Eighteen years of implementation of a control programme against Rift Valley fever, 2000–2018, Saudi Arabia: a review study

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Summary

Rift Valley fever (RVF) is a serious life-threatening disease with severe clinical manifestations and health consequences for humans and a wide range of domestic animals. In September 2000, an RVF outbreak was reported in the Jazan region in the south-west part of Saudi Arabia with 886 human cases including 124 deaths. This review provides: *a)* an overview of the RVF control programme in Saudi Arabia and *b)* an assessment of some of the control measures that have been launched since the early recognition of RVF. Currently, with the exception of Saudi Arabia, devastating outbreaks of RVF continue to occur and the number of countries reporting cases has increased rapidly. At least 19 large outbreaks including substantial numbers of human and animal deaths have been reported for the period between 2000 and 2018. In contrast to the aforementioned situation in endemic areas, the RVF control programme that was set up in Saudi Arabia has completely reversed the risk of re-occurrence of RVF over the past 18 years and provided long-term protection against Rift Valley fever virus (RVFV) exposure. The control programme involved: *a)* vector control campaigns (using conventional and microbial insecticides, drainage and filling of water swamps with soil, and mosquito surveillance), *b)* host-driven controls such as sustained vaccination campaigns, regular examination of sentinel herds, including seasonal surveillance

reinforcement (targeted sero-surveillance during rainy seasons), and serological examination of clandestine animal imports kept at Al-Twal quarantine station, at the border with Yemen.

The effectiveness of the current control programme can be demonstrated not only by the decrease in antibody prevalence of RVF virus-specific immunoglobulin M (IgM), from 12.3% (95% confidence interval [CI]: 6.8–17.8) in 2000 to 0.10% (95% CI: 0.01–0.2) in 2017, but also by the absence of human and animal cases since the 2000 outbreak. The mosquito infection rates with RVFV have also declined, from 0.045 per 1,000 for *Culex* in 2014 to zero from 2015 to 2018. Additionally, the integrated vector management methods targeting outdoor habitats in the Jazan region substantially contributed to vector control and should be considered one of the most important factors contributing to the significant reduction of malaria case incidence from 2000 to 2014. The Saudi current control initiative could be used as a guideline for control of RVF or as a suitable model for other endemic countries.

Keywords

Control – Outbreak – Prevention – Rift Valley fever – Surveillance.

Introduction

Rift Valley fever (RVF) is a serious infectious disease of humans and a wide range of domestic ruminants, caused by the mosquito-borne Rift Valley fever virus (RVFV) that belongs to the family Phenuiviridae, genus *Phlebovirus* and order Bunyavirales. Human beings can be infected either by mosquito bites or through exposure to blood, foetal aborted materials, body fluids or tissues of infected animals (1). The disease was first reported in Kenya in 1931, among livestock, and since then it has been reported in most African countries and has spread to the Arabian Peninsula, particularly Saudi Arabia and Yemen in 2000 (2, 3). This was the first time that RVF had appeared outside the African continent (4).

The Jazan region, located in the south-west of Saudi Arabia, was the hardest hit by the disease. About 65.6% of the total number of animal cases occurred in the Jazan region, whereas 26.9% occurred in the Asir and 7.5% in the Alqenfeda regions (5). High mortality rates due to RVF were observed in hospitalised patients, with 124 deaths reported. Among the hospitalised persons, some developed severe signs including haemorrhagic manifestations, retinitis and meningoencephalitis, and others died from progression of the disease to these severe clinical signs (19.4%, 9.7%, 4.2% and 33.9%, respectively). The main factors leading to deaths in humans were attributed to hepatocellular failure and acute renal disorders, in 75.2% and 41.2% of patients, respectively (6).

