the provinces with the highest incidence (Fig 4).

Age and sex of patients with brucellosis

From 2015 to 2023, more cases were reported in males than females (62% vs 38%, $p < 0.03$; sex ratio: 1.63). The most affected age groups were 20–44 and 45–64 years (Fig 5).

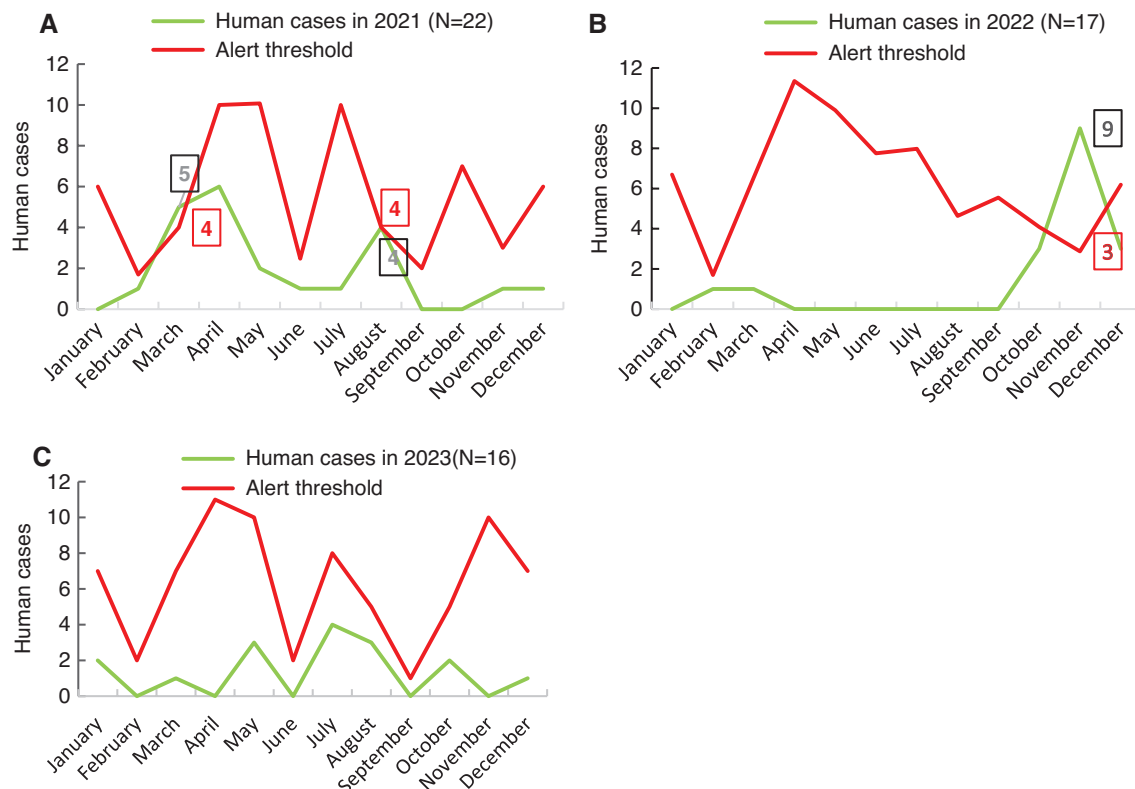


FIGURE 3 | Alert threshold for human brucellosis in Constantine in 2021 (A), 2022 (B) and 2023 (C).

