Chancroid – a rare sexually transmitted infection in the EU/EEA. Attention still needed when treating certain vulnerable groups

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Summary

Chancroid infrequently causes genital ulcer cases in European countries. Globally, endemic regions of Africa, Asia and America report most cases. Since 2015, migration flows from Asian and African countries to the European Union/European Economic Area (EU/EEA) have risen sharply. We therefore aimed to explore current chancroid epidemiology and define the possible impact of recent migration on chancroid prevalence in the EU/EEA.
We performed a PubMed and Embase systematic literature search without language restrictions to identify studies published after 2000 reporting chancroid prevalence in the EU/EEA and in the top-ten countries of origin of migrants arriving to the EU/EEA in 2015 to March 2016.
In total, seventeen studies were retrieved. In the EU/EEA, chancroid prevalence ranged between 0.0% in the Czech Republic (1994-2003) to 3% in France (1995-2005) among patients with genital ulcers. Sporadic cases of local transmission were reported from several countries.
In the countries of origin of recently arrived migrants, chancroid prevalence varied depending on population subgroup and country, ranging between 1% (2000) among STI clinic attendees in Nigeria to 56% among patients with genital ulcers in Senegal (1992).
While chancroid is rare in the EU/EEA, it should be considered by European healthcare providers, especially in patients with persisting genital ulcers who had previous sexual contacts in endemic areas.

Key words:
Haemophilus ducreyi. Chancroid. Sexually transmitted infection. Europe. Migrants. Refugees.

El cancroide – una infección de transmisión sexual rara en EU/EEA. Todavía necesita atención cuando se tratan ciertos grupos vulnerables

Resumen

El chancroide es una causa infrecuente de ulcera genital en los países europeos. Globalmente, regiones endémicas de África, Asia y América, reportan más casos. Desde el 2015, flujos migratorios desde países de Asia y África hacia países de la Unión Europea/ Área Económica Europea (EU/EEA) han aumentado bruscamente. Por ello, nos propusimos explorar la epidemiologia actual del chancroide y definir el posible impacto de la inmigración reciente sobre la prevalencia del chancroide en la UE/EEA. Para identificar estudios publicados después del año 2000, realizamos búsquedas bibliográficas sistemáticas en PubMed y Embase sin restricciones de idioma que reportaran prevalencias de chancroide en la EU/EEA en los diez principales países con mayor inmigración llegada a la EU/EEA desde 2015 hasta marzo de 2016. En total, se recuperaron diecisiete estudios. En la EU/EEA, entre los pacientes con úlceras genitales, la prevalencia del chancro blando varió entre el 0,0% en la República Checa (1994-2003) y el 3% en Francia (1995-2005). Se informaron casos esporádicos de transmisión local en varios países. En los países de origen de los inmigrantes recién llegados, la prevalencia de chancroide varió según el subgrupo y el país, oscilando entre el 1% (2000) entre las infecciones de transmisión sexual atendidas en Nigeria hasta el 56% entre los pacientes con úlceras genitales en Senegal (1992). Si bien el chancro blando es raro en la EU/EEA, debe ser considerado por los proveedores de atención médica europeos, especialmente en pacientes con úlceras genitales persistentes que tuvieron contactos sexuales previos en áreas endémicas.

Palabras clave:
Haemophilus ducreyi. Chancroide. Infecciones de transmisión sexual. Europa. Emigrantes. Inmigrantes. Refugiados.

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Introduction

Chancroid is a sexually transmitted infection (STI) caused by *Haemophilus ducreyi*, characterised by painful ano-genital ulcer(s)[1]. Diagnosis relies on the identification of *H. ducreyi* in ulcer exudates through laboratory cultures or nucleic acid amplification tests (NAAT) such as polymerase chain reaction (PCR)[2]. Appropriate antibiotic regimens can successfully cure the infection[3,4]. Asymptomatic carriage of *H. ducreyi* among female sex-workers showing no signs of genital ulcer while PCR-positive in cervical swabs has been described with unclear contribution to further sexual transmission[5].