This first outbreak of RVF in Saudi Arabia raised concerns about the potential incidence and establishment of the disease under different environmental conditions. It is possible that RVFV could affect areas that have never experienced the disease before as a consequence of climate change and globalisation of trade in animals and their products (7). Surprisingly, it has been demonstrated in a retrospective study that Saudi Arabia was free of RVF at least before 1995 and most probably before the 2000 epidemic (8). The virus was apparently introduced into Saudi Arabia during the religious festival of Eid Aladha through importation of live animals from countries of the Horn of Africa. The RVFV strain isolated from the first patients during the 2000 outbreak was similar to the one isolated in Eastern African outbreaks that occurred in 1997–1998 (9, 10). The adverse effects of the disease, and its serious socio-economic impacts, compelled the relevant veterinary authorities of Saudi Arabia to develop an effective control programme in order to break the transmission cycle and raise herd immunity.

This paper specifically aims to review the effectiveness and benefits of the control measures that were undertaken to control RVF in Saudi Arabia since the first occurrence of RVF in the country in 2000.

Methods

Data collection

A systematic review was conducted by searching Google Scholar (https://scholar.google.com/) up to 15 November 2018. The search terms 'RVF' and 'Saudi Arabia' were combined using the operator 'AND' to identify original research articles. A total of 1,610 articles were identified based on their relevance to the aim of the study and on their English-language edition. Of the 1,610 screened reports, only 17 articles were finally selected. Additional data were obtained from Veterinary Records of the Ministry of Environment, Water and Agriculture (MEWA) in Gizan city, Saudi Arabia, as well as from the World Health Organization (WHO) in Geneva, Switzerland, and the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, United States of America (USA).

Rift Valley fever control programme

Various control measures were implemented in Jazan over the past 18 years:

a) Sustained vaccination campaigns were accompanied by restriction of animal movements in the affected areas of Jazan, Tohamet Aseer, Tohamet Mekkah and Tohamet Al-Bahah and serological examination of smuggled animals that were kept at Al-Twal quarantine station, at the border with Yemen. Unvaccinated animals were not allowed to leave the outbreak zones.

b) Sentinel herds (sheep and goats) were set up, with regular examination and targeted sero-surveillance during rainy seasons for domestic animals such as sheep, goats, cattle and camels.

c) Vector control campaigns were routinely adopted, using ultra-low volume (ULV) sprays, fog and sprinkle sprayers in rural farms, cities and villages.

d) Water swamps were drained and filled with soil, in addition to biological control using living organisms such as the bacterium *Bacillus thuringiensis* var. *israelensis* (BTI).

e) Mosquito surveillance and virus detection in mosquitoes were implemented using molecular techniques.

Vaccination programme against Rift Valley fever

The Smithburn strain live-attenuated vaccine (Onderstepoort Biological Products [OBP], Pretoria, South Africa) has been used as the gold standard vaccine in the Jazan region and coastal areas of the Aseer region since December 2000. The annual vaccination programme for RVF in high-risk areas (high rainfall, reported positive RVF cases, water bodies and high vector density) is restricted to non-pregnant animals above six months of age before or during the mating season, to increase the chances of development of protective maternal antibodies and to prevent possible abortions. However, it has been proven through serological surveys that vaccination is effective and highly beneficial in controlling infections (11).

Sentinel herds

The sentinel animals used were unvaccinated sheep and goats, related to the local breeds and imported from regions free of RVFV infection. Most were females of the same age (six months). These animals tested negative for RVF specific immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies (using the ID Screen® Rift Valley fever Competition Multi-Species Capture) before they were placed at ideal habitats for RVF vectors, in order to investigate the potential circulation of RVFV during inter-epizootic periods (Fig. 1, Table I) (12).

