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A Systematic Review of epidemiology of Rabies in Arab countries

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ABSTRACT

Background: Rabies is an often neglected yet quite deadly infectious disease. Present in almost 150 countries around the world, with most of the deaths reported in Asia and Africa, it is clear that the disease is a serious, pressing issue worldwide. Underreporting, lack of surveillance and political neglect are the main issues that exacerbate the problem of rabies in many countries around the world.

Method: This systematic review, based on the literature published until June 2019, aims to assess the overall epidemiological situation of rabies, among both humans and animals in Arab countries. The literature search was done using PubMed, EMBASE, Google Scholar and other local journals. A total of 11 studies were included.

Results: Results showed that rabies was highly prevalent in Arab countries. However, very few studies which examined the prevalence of rabies are available or have been published in recent years. Dogs were the main reservoir in most of the Arab countries studied, except Oman, where most of the rabies cases occurred in foxes. Most of the human rabies cases were reported in children younger than 15 years of age.

Conclusion: Whereas some developed countries have eliminated rabies, it still constitutes a major problem in most of the Arab world. Most of the human and animal rabies can be prevented by vaccination and public health education on rabies. There is a need for further and more extensive research in Arab countries on the epidemiology of rabies, as the data available is outdated and insufficient.

Keywords: Rabies; Prevalence; Risk; Arab Countries; systematic review.

1. INTRODUCTION

Rabies is a deadly infectious disease with a case fertility rate of 100% [1]. It still remains one of the most important public health threats in the 21st century. Rabies is present throughout

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the world, but deaths mainly occur in Asia and Africa amongst younger children aged less than 15 years [1]. It still remains underreported in many regions of the world due to the lack of surveillance, political neglect and laboratory infrastructure, as well as being confounded by cultural and social taboos [2, 3]. Therefore, improved surveillance and reporting systems are a prerequisite for addressing the disease burden of rabies in many developing countries [4]. Estimated data by the World Health Organisation (WHO) showed that around 60,000 human deaths occur annually in around 150 countries, with most of the cases taking place in Africa and Asia [5].

Rabies is one of the 17 neglected tropical zoonotic diseases [6]. It was listed in the 2019 Office International Des Epizooties (OIE) diseases list and, at present, remains a constant risk to both humans and animals in most countries [7]. Moreover, rabies causes a serious and long-term societal and financial burden on patients in poverty-stricken countries [1]. Rabies virus (RABV) is an RNA virus of the genus *Lyssavirus*, belonging to the *Rhabdoviridae* family and the order *Mononegavirales* [8]. It is transmitted through an infected animal's saliva, either through a wound or mucosal contamination [8]. Dogs are the main vector of human rabies transmission [9].

Presently, dog-mediated rabies has almost been eliminated from Western Europe, USA, Canada, Japan and some Latin American countries [4, 8]. However, in the majority of the countries in Africa, Asia and the Middle East, the disease still wreaks devastation, as unvaccinated stray dogs and cats are a common sight [1, 5]. Globally the annual economic burden was estimated to be approximately 8.6 billion USD in 2010, and it was attributed to the premature deaths of infected animals, the cost of human post-exposure prophylaxis, loss of live stock, and other costs caused by rabies [10-12].

Challenges related to the control of rabies include its widespread host range, its global distribution, the growing population of free-ranging dogs and, most importantly, the limited resources for controlling the disease and public awareness [10]. Even though it is a preventable disease, it consistently causes the deaths of many humans and animals around the world, including Arab countries, every year [13]. Presently, the world can be categorized into three key zones related to rabies: zones with enzootic canine rabies; areas where canine rabies is controlled but there is rabies among wildlife; and, lastly, rabies-free countries/areas [10]. Arab countries are mostly present in enzootic places and in these countries, people are at risk of catching rabies both mediated by dogs and by other wildlife [10, 14].

In this regard, a study published in 2018 showed insight into the rabies situation and management only in the Middle Eastern countries and investigated the transboundary transmission of rabies by phylogenetic analysis of the rabies virus [13]. While this systematic review mainly focused on all the Arab countries and compiled all the articles published during the past years on human or animal rabies. The aim of this systematic review is to give an in-depth assessment of the situation regarding rabies in Arab countries, based on the published literature. The objective is therefore to aid in the development of strategies to combat rabies; for the control, prevention and elimination in the Arab world.

2. METHODS

This study used a systematic review research approach. To locate primary studies relevant to the present review, a systematic and comprehensive search of multiple electronic databases was performed, with each database searched individually. The databases included PubMed, Embase, and Google Scholar. Once completed, local journal searching, and cross-referencing was undertaken. The last search was done on the 20th of June 2019.