While the global prevalence has declined significantly[6], chancroid continues to be a cause of genital ulcer disease in resource-poor countries in Africa, Asia, Latin America and the Caribbean[2,7-9]. Behavioural changes, improved access to and better quality of sexual health services, and the adoption of syndromic management of STIs have contributed to the decline in chancroid reports[7,10]. Chancroid has been documented as a risk factor for HIV-transmission in studies from sub-Saharan African settings[4].

Chancroid is infrequent in the European Union*/European Economic Area** (EU/EEA), with sporadic, mostly travel-associated cases reported in recent years[8]. Underreporting cannot however be excluded as in many EU/EEA countries chancroid is not mandatorily notifiable, or the reporting has been discontinued[11]. Chancroid is not included among the sexually transmitted infections reported to The European Surveillance System (TESSy)[12].

In recent years, the European Union (EU) has seen a growing number of asylum seekers and refugees from countries in Africa and Asia, most of them reaching Europe after crossing the Mediterranean Sea. More than 1 million arrivals to the EU were reported in 2015 and more than 170 000 in the first quarter of 2016 - a significant increase compared to 21,000 arrivals in the respective quarter of 2015[13,14]. The majority of refugees originated from the Syrian Arab Republic, Afghanistan and Iraq (the three countries summing up to 80%), followed by Pakistan, Iran, Nigeria, Gambia, Senegal, Guinea and Mali (each country contributing with 1-3% of the arrivals).

This makes it increasingly important to understand the health determinants and the health needs of refugees and asylum seekers after their arrival in Europe, as these may vary quite significantly as compared to the general EU population[15-18]. In terms of sexual health, they are less likely to access sexual health services and are at higher risk to acquire STIs[15]. Data reported through TESSy on key infectious diseases among the foreign-born population in the EU/EEA has shown that individuals born abroad show a disproportionate risk of being affected by STIs such as HIV and hepatitis B. Conversely, only 11% of gonorrhoea and 7.3% of syphilis cases notified to TESSy in 2010 were reported among foreign-born cases[19].

In order to improve our understanding of chancroid epidemiology in the EU/EEA and in the light of the scarcity of surveillance data, we performed a literature review with an initial focus on the EU/EEA countries. Secondly, we aimed to describe the burden of the infection in the countries of origin of asylum seekers and refugees entering the EU/EEA, in order to identify any needs for clinical awareness and sexual health care provision among these individuals.

Methodology

A literature review for original research articles regarding chancroid epidemiology was conducted in PubMed® and Embase® (Embase.com platform) on January 19, 2016. Search strategies combined chancroid with epidemiology and case reports concepts. Controlled vocabulary available in the bibliographic databases (i.e. medical subject heading (MeSH) and Emtree terms) and natural vocabulary were used to represent the concepts in the search strategies. The results were limited to the records published from 2000 onwards; no language or country of report limits were applied. For full search strategies, see Table 1a and 1b. The electronic search was complemented by a manual search for additional studies through the reference lists of selected publications.

The publications regarding chancroid epidemiology in the EU/EEA retrieved through searches were independently screened and assessed for relevance in April 2016 by two reviewers against previously established inclusion and exclusion criteria. For inclusion, all articles published after 2000 from any EU/EEA country reporting outcomes such as chancroid prevalence estimates and positivity rates in any given population were considered. Individual case-reports were not considered within the main body of evidence, but were reviewed and listed as an addition to the main findings in order to highlight evidence of transmission in countries from which prevalence studies could not be retrieved.

Relevant publications regarding chancroid epidemiology in countries from where the most recent influx of refugees to the EU are originating were screened and reviewed in the same manner also

*https://europa.eu/european-union/about-eu/countries_en
**http://www.europarl.europa.eu/atyourservice/en/displayFtu.html?ftuId=FTU_6.5.3.html

Table 1a. Search strategy, PubMed.