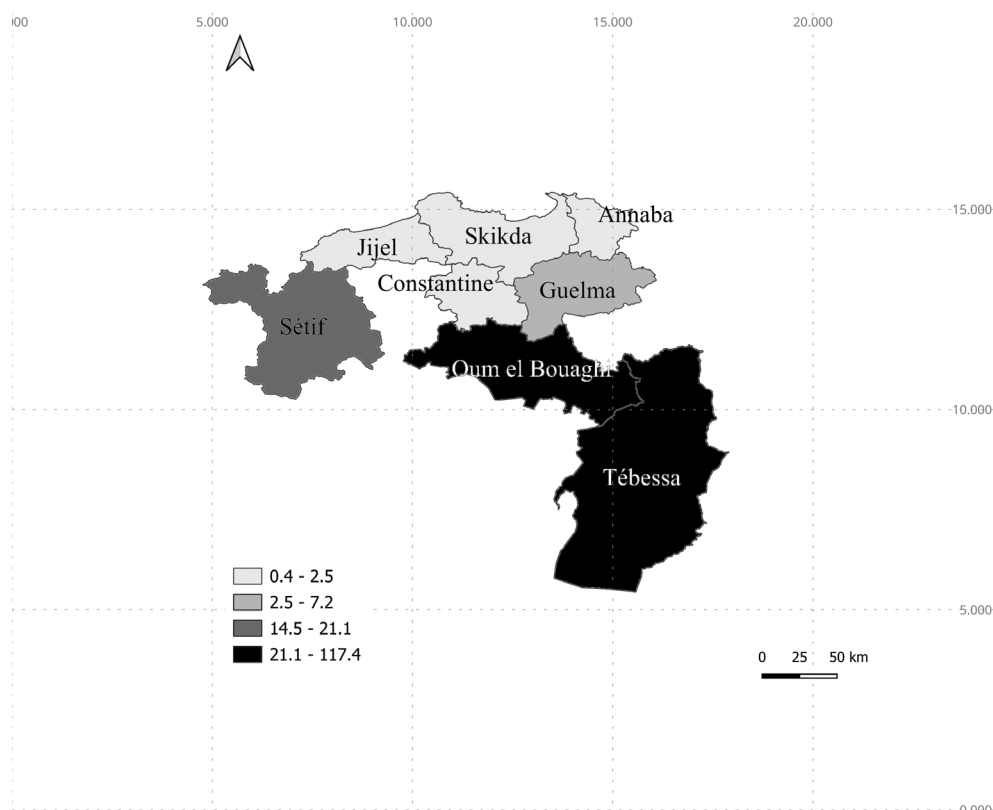


FIGURE 4 | Regional incidence of human brucellosis in eastern Algeria in 2023.

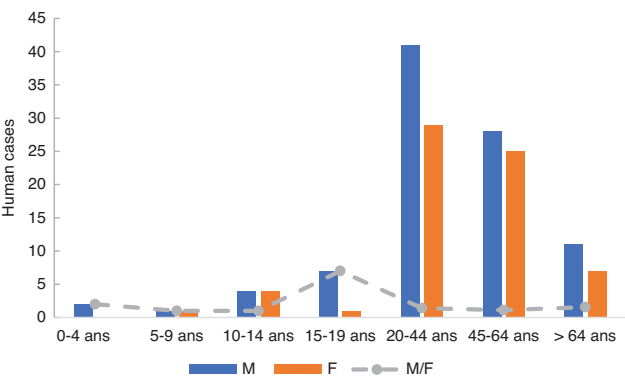


FIGURE 5 | Distribution of human brucellosis cases by sex and age in Constantine between 2015 and 2023.

Monthly trends

The incidence of human brucellosis tended to peak in April, May and November (Fig 6). No correlation was found between the number of reported human cases and the month of occurrence (Pearson correlation $r = -0.10$, $p = 0.9534$).

Characteristics of human brucellosis

Table 2 presents the only available data on the characteristics of patients with brucellosis in eastern Algeria between July and September 2019, and between July and December 2022 (total of 416 cases). The disease exhibited favourable

evolution in 44.47% of cases, and the consumption of raw milk appeared to be a contributing factor in 28.36% of cases.

Animal brucellosis in Constantine
Prevalence of animal brucellosis

A total of 59 cases of brucellosis in goats and 301 cases in cattle were reported between 2015 and August 2022. The mean prevalence in cattle was 1.32%. The total number of goat cases was recorded in only 2 years (58 cases in 2015), and a single case was reported in 2021, which corresponded to the year with the highest number of bovine brucellosis (128 cases) (Fig 7). No correlation was identified between human and cattle cases (Pearson correlation $r = 0.53$, $p = 0.878$). However, a negative correlation was observed between goats and humans ($r = -0.747$, $p = 0.33$).

Monthly trends

The number of bovine brucellosis cases fluctuated considerably between 2015 and 2022, and showed no correlation with the month of the year, although the highest value was reported in June 2021 (75 cases) (Fig 8).

Screening rate

A total of 20,546 cattle were screened for brucellosis, with an average coverage of 7.35% between 2015 and 2022 (Table 3).