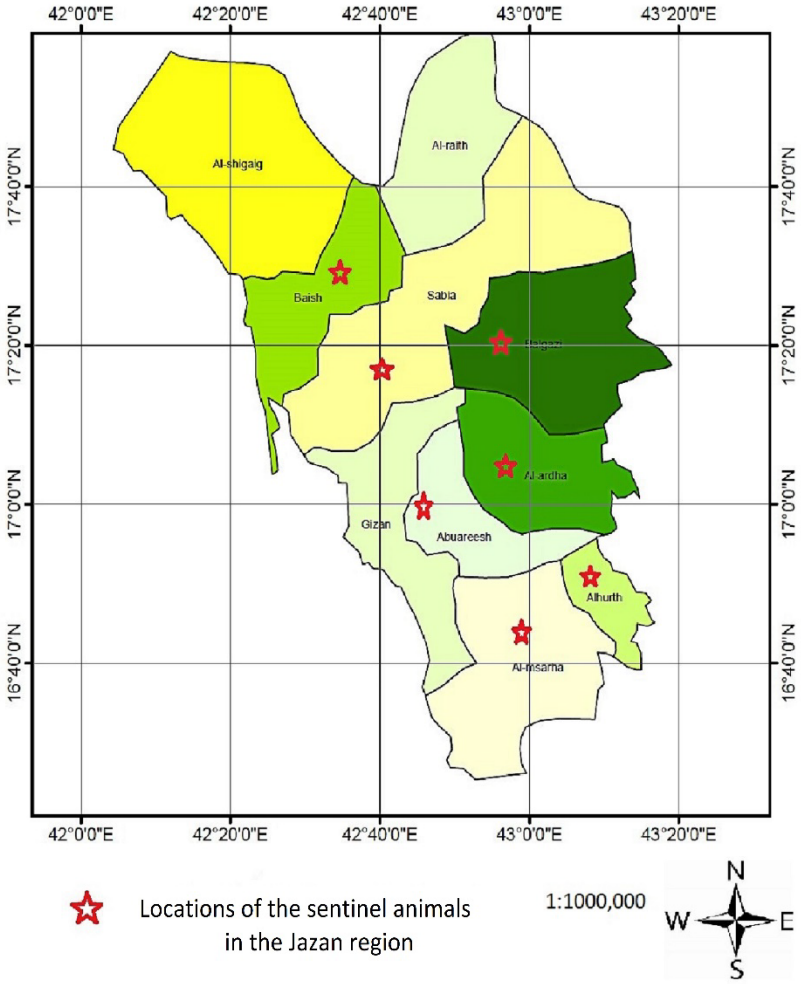

Fig. 1

Geographical distribution of sentinel animals in the Jazan region

Table I

Investigations of sentinel herds

Source: MEWA, Saudi Arabia

Number of herds	Number of animals in each herd (sheep and goats)	Total number of animals	Sampling programme
11	30	330	Monthly during rainy seasons

MEWA: Ministry of Environment, Water and Agriculture

Vector control

Vector control involved several types of measure: land spraying and aerial spraying with chemical insecticides, microbial insecticides and environmental management.

Vector control with land spraying

Outdoor land spraying with residual insecticides such as pyrethroids (cypermethrin 10%, deltamethrin 2.5% and cyfluthrin 5%) was used to control adult mosquito populations present in vegetation or at resting sites such as animal shelters at times associated with high mosquito activity, mainly 1–2 hours after sunset or 1–2 hours before sunrise. The ULV spraying and thermal fogging equipment used was mounted on ground vehicles.

Aerial spraying of insecticides

Aerial spraying of insecticides, as ULV aerosols of 10% alphacypermethrin that target adult and immature stages of insects, was used to reduce the insect populations over a large scale, notably in areas that were not accessible by roads or ground vehicles such as dense vegetation, forested land, valleys, streams, lakes and sewage stations. Helicopters and fixed-wing aircraft contributed substantially to vector control (Fig. 2).

Fig. 2

Aerial spraying of inaccessible areas by fixed-wing plane

Microbial insecticides

The numerous disadvantages of insecticides, such as increasing resistance to commonly used pesticides and the global growing concerns regarding the overuse of insecticides in the environment, have promoted the use of alternative tools such as microbiological insecticides that have less environmental impact than chemical compounds. Microbiological insecticides, developed to kill larvae without polluting or damaging the environment through the use of living organisms, such as the bacterium BTI, were applied in different aquatic habitats in the Jazan region with back-pack sprayers (Fig. 3, Table II).