Search	Query PubMed (19/01/2016)	Items found
#39	Search #36 OR #37 Filters: Publication date from 2000/01/01	213
#38	Search #36 OR #37	733
#37	Search "Chancroid/epidemiology"[Mesh] OR "*Haemophilus ducreyi*/epidemiology"[Mesh]	156
#36	Search #32 AND #35	731
#35	Search #33 OR #34	8199695
#34	Search "Case Reports" [Publication Type] OR case*[tw]	3874219
#33	Search "Epidemiological Monitoring"[Mesh] OR "Epidemiology"[Mesh] OR "Morbidity"[Mesh] OR epidemiolog*[tw] OR morbidity*[tw] OR prevalen*[tw] OR inciden*[tw] OR proportion*[tw] OR occurren*[tw] OR frequent*[tw] OR frequenc*[tw] OR rate[tw] OR rates[tw]	5388164
#32	Search "Chancroid"[Mesh] OR Chancroid*[tw] OR "ulcus molle"[tw] OR "soft chancre"[tw] OR *"Haemophilus ducreyi"*[Mesh] OR *"Haemophilus ducreyi"*[tw] OR *"Hemophilus ducreyi"*[tw] OR *"Coccobacillus ducreyi"*[tw] OR *"ducrey s bacillus"*[tw] OR " *ducrey s bacillus*"[tw] OR *"bacillus ulceris cancrosi"*[tw]	1529

Table 1b. Search strategy, Embase.

Search	Query Embase (19/01/2016)	Items found
#8	#5 OR #6 AND [2000-2016]/py	407
#7	#5 OR #6	987
#6	'ulcus molle'/exp/dm_ep	232
#5	#1 AND #4	917
#4	#2 OR #3	9425717
#3	'case report'/exp OR 'case study'/exp OR case*:ab,ti	4607070
#2	'epidemiological monitoring'/exp OR 'epidemiology'/de OR 'morbidity'/de OR 'incidence'/exp OR 'prevalence'/exp OR epidemiolog*:ab,ti OR morbidity*:ab,ti OR prevalen*:ab,ti OR inciden*:ab,ti OR proportion*:ab,ti OR occurren*:ab,ti OR frequent*:ab,ti OR frequenc*:ab,ti OR rate:ab,ti OR rates:ab,ti	6085880
#1	*'ulcus molle'*/exp OR chancroid*:ab,ti OR *'ulcus molle'*:ab,ti OR 'soft chancre':ab,ti OR *'haemophilus ducreyi'*/exp OR *'haemophilus ducreyi'*:ab,ti OR *'hemophilus ducreyi'*:ab,ti OR *'coccobacillus ducreyi'*:ab,ti OR *'ducrey s bacillus'*:ab,ti OR *'ducreys bacillus'*:ab,ti OR *'bacillus ulceris cancrosi'*:ab,ti	2036

in April 2016. All peer-reviewed publications reporting prevalence estimates and positivity rates published after 2000 were included.

The following countries which accounted for 95% of the recent migrants in 2015 and first quarter of 2016 were considered: Syrian Arab Republic, Afghanistan, Iraq, Pakistan, Iran, Nigeria, Gambia, Senegal, Guinea and Mali. Migration data were based on statistics as of the end of March 2016 from the Refugees/Migrants Emergency Response in the Mediterranean by the United Nations High Commissioner for Refugees (UNHCR)***.

Selected publications were evaluated concurrently by both reviewers for inclusion, discordances were solved through discussion. In total, 498 peer-reviewed references were returned from two databases, of which 199 were duplicates. Following their removal, 172 publications were excluded as they did not meet the inclusion criteria of study type, while 127 publications were assessed for eligibility. Of these, 110 publications were excluded based on the country of origin of the study, while 17 publications (8 from the EU/EEA and 9 from the top ten countries of origin or recently arrived migrants) fulfilled all the inclusion criteria and were included in the final review (Figure 1). Publications were grouped dependent on country of origin, following which data extraction and quality assessment was performed.

***https://data2.unhcr.org/en/situations/mediterranean

Figure 1. PRISMA Flow diagram showing the search strategy and number of studies included in the review.