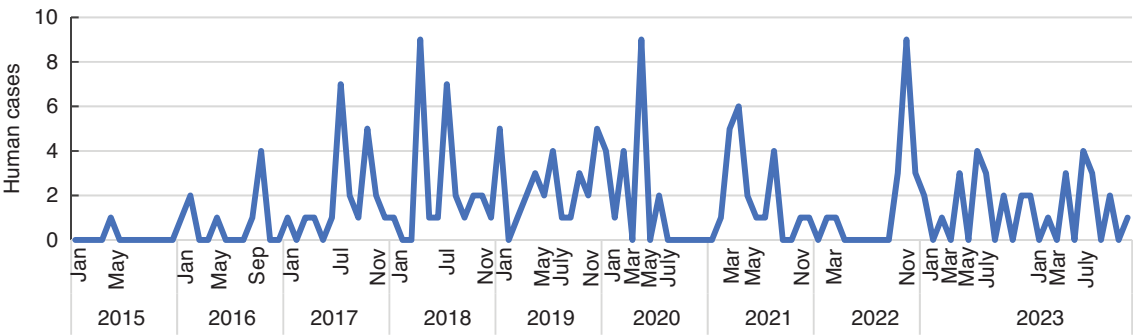


FIGURE 6 | Monthly trends in reported human cases between 2015 and 2023.

TABLE 2 | Characteristics of brucellosis cases recorded in the eastern region.

		July September 2019 (N = 285)		July December 2022 (N = 131)		Overall (N = 416)	
		Cases	%	Cases	%	Cases	%
Disease outcome	Favourable	138	48,4	47	35,8	185	44,47
	Recovery	92	32,3				
	Complication	2	0,7	0	0		0,48
	Death	0	0	0	0		0
	Unknown	53	18,6	84	64,1		32,93
Hospitalisation	Yes	64	22,5	28	21,3		22,11
	No	215	75,4	95	72,5		74,52
	NS	6	2,1	8	6,1		3,36
Probable source	Contact with animals	5	1,7	0	0		1,2
	Consumption of raw milk	44	15,4	74	56,4		28,36
	NS	236	83	57	43,5		70,43

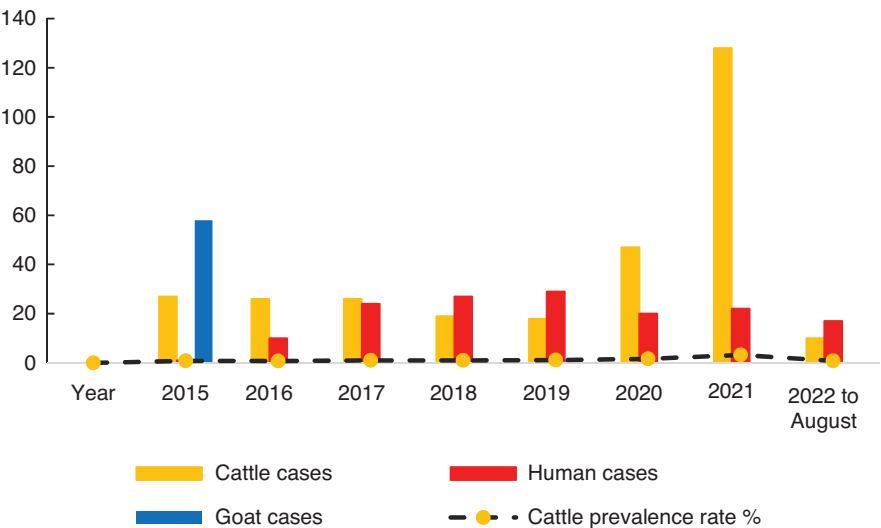


FIGURE 7 | Prevalence of animal brucellosis in Constantine between 2015 and August 2022.