Fig. 3

Application of microbiological insecticides, Jazan region

Table II

Vector control activities. *Bacillus thuringiensis* var. *israelensis* and aerial and land spraying with insecticides from 2000 to 2018

Source: MEWA, Saudi Arabia

Vector control activities	Land covered by aerial spray per hectare (cypermethrin 10%, deltamethrin 2.5% and cyfluthrin 5%)	Number of ponds treated with BTI	Animal shelters (sheep, goats, cows and camels) treated with cypermethrin 10%, deltamethrin 2.5% and cyfluthrin 5% insecticides (sprinkling spray)
2018	49,750	2,037	115,539
2017	50,200	2,422	211,215
2016	18,100	2,288	277,678
2015	40,000	1,954	278,556
2014	53,200	1,492	168,849
2013	48,800	3,146	193,139
2012	50,000	3,657	220,850
2011	67,200	3,890	236,179
2012	51,000	3,540	221,188
2011	40,200	4,250	195,123
2010	*	*	*
2009	39,100	7,882	219,911
2008	34,500	8,235	184,322
2007	67,600	7,858	201,874

2006	65,600	9,870	238,436
2005	123,710	*	*
2004	150,425	*	*
2003	183,963	*	*
2002	199,210	*	*
2001	288,043	*	361,580
2000	974,556	*	263,000

BTI: *Bacillus thuringiensis* var. *israelensis*
MEWA: Ministry of Environment, Water and Agriculture
* No information available

Environmental management

Environmental management is an effective approach in vector control to maintain permanent control of mosquitoes by altering or removing vector breeding sites, through different methods such as covering water containers, removing small used cans or tyres, flushing streams, draining water to follow natural flows, filling in ditches with soil or stones, subsoil drainage, and removing vegetation from water bodies. Heavy machinery, including wheel loaders, excavators, bulldozers and dump-trucks, contributed significantly to improving environmental conditions in the Jazan region particularly during rainy seasons (Fig. 4) (13). The aforementioned activities were monitored during swamp filling and treatment as part of the RVF control programme.

Fig. 4

Drainage of stagnant water in the Jazan region during the rainy season

Vector surveillance

Mosquito surveillance was conducted before insecticide treatments to evaluate the density of mosquitoes in breeding habitats, and post treatment to evaluate the efficiency of the insecticide spraying. Light carbon dioxide (CO_2) baited traps (Clarke, St. Charles, Illinois, USA) were placed overnight at different locations where mosquito breeding sites were identified (Table III). Additionally, molecular detection of RVFV in mosquitoes was performed in MEWA laboratories, using real-time polymerase chain reaction (RT–PCR) assay.

Table III

Mosquito surveillance activities, Jazan region, 2000–2018

Source: MEWA, Saudi Arabia

Trap type	Number of targeted trap sites per week	Number of investigated ponds targeted per week	Season of mosquito abundance	Genera of mosquitoes caught	Total number of mosquitoes caught from 2004 to 2018
CO_2 baited	48	24	From August to February	*Aedes*, *Culex* & *Anopheles*	1,771,790

CO_2: carbon dioxide
MEWA: Ministry of Environment, Water and Agriculture

Evaluation of the country-based Rift Valley fever control programme

Zero incidence of Rift Valley fever infection in humans

Currently, outbreaks of RVF continue to occur frequently in the 21st century and many countries are still hard hit by the disease. At least 19 large outbreaks with substantial numbers of animal and human deaths were reported for the period 2000–2018, with particular reference to Mauritania which was affected in 2010, 2012, 2013 and 2015 (Table IV).