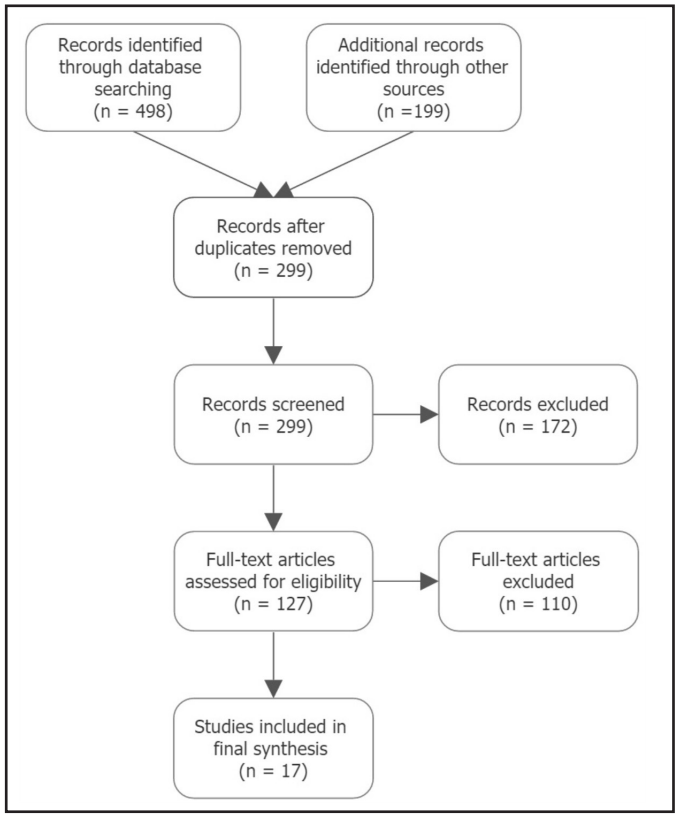

Table 2. Criteria used to assess representativeness and informative quality of studies included in the analysis.

Criteria		Score
Data are recent	Does the study report data collected after 2000? - all data after 2000 - data spanning before and after 2000 - all data before 2000	 2 1 0
Accuracy of the diagnosis	Which was the method used for the diagnosis? - NAAT (PCR) - culture/Gram-stain - Not reported/other	 2 1 0
Representativeness for the general population or for a specific sub-population group	Was the study population clearly defined? General population vs STI clinic attendees vs genital ulcer disease (GUD) patients Randomise sampling vs convenience sampling	1 or 0 3 or 2 or 1 1 or 0
Geographical coverage of the study (comprehensiveness of data)	National surveillance reports vs regional vs healthcare facility	3 or 2 or 1

Grading thresholds: poor 0-4, moderate 5-8, good 9-12.

The articles were assessed for the potential risk of bias using an appraisal checklist examining recency of data, accuracy of diagnosis, representativeness of the general population and comprehensiveness of data in terms of geographical coverage (Table 2). The quality was defined as "good" if the total score was between 12 and 9, "moderate" if between 8 and 5, and "poor" if between 4 and 0. As a result, studies reporting data after 2000, which had used PCR for laboratory diagnosis, had the study population clearly defined, were based on sampling from the general population through randomised sampling and were reporting nationally representative data would potentially achieve a higher score, compared to studies reporting data before 2000, which had used non-specified laboratory methods and reported cases on chancroid among conveniently selected patient groups in single clinical settings, which would be low-graded. Case-reports were not assessed.

Results

Chancroid epidemiology in the EU/EEA

Eight studies from six European countries meeting the inclusion criteria were selected (Table 3a). Most studies reported data collected from patients attending STI clinics with either sexually transmitted infections or genital ulcer disease (GUD). Several studies, although published from 2000 onwards, reported data collected in the 1990's.

Low rates of chancroid infections were reported by all authors, with proportions ranging from 0% to 0.5% among patients attending STI clinics, and from 0% to 3% among those attending STI clinics diagnosed with genital ulcers. Reported data suggested a decreasing trend over time. These studies were assessed as of moderate quality, mainly due to old data (some data stemming from before the year 2000) and limited coverage (sub-population groups from singular or selected settings).

In England, the United Kingdom (UK), 79, 146 and 83 cases were reported to the Health Protection Agency in 2009, 2010 and 2011, respectively. However, only a small proportion of these cases were confirmed and several others were assessed as reporting errors (i.e. misclassifications)[4]. In contrast, a more recent study showed no positive *H. ducreyi* samples among 636 patients presenting with genital ulcer disease in two London clinics during January 2010 to January 2014[20]. This is more in line with findings from a Health Protection Agency study that used a multiplex PCR assay in a referral service for genital ulcer disease and found no cases of *H. ducreyi* among the 100 genital ulcer disease patients registered in the patient database between 2010 and 2013[21].