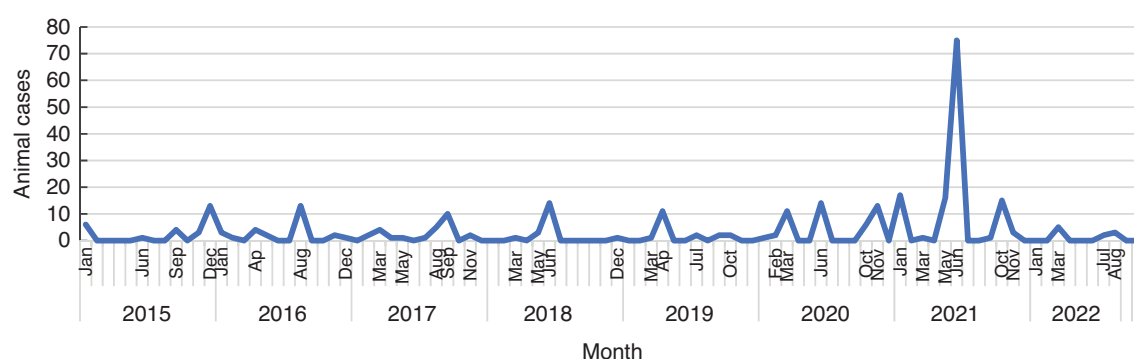


FIGURE 8 | Monthly trends in bovine brucellosis cases in Constantine between 2015 and August 2022.

TABLE 3 | Bovine brucellosis screening rates in Constantine between 2015 and 2022.

Year	Number of screened cattle	Number of screened farms	Number of positive cases	Screening rate %	IC 95 %
2015	3.237	186	27	7,29	7,05–7,53
2016	3.461	204	26	7,80	7,55–8,05
2017	2.488	180	26	5,80	5,58–6,02
2018	1.828	110	19	5,76	5,50–6,02
2019	1.537	89	18	4,56	4,34–4,78
2020	2.878	143	47	8,54	8,24–8,84
2021	3.942	183	128	11,70	11,36–12,04
2022 to August	1.175	60	10	3,50	3,30–3,70
Total	20.546	1.155	301	6,89	6,80–6,98

Distribution of human and animal brucellosis

All 12 localities in Constantine recorded cases of human brucellosis at markedly differing rates. The three localities recording the highest numbers of both human and animal cases were El Khroub (38 human cases/36 bovine cases), Ouled Rahmoune (27 human cases/3 bovine cases) and Constantine (26 human cases/124 bovine cases/59 goat cases) (Fig 9).

DISCUSSION

The aim of this study was to describe the epidemiological features of human and animal brucellosis in eastern Algeria, particularly in Constantine province.

Human brucellosis

At the national level, the annual incidence of human brucellosis varied countrywide between 2015 and 2023. On average, 21.81 cases per 100,000 people were recorded over 8 years. The highest incidence was recorded in 2020, and the lowest incidence was recorded in 2015. The incidence has shown an upward trend since 2006 but has decreased considerably since 2011, as previously described [18]. A comparison among countries worldwide revealed that Algeria is among the most endemic regions, alongside Syria, Turkey, Iraq, Saudi Arabia and Oman; however, the

status remains less severe in Algeria than in several Asian and African countries, such as Kenya, which had an incidence as high as 293.1 in 2019, and Yemen, which had an incidence of 157.59 in 2018 [10]. In the Maghreb countries, brucellosis persists as a major public health concern. National incidence rates in Tunisia varied from 2.9 to 3.9 per 100,000 inhabitants in 2008 and 2015 but remained elevated in certain regions, such as Gafsa (30.8/100,000) [33]. In Morocco, the estimated incidence was 3.3 per 100,000 inhabitants [34], and the range was 0.003 to 0.394 between 2002 and 2019 [35]. In Algeria, although molecular biotyping of *Brucella* spp. is not a routine diagnostic test, the available published research has identified *B. abortus* biovar 3 and *B. melitensis* biovar 2 strains, which cluster with those from African (Morocco and Zimbabwe) and European (France, Germany, Portugal and Italy) countries [20]. *B. melitensis* biovar 3 was also circulating in cattle (Lounes 2021). In humans and small ruminants, the dominance of *B. melitensis* biovar 3 was demonstrated, as in Morocco and Tunisia [22,34]. The clustering of strains from the Maghreb in two geographical lineages suggested the existence of an autochthonous Maghreb group and a lineage resulting from socio-historical links with Europe. This lineage diversity and connectivity between Mediterranean countries has been confirmed in other studies. For example, in Turkey, the isolates were highly