The searched terms, based on Medical Subject Headings (Mesh), included:

- **Disease:** Rabies, rabies disease, rabies virus.
- **Geographical locations:** Arab countries, Saudi Arabia, epidemiology, prevalence. Middle Eastern countries were systematically applied line by line and replicated in every source database using Boolean operators; (rabies or rabies virus) AND (Algeria or Bahrain or Egypt or Iraq or Jordan or Kuwait or Lebanon or Libya or Morocco or Mauritania or Oman or Palestine or Qatar or Saudi Arabia or Somalia or Sudan or Syria or Tunisia or United Arab Emirates or Yemen)
- AND (epidemiology or risk or burden or prevalence or incidence or impact or prognosis).

2.1 Inclusion and Exclusion Criteria

The inclusion criteria were: original research studies published in peer-reviewed journals mainly focusing on epidemiology; burden; prevalence; risk factors; incidence or prognosis of rabies in Arab countries. Observational studies; retrospective and prospective studies published in English were included. Studies which focused on non-Arab populations, enclosed case reports, case series, and quasi-experimental research designs were excluded from our review.

Furthermore, we also excluded unpublished material and articles, as well as studies reporting results aggregated from different countries or global studies.

2.2 Study Selection

Initially, the titles/abstracts of the search outcomes were studied, and when the suitability of the article was in question, full text articles were demanded and evaluated. Based on the exclusion and inclusion criteria, relevant full-text articles were assessed, screened and reviewed by two researchers for inclusion. Any disagreements between authors were resolved through discussion with the third author. This ensured that only articles relevant to the research questions were included. In total, 248 papers were retrieved. Of these, 11 were deemed by both reviewers suitable for analysis and relevant for inclusion into our documented review.

2.3 Data Analysis

All analyses and reviews of the literature were conducted based on the PRISMA “(Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [15]. Extracted relevant papers were synthesized systematically. The collected data was tabulated through narrative with an overview of geographical location, study design, populations, sample sizes, and key study findings. Due to the heterogeneity of the presented data, statistical meta-analysis was not possible.

3. RESULTS

3.1 Overview

The PRISMA flowchart shows the screening and selection processing of identified articles (Figure 1). We retrieved 248 articles, 11 of which met the objective of this systematic review. These studies were categorized into two groups according to the prevalence of rabies in humans and animals (Table 1 and 2).