In France, chancroid prevalence was 3% (8/278) among patients with genital or anal ulcerations lasting for less than 6 weeks, who attended an STI clinic in Paris during January 1995 and December 2005. Seven cases were of African origin and two presented with co-infections of genital herpes and primary syphilis respectively. The authors also highlighted the similar clinical characteristics among the cases of chancroid, syphilis and herpes[22].

In Italy, data collected through the National STI Surveillance System on all cases of STIs during January 1991 and December 1999 revealed a prevalence of 0.01 to 0.08% (2/23,748 - 26/31,202) among the Italian citizens. Comparisons with individuals born outside of Italy and who did not possess Italian citizenship showed a higher prevalence within these groups, ranging between 0.1% (3/2,503) for non-Italian women, to 0.5% (21/4,344) for non-Italian men. Of the total of 61,798 individuals newly diagnosed with STI during the reporting period, 11.2% (6847) were non-Italians, the majority of those originating from Africa[23].

In a study from Greece, chancroid frequency among patients with laboratory confirmed STIs, registered in a hospital outpatient database in Athens during 1990-1996, was 0.5% (32/5831). Majority of chancroid cases had a foreign background, with North Africa and Asia being the most common geographic origins[24].

In the Netherlands, 0.9% (3/346) of the patients with genital ulcer disease attending an outpatient clinic during February and November 1996, tested positive for *H. ducreyi*[25].

In the Czech Republic where chancroid is a mandatory notifiable disease, no cases of *H. ducreyi* were reported at national level between 1994 and 2003[26].

Table 3a. Chancroid epidemiology in EU/EEA countries – prevalence studies.

Country	Year of study	Positive population	Subgroup	Diagnostic method	Study type	Reference	Quality grade (max: 12)
Czech Republic	1994-2003	0/NA (0.0%)	VDP	PCR	Surveillance study	Zakoucka *et al.* 2004	Moderate (score 8.3)
France	1995-2005	8/278 (3%)	GUD	Gram-stains/ Culture	Cross-sectional	Hope-Rapp *et al.* 2010	Moderate (score 6)
Greece	1990-1996	32/5831 (0.5%)	STI	Gram-stains/ Culture	Cross-sectional	Kyriakis *et al.* 2003	Moderate (score 5.5)
Italy	1991-1999	21/4344 (0.5%)	STI (non-Italian males)	NR	Surveillance study	Giuliani *et al.* 2004	Moderate (score 6)
		26/31202 (0.1%)	STI (Italian males)				
		3/2503 (0.1%)	STI (non-Italian females)				
		0/23748 (0.0%)	STI (Italian females)				
Netherlands	1996	3/346 (0.9%)	GUD	PCR	Cross-sectional	Bruisten *et al.* 2001	Moderate (score 5.5)
United Kingdom	2009-2011	79/NA,146/NA 83/NA	NR	NR	National surveillance report	O'Farrell & Lazaro 2014	Moderate (score 5.5)
	2010-2014	0/636 (0.0%)	GUD	PCR	Retrosp. review	Dufaur *et al.* 2015	Moderate (score 7)
	2010-2013	0/100 (0.0%)	GUD	PCR	Retrosp. review	Rayment *et al.* 2013	Moderate (score 7)

NA: Denominator not available.
VDP: Venereal disease patients (syphilis, gonorrhoea, chancroid and *lymphogranuloma venereum*).
GUD: Patients presenting with genital ulcer disease.
STI: Patients presenting with STD/STI.
NR: Information not reported.

Table 3b. Chancroid epidemiology in the EU/EEA - case reports.

Country	Year	No. of patients	Travel history	High-risk group contact	Diagnostic method	Reference
Belgium	2009	1	Yes (to Maghreb)	Unknown	Gram-stain	Henry *et al*. 2009
Croatia	2000	1	Yes (to Guinea)	Yes*		Marasovic *et al*. 2000
Denmark	2010	2	Yes (to Pakistan), No	Yes* No	PCR	Knudsen *et al.* 2010
	2007	1	Yes	Unknown	PCR	Holst *et al.* 2007
France	2015	1	Yes (to Madagascar)	Unknown	PCR	Fouéré *et al.* 2015
Portugal	2012	1	No	Unknown	PCR	Canhoto *et al.* 2012
United Kingdom	2014	1	No	No	PCR	Barnes *et al.* 2014