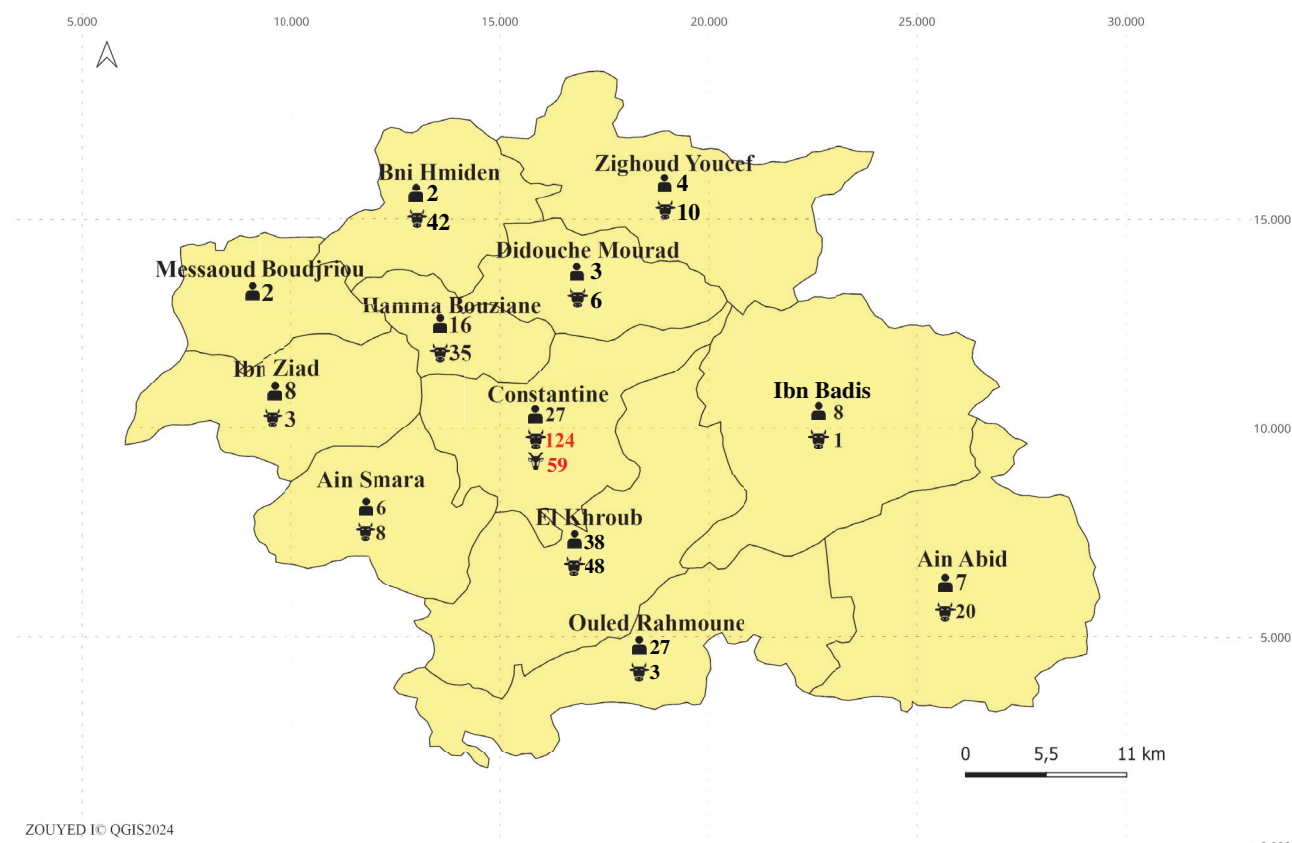


FIGURE 9 | Distribution of human and animal brucellosis cases in Constantine localities between 2015 and 2022.

similar to those from Greece and Portugal, thus demonstrating that the endemicity of *B. melitensis* in the region is due to socio-historical links among these countries [36].