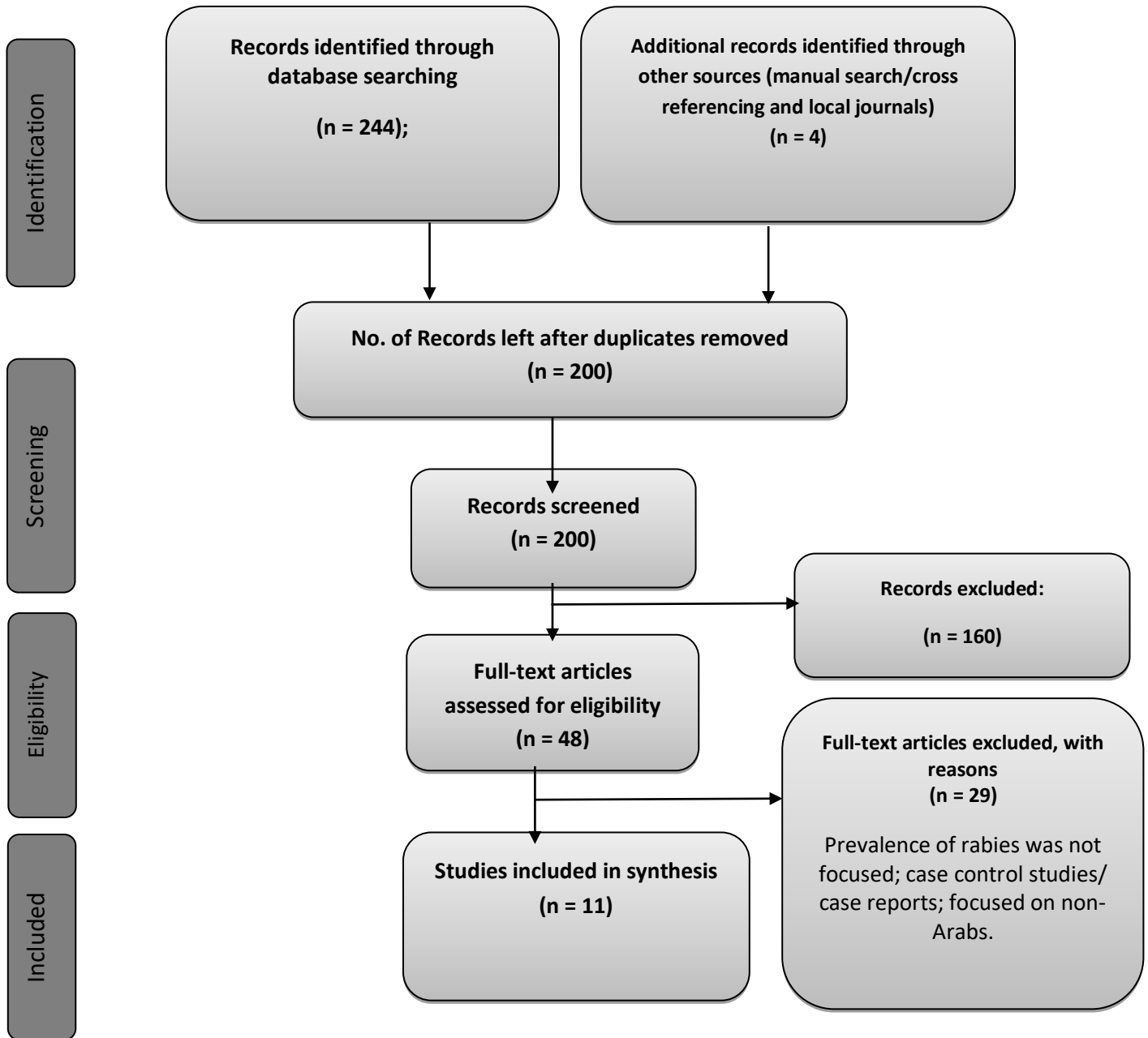


Figure 1 Flow diagram of the included studies.

3.2 Prevalence of Human Rabies

Six studies discussed the prevalence of rabies in human. Two studies were conducted in Lebanon, and one each in Algeria, Oman, Iraq and Yemen. The majority of the rabies cases reported was due to dog bites. The average of rabies cases reported in all the studied countries were 8-11 cases per year, except Algeria where 131 cases were reported per year during the study period, which spanned over six years. Most studies observed an increase in prevalence among children younger than 10 years, while the study conducted in Yemen reported that males were predominantly attacked more than females [16] (Table 1).

Table 1: Prevalence of Human Rabies

Author (year)	Year	Country	Study design	Sample size	Study Key Findings
Yahiaoui F et al [17]	2010-2016	Algeria	Retrospective National study	All animal bite cases.	<ul style="list-style-type: none"> • 131 cases of rabies per year.
Abaidani IA et al [18]	1991-2013	Oman	Cross-sectional study	All animal bites cases	<ul style="list-style-type: none"> • There were 8 rabies cases reported out of total 22,788 animal bites. • Mostly due to wild animal bites with 100% mortality.
Horton DL et al [3]	2001-2010	Iraq	Cross-sectional study	Data from 18 governorate	<ul style="list-style-type: none"> • Average 17 human rabies cases reported annually. • In 2009, estimated 0.89 deaths/ million populations were reported. • Around 40% of the population is younger than 15 years of age, with 63% of cases occur in this age group ($X^2= 48.4, p = 0.0001$).
Bizri A et al [19]	2001-2012	Lebanon	Cross-sectional study	5280 animal bite cases	<ul style="list-style-type: none"> • Eight rabies cases were reported out of 5280 animal bites • Dogs were the only vector reported.
Bizri AR et al [20]	1991-1999	Lebanon	Cross-sectional study	All cases reported during study period.	<ul style="list-style-type: none"> • 11 cases of rabies were reported during the study period. • Majority of the dog bites cases were reported in 1102 animal bites cases to human.
Al-Shamahy HA et al [16]	2011	Yemen	Cross-sectional study	180 individuals, who were attacked.	<ul style="list-style-type: none"> • Males to females attacked reported ratio was 2.2:1. • Most of the bites (56.1%) observed in children ≤ 10 years of age, of which 73.3% were by rabid animals.

3.3 Prevalence of Animal Rabies

Nine studies reported the prevalence of rabies in animals. All data were collected from the suspected animals and animal bite cases. Four studies were conducted in Oman, while one each in Saudi Arabia, Egypt, Algeria, Iraq and Yemen. Dogs were the main reservoir, but rabies was also found in camels, foxes, cattle, sheep, and goats. In KSA, cases of rabies were also

reported in Procaviacapenis and monkeys, while in Egypt, the rabies virus was reported in gerbils. In Oman, the highest numbers of rabies cases were reported in foxes (Table 2).