*contact with CSW in the country of travelling

Case reports describing individual chancroid cases have been published from Belgium (2009), Croatia (2000), Denmark (2007, 2010), France (2015), Portugal (2012) and the UK (2014), with most cases being travel-associated (Table 3b)[27-34]. Some reports, however, show evidence of locally-acquired infections. For example, in a case report from the UK, a male from the North East of England tested positive for chancroid following several repeated examinations where he was provisionally diagnosed with the *Herpes simplex virus* (HSV) despite negative PCR results. The man reported no recent contact with any non-UK individuals as well as no contact with commercial sex workers[32]. A similar case was reported from Portugal in a patient with no recent travel history, where the diagnosis was made upon readmission of the patient following two weeks with persisting symptoms, as the test was

Table 4. Chancroid epidemiology in the top-ten countries of origin of recently arrived migrants* to EU/EEA.

Country	Year	Positive population	Subgroup	Method of diagnosis	Study type	Arrivals 2016 (%)**	References	Quality grade (max: 12)
Pakistan	2006-2009	20/1532 (1.3%)	STI	Culture, IF, COAG	Cross-sectional	3%	Maan *et al.* 2011	Moderate (score 8)
	2000-2009	40/4288 (0.93%)	STI (males)	GS/Culture	Cross-sectional		Bhutto *et al*. 2011	Moderate (score 7.5)
	2004	1/500 (0.45%)	FGTI	GS	Cross-sectional		Sami & Baloch 2005	Moderate (score 7.5)
	2010-2014	25/512 (4.9%)	STI	Unknown	Cross-sectional		Razvi *et al.* 2014	Moderate (score 6.5)
	1999	80/465 (17.2%)	STI	Unknown	Cross-sectional		Rehan 2003	Moderate (score 5)
Nigeria	NR	NR/300 (21.1%)	HIV+	Unknown	Retrospective review	1%	Awolade *et al*. 2012	Poor (score 4)
	2002-2003	9/64 (14.1%)	HIV+ CSW	Unknown	Retrospective review		Fayemiwo *et al.* 2011	Moderate (score 8)
		14/250 (5.6%)	CSW	Culture	Cross-sectional			
	2000	3/286 (1%)	STI	Unknown	Retrospective review		Fatiregun & Afolabi Bamgboye 2004	Moderate (score 6.5)
Senegal	1992	22/39 (56%)	GUD	PCR	Cross-sectional	1%	Totten *et al.* 2000	Moderate (score 5)

Note: no studies were identified from Syria, Afghanistan, Iraq, Iran, Gambia, Guinea or Mali.
*Data on Mediterranean Sea arrivals retrieved from UNHCR http://data.unhcr.org/mediterranean/regional.php
** Percentage of total Mediterranean Sea arrivals from the top-ten countries of migration during January to March 2016
GUD: Patients with genital ulcer diseases; HIV+: Individuals with a HIV positive diagnosis; CSW : Commercial sex workers; STI: Patients presenting with STD/STI diagnoses; FGTI: Female patients presenting with genital tract infections; GS: Gram stain; IF, COAG: Direct immunofluorescence, coaglutination; NR: Not reported

not included as a part of the initial screening[31]. In addition, one of the patients described in a report from Denmark appears to have contracted the infection within the country[28,30]. These case-reports document the possibility of chancroid to occur within a country through sporadic introduction and the potential of local circulation to go unnoticed due to lack of awareness and mandatory disease notification.

Chancroid epidemiology in the ten countries with highest number of migrant arrivals to the EU/EEA

Epidemiological data on chancroid from the three countries of origin of the majority (80%) of refugees entering the EU/EEA by the Mediterranean Sea (i.e. Syrian Arab Republic, Afghanistan and Iraq) are largely unavailable and no studies were retrieved. We identified, however, nine studies conducted in Pakistan, Nigeria and Senegal (Table 4), countries that contributed with relatively low percentages to the migrant influx (3%, 1% and 1% respectively). Our quality assessment indicated a moderate risk of bias for all studies except one study from Nigeria that was of poor quality due to both the year of data collection and the diagnostic method not being reported.