Analysis of regional incidence indicated considerable variation among the eight eastern provinces, from the lowest incidence in Constantine, Jijel and Skikda, to the highest incidence in Tébessa, Oum El Bouaghi and Sétif; these province has a large cattle population of 151,446 heads, many slaughterhouses, livestock markets and milk production estimated at 281,865 litres in 2019. Tébessa and Oum El Bouaghi are the leading provinces for small ruminant production, and have large populations of sheep and goats [37]. Notably, Tébessa has long been classified as an endemic province with epidemic potential for brucellosis, and had a high incidence rate of 246.7 per 100,000 inhabitants in 2005 [22]. The agro-pastoral characteristics of this province are associated with its geographical location at the border with Tunisia, where illegal trade and uncontrolled movement of animals occur. The highest national incidence of brucellosis was observed in the steppe region, where high populations of small ruminants have contributed to the rise in cases [26]. For example, in 2021, when the incidence rate in Constantine was 1.65, four provinces in the steppe region had the highest rates in the country (M'Sila: 128.45; El Bayadh: 121.55; Laghouat: 110.63; and Djelfa: 91.57 [38]. In the west, the values for Constantine were similar to those for Oran.

Some regions, including Saida, Sidi Belabbas and Tiaret, reported relatively high incidences in 2022 (31.44, 23 and 28.06, respectively) [39]. Observations were similar in El Oued, southern Algeria, where a 21-year study found an average incidence rate of 12.26 cases per 100,000 inhabitants [40].

The low incidence of brucellosis in Constantine is due to the province's control measures prioritising brucellosis. In 2021, a decree (No. 1679 of 18/04/2021) established a local committee for the prevention and control of zoonoses. After a diagnosis is confirmed, the committee implements the necessary measures, which may include isolation, tagging and slaughter of positive animals, and compensation to their owners. The number of human cases of brucellosis is likely to be underestimated. Reported cases should be investigated to determine their origin. Similar findings have been reported in several studies in Algeria, such as in Tébessa, where the most affected age group was 15–44 years [22]. Similar findings have been reported in El Oued [40] and the eastern Algerian plateau. The highest incidence was observed in individuals 30–39 years of age [17]. The mean age of affected individuals in the Tunisian region of Gafsa was 39 years [33], and that in Morocco was 41.7 years [35]. In Italy, the age group most exposed to risk factors was 25–64 years [41]. Men were more affected than women in all these studies, because pastoral practices are typically

performed by men in Algeria and many other African countries [42]. The link between environmental risk factors and human brucellosis infection with monthly variations is well established [43]. Our study indicated that human brucellosis cases peaked in the spring and autumn, seasons associated with parturition and lactation, which peak in spring and decline in summer. People working with animals and consuming their milk have the highest risk [44]. The timing of epidemics might be associated with sheep shearing and the optimal climatic conditions for *Brucella* survival [45]. A similar seasonal pattern has been observed in Algeria, as described in prior studies [22,40], as well as in other countries, such as Italy [41], Tunisia [33] and Morocco [35]. In addition, between 2016 and 2023, the festival of Aid El-Adha, during which close contact occurs between humans and animals, coincided with the warmer months of the year (June to September). The number of human brucellosis cases peaked in 2019, but the ET was exceeded in 2021 and 2022. This finding indicated a transition from enzootic to epizootic status. Consequently, the Algerian authorities, on 22 November 2002, decreed brucellosis as a priority disease, and set up a committee for the prevention and control of zoonoses. A comparison of the monthly trends in human and bovine brucellosis in 2021 indicated that the bovine brucellosis peaks preceded those of human brucellosis by 2 months (January and March for bovine brucellosis, compared with March and August for human brucellosis); this difference in peaks was associated with the incubation period and delays in consultation and diagnosis after symptoms appear. In 2021 intensified global effects of the COVID-19 pandemic led to considerable increases in hospitalisation and medical investigations, and consequently the likelihood of identification of previously undiagnosed diseases, including brucellosis.

Animal brucellosis

We observed a brucellosis prevalence of 1.32% in cattle in Constantine, a rate comparable to the national average reported between 1995 and 2020 (1.26%) [12,22]. WAHIS reported a notable increase in animal brucellosis cases in the first half of 2021 (3,548), predominantly in cattle and goats. For bovine brucellosis, outbreaks decreased between 2018 and 2020, but subsequently increased, reaching 559 cases in 2022. In contrast, caprine brucellosis decreased, from 382 cases in 2019 to 187 in 2022 [46]. Bovine brucellosis was found in 18.6% of herds and 4.0% of individuals in the western region of Algeria. However, many variations were observed across the surveyed areas, ranging from 8.3% in Tiaret city to 24.1% in northern Tiaret. The average screening rate for cattle in Constantine (7.35%) was in line with the previously reported national average (4% or 6%) [25]. The highest screening rate, in 2021, revealed an expected increase in the number of cases.

