Journal of the Egyptian Society of Parasitology, Vol.43, No.1, April 2013
J. Egypt. Soc. Parasitol., 43(1), 2013: 41 - 56

THE RIFT VALLEY FEVER: COULD RE-EMERGE IN EGYPT AGAIN?

By
MAMDOUH M. EL-BAHNASAWY[1], LAILA ABDEL-MAWLA MEGAHED[2], HALA AHMED ABDALLA SALEH[2]AND TOSSON A. MORSY[3]
The Military Medical Services For Preventive Medicine[1], The Military Medical Academy[2] and Department of Parasitology, Faculty of Medicine, Ain Shams University, Cairo 11566[3], Egypt

Abstract

The Rift Valley fever (RVF) is a neglected, emerging, mosquito-borne disease with severe negative impact on human and animal health and economy. RVF is caused by RVF virus of the family of Bunyaviridae, genus *Phlebovirus.* RVF is an acute, febrile disease affecting humans and a wide range of animals. The virus is trans-mitted through the bites from mosquitoes and exposure to viremic blood, body fluids, or contact with tissues of infected animals or by inhaling natural virus aerosols, also possibly by consumption of infected unpasteurized milk.

The RVF-virus replicate at the site introduction and in local lymphatic followed by viremia and spread to other organs as the liver and central nervous system, causing the hepatic necrosis and eosinophilia cytoplasmic degeneration. The main signs and symptoms are fever, headache, myalgia, arthralgia, photophobia, bradycardia, conjunctivitis and flushing face. Main complications include jaundice, hemorrhagic, meningoencephalitis and retinal lesions.

Generally speaking, in the21stCentury, the vector-borne infectious diseases, was accepted as the disaster issues with the considerable significant morbidity and mortality. These facts should be considered by the public health, veterinary and agricultural authorities

Key words: Egypt, Rift Valley fever, Mosquitoes, Re-emergency.

Introduction

The Rift Valley Fever (RVF) has been reported in many savanna regions of the sub-Saharan Africa, mainly following heavy rainfall. Outbreaks have also been documented in West Africa. The outbreaks occurred in Ken-ya and Somalia; largest one occurred in Keya during the years 1997-1998 seasons when approximately 89,000 people were infected and 473 died. In the Kenyan outbreak, more than 404 cases were reported with 118 deaths from November 2006 to January 25, 2007, a case fatality rate of 29%. The most frequently reported symptoms among the first 97 cases included fever, headache, bleeding, malaise, muscle pain, back pain, vomiting, and joint pain. The diagnosis of RVF was confirmed by the detection of viral

RNA-PCR and/or by the detection of ELISA-IgM antibodies against RVFV (Faye *et al*, 2007).

In Egypt

Imam and Darwish (1977) gave a preliminary report on an epidemic of Rift Valley Fever (RVF) in Egypt. Hoogstraal *et al*. (1979) concentrated on the vector, and isolated RVF virus from unengorged *Cx. pipiens,* and demonstrated laboratory transmission of the virus by this species, strongly implicate it as the chief vector and that transmission to man also occurs by contamination when handling infected meat and by inhaling natural virus aerosols. They added that over 30% of the camels sampled at the southern border of Egypt were serologically positive and that the virus was introduced into Egypt, either by these imported animals or by other vehicles from the south border.

El-Gebaly (1978) reported an outbreak of RVF among the military personnel. Niklasson *et al*. (1979) serologically tested Swedish United Nations Emergency Forces Soldiers serving in Egypt and Sinai Peninsula for hemagglutination-inhibiting antibodies to RVF virus. Eight of 170 were positive. RVF has not been reported outside Africa, and a survey of 500 Swedish Soldiers who had not served in the Middle East or Africa revealed no RVF virus anti-bodies. There were extensive RVF epidemics in Egypt in 1977 and 1978, and it is considered that these serologically positive soldiers contracted the RVF disease while on duty in the Eastern Mediterranean Countries.

Meegan *et al.* (1979) reported that a disease causing increased mortality and abortion in domestic animals during a 1977 epizootic in Egypt was identified as RVF virus. The epizootic included extensive human involvement reflected clinically as either an acute febrile, ocular, encephalitic, or fatal hemorrhagic form of RVF disease. The virus was again isolated from humans and animals during a second RVF epizootic in the summer of 1978.

Siam *et al*. (1980) studied ocular manifestations resulting from the RVF virus infection during an extensive RVF epidemic in Egypt on 1977. The color photography and the fluorescein angiography of seven serologically diagnosed patients showed commonest manifestations to be macular, paramacular, and/or extra-macular retinal lesions, often occurring bilaterally.

The hemorrhages and edemas were usually associated with the lesions, and vasculitis, retinitis, and the vascular occlusion were also observed. Patients were monitored during 6-month convalescence, and, though resorption of the lesions occurred, approximately half the patients experienced the permanent loss of visual acuity. Ocular disease was one form of the clinical spectrum of RVF; acute febrile, encephalitic, and fatal hemorrhagic RVF illnesses were also observed during the epidemic.