Table IV

Worldwide human Rift Valley fever outbreaks, 2000–2018

Sources: OIE, France; WHO, Switzerland; CDC, United States of America

Year of occurrence	Affected country	Human deaths	Human cases	References
2003	Egypt	38	153	(14)
2007	Kenya	155	684	(15)
2007	Tanzania	109	264	(15)
2007	Sudan	222	698	(16)
2008	Mayotte	0	10	(17)
2008	Madagascar	17	418	(18)
2008	Swaziland	*	*	(19)
2010	Mauritania	13	63	(20)
2010	South Africa	25	250	(20)
2010	Botswana	*	*	(21)
2012	Mauritania	17	34	(22)
2013	Senegal	*	11	(23)
2013	Mauritania	*	*	(24)
2014	Botswana	*	*	(25)
2015	Mauritania	8	31	(20)

2016	Uganda	*	5	(20)
2016	Niger	32	266	(26)
2016	Mali	*	*	(27)
2016	People's Republic of China	*	1	(28)
2018	Gambia	1	1	(29)
2018	Kenya	6	26	(30)

CDC: Centers for Disease Control and Prevention
OIE: World Organisation for Animal Health
WHO: World Health Organization
* No information available

By contrast, neither human fatalities nor RVF-specific IgM seroconversion have been reported in Saudi Arabia since the 2000 outbreak. Furthermore, a zero prevalence of specific IgM and IgG has been reported among children born after the 2000–2001 outbreaks (31). These findings support the notion that the control programme that was implemented has played a significant role in RVF prevention over the past 18 years. This was despite the recent climate change in the Arabian Peninsula and early warning alerts that were issued from the National Aeronautics and Space Administration (NASA), which indicated the elevated risk of RVF activity in Saudi Arabia due to above normal rainfall in 2005 and 2015 (32, 33).

Low seroprevalence of Rift Valley fever in local herds and sentinel animals

The efficacy of the current control programme can be demonstrated not only by the absence of human cases, but also by the strong decrease in specific RVF antibody prevalence in local herds from 12.3% (95% confidence interval [CI]: 6.8–17.8) in 2000 (5) to 0.10% (95% CI: 0.01–0.2) in 2017 (source: MEWA, Gizan city, Saudi Arabia). Currently, RVFV circulation seems to be mainly restricted to sporadic

cases without clinical signs, mostly in sentinel herds (34). From 2004 to 2018, the sentinel surveillance system identified 36 out of a total of 330 sentinel animals to be seropositive for RVFV-specific IgM and IgG antibodies. Out of a total of 36 seropositive cases for RVF in sentinel herds, most of them were reported in Alardah, Abuareesh and Alqunfidah, with percentages of 36.1% (95% CI: 29.2–42.9), 16.7% (95% CI: 9.8–23.6) and 13.9% (95% CI: 7.03–20.8) of the total number of cases, respectively (35). The absence of clinical cases in humans as well as in animals since the 2000 outbreak of RVF reflects the high performance of the control programme (36).

Vaccination efficacy from a pooled analysis of cross-sectional surveys

A pooled analysis of seropositive cases of RVF that were diagnosed through cross-sectional surveys in high-risk areas and in sentinel herds (source: MEWA, Gizan city, Saudi Arabia) was done to evaluate whether or not vaccination had a significant effect on the occurrence of clinical cases, thus preventing outbreaks, when both sentinel herds and local (vaccinated) animals were exposed to the same levels of RVFV under natural conditions (Table V).

Table V

The risk of Rift Valley fever in local vaccinated herds and sentinel animals (sheep and goats), Jazan region, 2000–2018 (35)

Groups of animals	Positive cases of RVF	Negative for RVF	Total
Local herds (vaccinated animals)	53	18,234	**18,287**
Sentinel herds (unvaccinated animals)	36	294	**330**
Total	**89**	**18,528**	**18,617**

RVF: Rift Valley fever

The rate of RVF infection in sentinel herds was 36/330 = 10.9 cases per 100 animals, while the rate of infection in vaccinated animals was 53/18,287 = 0.29 cases per 100 animals. The odds ratio (OR) is 0.02 at a value of $p < 0.05$, which demonstrates that vaccination seems to be protective against RVF.