The unexpected inverse correlation between goat and human cases is due to the lack of systematic screening

of reported goat cases. The peak in 2015 (58 cases) was circumstantial and was documented after the identification of human cases associated with goat's milk consumption in the region. This hypothesis is supported by the absence of reported goat cases between 2016 and 2021, when the goat population of Constantine increased (from 10,539 in 2016 to 12,196 in 2021). A Department of Veterinary Services report covering an 8-year period has indicated only five cases of caprine brucellosis detected in 114 animals tested in 2001, compared with a national goat prevalence estimate of 5.18 in 2001 and 4.36 in 2002 [29]. In Algeria, goats are considered an important reservoir of human brucellosis [22], as previously confirmed in the eastern Algerian plateau [17], the southeastern region [19] and the western region [15]. Importantly, the prevalence values for brucellosis in small ruminants underestimate the true prevalence in the population. Cases are underreported by veterinarians for several reasons, including fear of consequences (culling of cattle and inadequate compensation for the purchase of replacement animals), and the long interval between sampling and diagnosis [13,15]. Vaccination of small ruminants in Constantine is not regularly conducted or widespread. In 2015, 6,327 goats were vaccinated, and only 1,713 were vaccinated in 2016 [29]. The estimated vaccination coverage for small ruminants was only 19.79%, a very low percentage, given that vaccination coverage of animals must exceed 30% to decrease human brucellosis incidence. In Greece, for example, increased vaccination coverage from 18% in 1999 to 51% in 2022 decreased the prevalence of the disease by approximately 50% [47,48]. From 2006 to 2013, vaccination programmes covered 32 of Algeria's 48 districts and resulted in a moderate decline in brucellosis prevalence in small ruminants, to 3.33% in 2014 [26]. However, the number of regions covered and the vaccination rates decreased in subsequent years, partly because efforts focused on vaccination campaigns against other diseases. In 2019, the region of Constantine was declared a protection zone to prevent the introduction of the Peste des Petits Ruminants (PPR) virus, and 198,250 small ruminants were vaccinated [29].

Another challenge is the inadequacy of diagnostic methods, as evidenced by the inability of any of the serological tests used for the diagnosis of brucellosis alone to identify all positive cases [13,25]. A common error is the use of a confirmatory testing strategy, typically combining RBT for screening with a poorly sensitive confirmatory test, such as a complement fixation test, ELISA, cELISA or SAT [49]. We identified deficiencies in the epidemiological monitoring of brucellosis. Data on the characteristics of cases were unavailable until 2019 and 2022; these irregularities have previously been reported in Algeria [25]. Typically, after notification of a human outbreak, an investigation should be conducted among a patient's contacts to identify affected individuals and determine potential infection sources. The main source

of infection was identified as raw milk, thus reflecting the culinary traditions of the region. For example, raw milk is used in the preparation of couscous at wedding feasts in and around Sétif, and ‘bouhazza’, a traditional soft cheese, is also widely consumed in regions such as Oum El Bouaghi, Khenchela and Batna [50]. In Algeria, ingestion of raw milk and dairy products remains the primary mode of contamination, even among veterinarians [12]. Despite the authorities’ formal ban on the marketing of raw milk in Constantine, the informal practice of selling and distributing this product is a major challenge that must be addressed.

At the regional level, all 12 localities in Constantine were affected by brucellosis, with the exception of Messaoud Boudjeriou, which did not report any animal cases despite the observation of cases in humans. The southern region of the province initially reported the highest incidence (Constantine, El Khroub and Ouled Rahmone). The geographical distribution of cases is explained by the presence of a livestock market in El Khroub, which is one of the country’s largest and serves as a regional livestock trade hub. This market facilitates the movement of animals among these provinces, thereby enhancing the likelihood of transmission. Ouled Rahmone has the largest livestock population, which might contribute to the prevalence of the disease. The high incidence of human brucellosis in Constantine might be attributable to the town’s hospital, which serves eastern Algeria. The true prevalence in the region might be underestimated if patients do not report their place of residence or if information is not collected consistently. Our study confirmed that brucellosis is among the most important zoonotic diseases in Constantine, in line with evidence from western Algeria and at the national level.