Table 2: Prevalence of Animals Rabies

Author (year)	Year	Country	Study design	Sample size	Diagnostics used	Study Key Findings
Kasem S et al [21]	2010-2017	Saudi Arabia	Cross-sectional study	199 animals sample	Samples were analyzed using Direct Fluorescent Antibody Test (DFAT)	<ul style="list-style-type: none"> • Positive cases of rabies were 79.4%. • Mostly found in AL-Qasim, Eastern region, Riyadh and Al-Madina. • Main reservoirs of rabies were found in Dogs and camels. While it is also found in Procaviacapensis and monkeys.
Botros BA et al[22]	1977	Egypt	Cross-sectional study	532 rodents and 112 other wild mammals		<ul style="list-style-type: none"> • Rabies Virus Was Found In 1-2% Of Gerbils and 1-8% Of Foxes <i>Vulpes</i> species.
Yahiaoui F et al [17]	2010-2016	Algeria	Retrospective National study			<ul style="list-style-type: none"> • 30.8% of vaccinated dogs and 47.98% of all studied dogs showed less than 0.5 IU of rabies antibodies titers.
Abaidani IA et al [18]	1991-2013	Oman	Cross-sectional study	All animal bites cases		<ul style="list-style-type: none"> • 56.1% were positive for rabies out of 758 suspected animal test. • Highest rate of rabies found in foxes 70.1%
Hussain MH et al [23]	2006-2010	Oman	Cross-sectional study	444 samples of suspected animals	Fluorescent antibody test, histopathology; Reverse transcription PCR	<ul style="list-style-type: none"> • Overall 63% confirmed as rabies during the study period. • Monthly reports of fox rabies cases were highly associated ($r_{SP} > 0.5$) with of camel, cattle, sheep and goat rabies reports.
Ata FA et al [24]	1990-1991	Oman	Cross-sectional study			<ul style="list-style-type: none"> • 127 cases were confirmed in 99 foxes, 2 dogs, 6 cats, 2 camels, 7 cattle, 6 goats and 5 in other species. • Data indicated that the red fox (<i>Vulpes vulpes</i>) was essentially the vector and transmitter of the disease; interspecies spread was also reported.
Body M et al [25]	2011-2012	Oman	Cross-sectional study	257 suspected cases	DFAT	<ul style="list-style-type: none"> • 135 were positive for rabies. • One genetic group (with 99% of homology) of virus appeared to be circulating in the Sultanate of Oman. • Rabies virus is closely related ($> 97\%$ homology) to

						viruses isolated from Saudi Arabia, Jordan and Israel.
Horton DL et al[3]	2001-2010	Iraq	Cross-sectional study	40 animal samples (38 dogs and 2 cattles).	fluorescent antibody test, and reverse transcription Polymerase Chain Reaction (RT-PCR)	<ul style="list-style-type: none"> • 3 out of forty were positive for rabies.
Al-Shamahy HA et al[16]	2011	Yemen	Cross-sectional study	180 animals brain samples	DFAT	<ul style="list-style-type: none"> • 63% were positive for rabies. • 92% were dog bites with 63% positive rabies cases. • Animals involved in bite cases, 70.6% males (60.6% were positive), and 29.4% females (69.8% were positive). • Major risk factor for the spread and transmission of rabies include poultry carcasses and food waste (prevalence 84.8%, PPR=9.5, P-value= >0.001). • Animal bites also increased during the school vacation time of the year (PPR =3.8).

4. DISCUSSION

Recent data from literature showed that rabies is still endemic in the Arabian Peninsula. We aimed to evaluate the prevalence of rabies in humans and animals in Arab countries reported during the past years. A total of 11 out of 248 studies that discussed prevalence of rabies in Arab countries were found. This shows that there are very few published studies which examined the prevalence of rabies. It is a major zoonotic and public health problem all over the globe [10, 26]. The majority of human rabies cases occur in developing countries in which the number of stray dogs is higher [6, 10]. This is reported in most of the Arab countries as well. One reason for this endemic is due to dog-to-dog transmission of rabies virus between rabid and unvaccinated dogs. This may become a risk to humans due to dog bites [1]. Most studies of the Arab world showed an increased burden of disease among children, which is inconsistent with other parts of the world as well [27]. Very little, if any, accessible information was available from Palestine and Syria, especially after the political unrest there [13]. In some countries like Iraq, Oman and Yemen, very few studies to evaluate the rabies situation have been published in recent years, and currently, no new updated data is available on the situation of rabies [3, 18]. It is also suspected that the situation has intensified in these countries (Iraq and Syria) as the number of

unvaccinated dogs increases due to the unavailability of proper veterinary facilities, as well as the decrease in sanitary and municipal infrastructure and responsibilities[13].In Egypt, we could not find any new data about the prevalence of rabies; however, a report published in 2011 depicted a stable situation during the years 2000 to 2010, which translates into 80 human cases of rabies[13, 28].