In Pakistan, the identified chancroid prevalence estimates are widely divergent, possibly dependent on the sub-population group studied and the years when the studies were conducted. While a study of 1532 patients attending STI clinics in Faisalabad from July 2006 to September 2009 revealed a chancroid prevalence of 1.3% (20/1,532)[35], a prevalence of 0.93% (40/4,288) was described among male STI patients presenting to a male-only STI clinic in the Sindh province during January 2000 to December 2009. Noteworthy is that 92% of the males reported having extramarital sexual contacts, of which the majority involved female sex workers[36]. A study involving 221 symptomatic women presenting to a gynaecology clinic in Quetta with lower genital tract infections during 1 April to 31 October 2004, reported only one case of chancroid (0.45%)[37], while a more recent study with data reported from a hospital in Abbottabad found a prevalence as high as 4.9% (25/512) among patients of both genders attending with an STI during a five-year period (2010-2014)[38]. In sharp contrast to these findings, a study conducted during June 1999

to September 1999, involving data collected from 465 male STI patients from hospitals and clinics throughout Lahore, Karachi, Peshawar and Quetta, reported a prevalence of 17.2% (80/465) with a similar distribution over the four areas[39].

In contrast with the figures from Pakistan, prevalence estimates reported from Nigeria appear to be relatively high. Important to note, however, is that the majority of the studies are focused on specific high-risk subgroups. For example, a seven-year retrospective study conducted in 2012, involving 300 HIV-positive women attending STI clinics in two Nigerian hospitals, revealed a chancroid prevalence of 21.1%[40]. Another study conducted during November 2002 to July 2003 in Ibadan, involving a high risk group of 250 commercial female sex workers, showed a prevalence of 14.1% (9/64) among HIV-positive individuals and 5.6% (14/250) among HIV-seronegative individuals. The lower prevalence among seronegative individuals may partially be explained by the fact that chancroid, as a genital ulcer disease, is a risk-factor for HIV, as supported by a significant association between HIV-positivity, syphilis and chancroid[41]. Another study on patients retrospectively examined after presenting to a sexually transmitted diseases clinic in Ibadan during 1 January to 31 December 2000, showed a significantly lower prevalence of merely 1% (3/286), with all of the cases recorded among males[42].

In Senegal, 56% (22/39) of the samples collected from genital ulcer disease patients attending the STD clinic at the Public Health Institute in Dakar during May to September 1992, were PCR positive for *H. ducreyi* as compared to rates of 15% and 13% for cases with syphilis and herpes, respectively, leading the authors to conclude that chancroid appeared to be the most common cause of genital ulcers in Dakar[43].

Discussion

Our review retrieved a small number of epidemiological studies on chancroid in the EU/EEA. The reported prevalence of chancroid ranged from 0.0% to 0.5% among STI clinics attendees and from 0.9 to 3% among patients presenting with genital ulcer between 1990 and 2011 in the six countries from which literature was available. In studies from the UK covering the period 2010 to 2014, no cases of chancroid were reported among patients with genital ulcers.

These findings are consistent with the global decline in the prevalence of chancroid. The few cases that occurred in the EU/EEA in recent years were sporadic and majority also travel-associated. However, considering the lack of mandatory notification of chancroid in many European countries and the possibility of some cases to go unnoticed or misdiagnosed, an under-ascertainment cannot be excluded[11,29,31,44-46]. As exemplified by Barnes *et al.* (2014) HSV infection was presumptively assumed in a sporadic chancroid case[32]. The presence of mixed chancres may further complicate the clinical picture and mislead the diagnosis[22,31,34]. The potential for atypical clinical presentation of chancroid combined with the reported occurrence of locally-acquired cases[30-32], emphasize the need for improved awareness amongst clinicians when faced with patients presenting painful genital ulcers. Particular vigilance should be placed on the correct diagnosis of individuals with a travel history to countries where the disease is endemic.

One study from Greece and one from Italy, both reporting 1990 to 1999 data, indicated some sub-population groups like commercial sex workers and migrants originating from endemic settings as disproportionately affected by chancroid[24]. In the study by Kyriakis *et al.* (2003) the majority of chancroid positive diagnoses were among foreign-borne STI patients. Similarly, Giuliani *et al.* (2004) found higher rates among individuals of foreign origin, mostly migrants from African countries. Implementation of targeted prevention strategies and addressing sexual health needs of non-native populations were recommended by the authors.