Huge decline in mosquito infection rates and mosquito numbers following vector control programme

A continuous decrease in mosquito infection rates occurred after the vector control measures were undertaken to control RVF in the country in 2000. The mosquito infection rates with RVFV declined from 0.30–13.8 cases per 1,000 for *Culex tritaeniorhynchus* and 1.94–9.03 per 1,000 for *Aedes vexans arabiensis* in 2000 (37) to 0.045 per 1,000 for *Culex* and to zero for *Aedes* in 2014 (source: MEWA, Gizan city, Saudi Arabia). All mosquitoes collected between 2015 and 2018 tested negative for RVFV. Interestingly, the numbers of mosquitoes have declined gradually over the period of the vector control programme from 2004 to 2018 (Table VI).

Table VI

Adult mosquito collections per year, 2000–2018

Source: MEWA, Saudi Arabia

Year	Total number of mosquitoes
2018	69,153
2017	79,876
2016	68,052
2015	55,336
2014	78,643
2013	79,000
2012	111,681

2011	92,195
2010	111,022
2009	111,747
2008	132,606
2007	126,471
2006	143,463
2005	141,300
2004	189,353

MEWA: Ministry of Environment, Water and Agriculture

A significant decrease in malaria incidence

The One Health strategy to overcome mosquito disease vectors in Saudi Arabia was based on the collaboration between the Ministry of Municipal, Rural Affairs and Housing (indoor habitats) and MEWA, which is entirely responsible for the vector control programme in outdoor habitats. Consequently, the integrated vector control programme implemented for RVF control has also significantly contributed to malaria vector control and should be considered as a main factor contributing to the decreased number of malaria cases from 2000 to 2014. This is especially true for locally acquired cases wherein a significant decline was observed from 2,756 cases (35.3 per 10,000 human population) in 2000 to 15 cases (0.11 per 10,000 human population) in 2014 (38).

Conclusion

To summarise, this study has provided some evidence of the efficacy of the RVF control programme implemented in Saudi Arabia. It was shown that RVF can be controlled through routine vaccination and vector control in high-risk zones by using a combined sentinel herd-based and mosquito-based surveillance strategy during the rainy

seasons corresponding to the peaks of mosquito abundance which facilitate RVF outbreaks.

The control programme that was set up in Saudi Arabia during the period 2000–2018 has shown its effectiveness in preventing outbreaks with *a)* no clinically active cases of RVF in humans and animals recorded since the first outbreak in 2000 and *b)* a remarkable decrease in RVFV antibody prevalence in ruminants from 12.3% (95% CI: 6.8–17.8) in 2000 to 0.10% (95% CI: 0.01–0.2) in 2017. The integrated vector control strategies that have been implemented in the region could help to reduce the incidence of emergent mosquito-borne diseases as well as endemic diseases such as malaria.

The ongoing RVF control programme could be used as a successful model to be considered by other RVF endemic countries.

A lack of recent information on RVF seroconversion in humans is an inherent limitation of this study. It is necessary to conduct further sero-epidemiological investigations of RVF in humans on a regular basis, to address the disease from the perspective of a One Health approach.

Moreover, future studies should examine the residual insecticides in soil, water and agricultural products. A regular insecticide resistance monitoring programme should also be considered to limit insecticide resistance along with broadening the spectrum of biological controls such as the use of fish predators to control mosquito populations.

Furthermore, a geographical information system (GIS) is needed to identify potential epizootic areas for RVF and the boundaries of intervention activities, to improve the surveillance network and favour decision-maker policies. Further research is needed to develop and bring new vaccine candidates to the market in the near future to improve vaccine safety and immunogenicity.

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