Unfortunately, despite efforts to control brucellosis since the 1970s, Algeria remains an endemic country [10], because of factors such as uncontrolled animal movement, poor animal management and the existence of mixed herds, and deficiencies in the implementation of measures for permanent identification and control of animal movement. Further complications include a lack of cooperation between the public health and veterinary sectors, as well as a lack of information sharing between neighbouring countries [9,25].

The worldwide success of brucellosis eradication programmes, as evidenced in the United States, has demonstrated the critical role of effective surveillance and prevention strategies. In contrast, the eradication efforts in countries such as Egypt, Sudan, Ethiopia and Tanzania have encountered major challenges, primarily because of a lack of collaboration among policymakers, health officials, the veterinary sector and farmers [51].

To achieve complete eradication of brucellosis, as successfully accomplished in other countries, a comprehensive awareness campaign must be implemented among relevant stakeholders, including public health and veterinary services. Ensuring that diagnostic, epidemiological

and prophylactic tools are used correctly is also crucial. A strategy might be based on individual animal identification, rigorous control of animal movement, and the allocation of a substantial budget for the logistics and compensation associated with the slaughter of infected animals [14,52]. In the context of Algeria, the current prophylaxis programme, which relies on the screening and slaughter of cattle and the vaccination of small ruminants, must be enhanced through the implementation of several key measures, such as the identification and screening of all national livestock, as well as the prompt declaration of any positive cases in humans. Early diagnosis and effective diagnostic methods, particularly molecular laboratory techniques for identifying circulating strains among humans and animals, will be crucial. To improve the effectiveness of the programme, the screening-slaughter control programme should be strengthened to include more animals and increase compensation rates for farmers. Farmers must adhere to obligatory prophylaxis programmes to ensure the success of the initiative. In addition, field surveys will be crucial for identifying the specific strains and detecting the lineages between isolates in Algeria and other neighbouring countries, thereby enabling the tracing of infection sources, and ensuring the selection and implementation of appropriate vaccines for herds at the national level. Awareness campaigns for the public and crucially for livestock farmers are necessary to explain the dangers of certain everyday practices, particularly the consumption of raw milk and its by-products, because this zoonosis will persist as long as the animal reservoir is not controlled. The management and prevention of human brucellosis are inextricably associated with the management and prevention of animal brucellosis [9,25,49].

CONCLUSION AND RECOMMENDATIONS

Despite eradication efforts, brucellosis remains endemic in Algeria. Management of the disease in Constantine has several shortcomings: the screening programme only covers cattle and has a low and irregular screening rate. Vaccination of small ruminants with Rev1 has not been pursued, goats are not screened, and case detection depends on alerts following the identification of human cases and therefore does not reflect the true status. Data on sheep are also unknown.

The effectiveness of the screening and slaughter control programme used by the Algerian authorities could be improved by making it compulsory, increasing the number of animals and species covered, identifying and tagging these animals, and controlling their movements. An increase in the compensation rates for farmers is also essential. Vaccination should cover a larger number of small ruminants. Surveys are essential to identify the specific strain using molecular tools to select appropriate vaccines for herds at the national level. Awareness campaigns are needed to educate the public about the dangers of consuming raw milk and its

by-products, and the early warning system must be effective. Intersectoral collaboration within a One Health approach will be essential to control this zoonosis, which will persist until the animal reservoir is controlled. Further studies in other geographical parts of Algeria and in other mammals will be necessary to obtain a complete epidemiological overview of brucellosis in Algeria.

Data on cases of caprine brucellosis are biased and therefore do not accurately reflect the true status. Farmers are not obliged to participate in prophylaxis programmes. As a result, screening rates refer only to registered farms and lead to an underestimation of the true prevalence. In addition, there is a lack of available data on the status of sheep. Unfortunately, our study was limited by the paucity of data on small ruminants, particularly goats, which prevents a full understanding of the epidemiology of the disease. Further studies are needed to fill these knowledge gaps and provide a more complete epidemiological picture of brucellosis in Algeria.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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