The European guideline for the management of chancroid (IUSTI [The International Union against Sexually Transmitted Infections] Europe)[47] recommends nucleic acid amplification techniques (NAAT) for *H. ducreyi* as the preferred diagnostic method, although due to very low frequency of the disease, it is likely that only a limited number of laboratories would be able to provide these NAATs[8,48]. It was difficult to estimate the diagnostic capacity within the EU based on the few studies retrieved, however culture and/or Gram-stain microscopy were used in the Czech Republic (1994-2003), France (1995-2005) and Greece (1990-1996), and PCR in the Netherlands (1996) and the UK (2010-2014).

This review did not identify compelling evidence to suggest that chancroid is a priority in the context of public health needs of migrant populations. This conclusion is however limited by the lack of studies on chancroid from the three countries of origin of the majority of refugees entering the EU/EEA. Only three of the countries in the top-ten but contributing with much lower numbers of refugees had such studies.

Several factors suggest that studies retrieved from Pakistan, Nigeria and Senegal may not accurately describe the true prevalence of infection. Senegal appeared to be the only country to have used PCR methods for chancroid diagnosis (1992). This unequal access to more sensitive diagnostic tests and the potential variation in the accuracy of diagnosis, require a cautious interpretation of the prevalence estimates[10,49]. Several studies where higher estimates were observed, were conducted among

sub-population groups at high-risk such as HIV-positive patients and HIV-positive sex workers (Nigeria). As an exception, one study from Senegal reported 56% chancroid cases among patients attending with genital ulcer disease[43].

The study from Senegal by Totten *et al* reporting 56% chancroid among patients with genital ulcer in 1992 and the study from Pakistan by Rehan *et al* reporting 17.2% among patients presenting with STIs in 1999, may not appropriately reflect the current epidemiology in the country. A recent review by González-Beiras *et al.* (2016) of global trends of chancroid that included 49 studies on genital ulcer etiology between 1980 and 2014, showed a clear decline in worldwide prevalence with majority of studies published during 2010-2014 indicating a prevalence below 10% as compared to 0.0%-68.9% during 1980-1999[9].

This review has some methodological limitations. The search did not cover African or Asian databases nor the grey-literature sources from the countries of origin of the migrants entering the EU/EEA, and only captured publications available in English which were peer-reviewed. A limited number of studies were retrieved from the European region and from the countries of origin of the majority of migrants entering the EU/EEA. In addition, most studies were of moderate quality as a large proportion of data described time-periods prior to the year 2000, which may not appropriately reflect current epidemiological patterns. Moreover, the choice of diagnostic method and the sensitivity of the test may have influenced the prevalence estimates. Some studies were conducted in specific locations or in particular patient subgroups; this may reduce the generalizability of the data and may not appropriately reflect the true national estimates.

In the context of migration, it has been documented that there are unmet needs in terms of provision of essential sexual health services. As such, migrants residing in camps across the EU may lack access to the minimum standard of care which should be provided within a disaster response according to the Interagency Working Group in reproductive health[50,51]. Limited provision of tests and treatment for sexually transmitted infections render the migrant population more vulnerable to sexual health related morbidity[50]. Even though chancroid cases among refugees cannot be excluded, the global decline in the prevalence suggests that it is unlikely that such cases will have a real impact on the epidemiology of chancroid in the EU/EEA. A cross-sectional survey including 452 Syrian refugee women aged 18-48 years attending six health clinics in Lebanon (June –August 2012) reported that 53.3% of women had reproductive tract infections during the conflict and, of those seen by a gynaecologist in the last six months, 27.2% were diagnosed with a reproductive tract infection[52]. Further research is needed to shed light on the STIs burden among recently arrived migrants.

Conclusion

In conclusion, chancroid is a sporadic cause of genital ulcer in the EU/EEA region. Heightened awareness among clinicians, especially when diagnosing genital ulcers among vulnerable populations or travelers to endemic areas, is recommended. Additionally, the unmet sexual health needs among migrants newly arriving to the EU, the type and rates of infection, as well as the potential impact this may have on the general STI patterns in European region still remain to be further elaborated.

Declarations

Conflict of interest

The authors declare that they have no conflicts of interest.

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