Aylan et al also reported that, in most countries, human rabies cases were present at the national level but not at the international level [28]. In this systematic review, it was observed that human cases of rabies are still present in Arab countries, where rabies occurs in dogs despite vaccination coverage and rabies immunoglobulin (RIG) availability. In the literature, we also found studies where rabies was present in dogs imported from Arab countries like Egypt [29, 30]. Likewise, in other regional non-Arab countries like Iran, privately owned dogs were vaccinated up to some extent (40%), while there were no vaccination programs for stray or unowned dogs [31]. However, for the effective control of rabies the vaccination of at least 70% of the whole population of dogs is necessary [32]. In 2015, WHO-OIE-FA announced a joint project to control and eradicate human rabies mortalities worldwide by the year 2030 [1, 33, 34]. In Lebanon, two studies reported cases from 1991 to 2012, around 8-11 of which were during the study period [20]. However, it was also reported that the vaccination of dogs is not enforced, despite evidence showing that vaccination may lead to a state of near elimination, or at the very least, infrequent reemergence [20] of rabies, as in the case of foxes in Turkey [35]. Similarly, Israel also reported the foxes acting as reservoirs [36]. This is called host switching, in which a second species of reservoir is disease-ridden and is therefore accountable for the presence of the virus in other wildlife like foxes and skunks, which originate from dogs and bats in the US [37, 38]. This stresses the need to observe the spread of rabies virus in other wildlife for the prevention of rabies overall.

In high income Arab countries like the United Arab Emirates, Kuwait, Jordan and Qatar, human rabies is considered rare [13, 39, 40]. In the past decade, no human rabies cases have been reported by the Saudi Ministry [40]. However, the first confirmed human rabies case in Saudi Arabia was reported in 2018 [41]. Nevertheless, animal rabies is still commonly present in Jordan and Saudi Arabia [13]. Arab countries like Egypt and Iraq have begun working together with Non-Arab regional countries like Iran and Turkey to prevent the movement of rabid animal across countries borders [3, 42].

Due to cultural diversity, political instability and extreme socioeconomic disparity (from the richest nations to severely poor ones) in many Arabian countries, rabies has become much more neglected [40]. Not only is there a scarcity of information about the rabies situation but the accessible studies were also outdated [40]. Even though rabies is a reportable disease, under-reporting is still a main concern in these areas. This situation is even worse in rural areas, where the incidence of rabies tends to be higher and people are less aware of the manifestation of the disease, as compared to urban areas [18, 19].

The few limitations of this systematic review include the fact that most studies did not geographically cover the entire country; therefore, we could not find the true burden of disease. Secondly, we only included studies published in the English language, thereby excluding other languages and grey literature. Although we tried to search in both databases and local journals, we cannot exclude the chance of having missed some articles.

5. CONCLUSION

Rabies is a neglected zoonotic viral disease that is present in most Arab countries. This systematic review presents the prevalence of human and animal rabies. Although it has been eradicated from some developed countries, it still constitutes a problem in most of the Arab World. This study shows that rabies can be eliminated from high-risk countries by simply taking preventive measures as well as the vaccination and control of the population of stray dogs. It is also recommended that there be cooperation between the Human Health sector, the Veterinary Sector and environmental authorities to set action plans to eradicate rabies from the whole world by 2030.

The majority of human and animal rabies can be prevented by public health education about the rabies transmission route, exercising caution when coming into contact with wildlife, proper veterinary care, and dog vaccination. Local governments in each Arab country should initiate effective vaccination programs for all dogs, cats [42], and cattle as well as controlling stray dogs and unwanted animals. Social media can also play a role in raising awareness in order to control and eradicate rabies in the Arab world. Moreover, it is important to maintain a sufficient surveillance system for rabies cases in order to facilitate reporting and control of the disease. There is also a need to strengthen the cooperation between Arab countries for more

research projects on the control of rabies, as the data currently available from Arab countries are not enough.

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7. CONFLICT OF INTEREST:

“The authors declare that they have no competing interests.”

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