Digoutte *et al*. (1985) reported that among the viruses which can provoke human hemorrhagic fevers, the Congo-Crimean Hemorrhagic Fever and Rift

Valley Fever viruses were discovered relatively recently in West Africa. Two human cases of severe hemorrhagic fever have been connected with the Congo-CHF, in Mauritania and Burkina-Faso. Epidemiological enquiry performed in Mauritania, consequent to the appearance of the first case, has demonstrated that the patient had been contaminated by contact with camels. Twelve strains of Congo-CHF virus have been isolated from ticks taken on bovines and dromedaries in that area. The serological enquiries realized on man showed that the incidence was relatively feeble; on the other hand, among animals, one finds a large distribution among small ruminants in Mauritania as well as in Senegal. Recent realization of a complete identity between the Zinga and Rift Valley Fever viruses has broadened the geographical distribution of this virus to the whole of inter-tropical Africa including Madagascar. The serological enquiries realized among men and animals in areas where the virus has been isolated from wild vectors show that the presence of antibodies is faintly superior. On the other hand, in southern Mauritania, the virus prevails among men, who get antibodies of the IGM type, which proves a recent circulation. Immunological enquiries on camels seem to corroborate these data. The Rift Valley Fever epidemic which broke out in 1978 among the human and animal populations of Egypt has, apparently, been connected with the passage of camels coming from Sudan through the intermediary halting-place of the Aswan dam.

Feinsod *et al*. (1986) mentioned that epidemic RVF was generally recognized when a higher than expected frequency of abortions and hemorrhages occurring in sheep and other livestock. Other infectious agents can cause similar clinical signs. In Egypt, an outbreak of abortions and hemorrhages in sheep and goats in 1982 was traced to intoxication with the rodenticide Brodifacoum. The epidemic lasted for three weeks and resulted in 120 deaths. The epidemic end coincided with the heavy rainstorm. The outbreak showed the need for the strict control of the use of rodenticides and widens the differential diagnosis of the epidemic abortion in sheep and goats.

Scott *et al*. (1986) examined serum samples obtained from 418 sheep in the Nile Delta using five tests to determine the accuracy of serological methods in detecting RVFV antibodies. Plaque Reduction Neutralization Test (PRNT) was considered the standard serological method against which the four other tests were compared. The twenty-four serum samples had RVF viral antibodies detected by PRNT. The hemagglutination inhibition and the enzyme-linked immunosorbent assay antibodies to RVF virus were also present in the same 24 serum samples. The indirect immunofluorescence was less sensitive in comparison with PRNT, and the complement fixation was the least sensitive. The outcome data extended observations made with the laboratory animals to a large field-collected group of Egyptian sheep.

Gad *et al*. (1986) mentioned that RVF, which was enzootic in Sudan in

1976 and epidemic in Egypt in 1977-78, might have been introduced into Egypt from Sudan via sheep transported along Lake Nasser. A hypothesis is presented which describes sheep transport from holding areas in north-central Sudan, where RVF was epizootic, to live animal markets in southern Egypt. Travel time from north-central Sudan to the Aswan area was less than 5 days, approximating the incubation period of RVFV in sheep. Reintroduction of RVF or other diseases from Sudan into Egypt could be facilitated by the construction of new roads linking the two countries.

Gad *et al*. (1987) tested 4 Egyptian mosquito species for their ability to transmit the Egyptian ZH-501 strain of RVFV to golden Syrian hamsters. *Cx. antennatus* was the most efficient vector, showing a 37.5% transmission rate following a hamster blood meal containing ten suckling mouse intracerebral 50% lethal doses (SMILD50) per ml. Fully engorged mosquitoes of this species showed an infection rate of 85% with mean viral titers of transmitting mosquitoes 100-fold higher than non-transmitters. The autogenous and anautogenous populations of *Ae. caspius* were tested separately, and the transmission rates were 23.1% and 9.7% respectively, following feeding on hamsters with similar levels of viraemia. The two anopheline species, *Anopheles multicolor* and *An. pharoensis,* showed 12.5% and 3.5% transmission rates under similar conditions. In the three species infection rates exceeded 75% and mosquitoes' transmitting had a high average titer than those not transmitting.

Woodruff *et al*. (1988) reported that patients presenting at the Juba Teaching Hospital, either with the fever of undetermined origin or with a clinical cause of fever, gave evidence of exposure to a wide range of viral and rickettsial agents. The serological tests showed high antibody levels to flaviviruses (56.9%) and alphaviruses (29.2%), with lesser levels of bunyamwera-viruses (3.8%), RVF (2.3%), and sand fly fever (0.75%). Flavivirus exposure was significantly associated with clinical evidence of liver disease; repeated exposure to flaviviruses was particularly prevalent in those with poor sanitation and who had received previous injections. A significant focus of Ebola and Marburg exposure in Juba has been identified. Clinical evidence of liver disease was evident in 37% of patients studied and 24.6% were HBs-Ag positive. The first 2 HIV-positive individuals from the southern Sudan are reported including one with clinical AIDS. A high prevalence of positive antibodies to *Rickettsia typhi* in the population indicated that the murine typhus was common locally. This study indicates the need for further public health measures in the southern Sudan to control the spread of infections.

Botros *et al*. (1988) stated that from October 1985 through November 1986, 1714 presumably unvaccinated sheep in 13 nomadic flocks located in four provinces in Dakahlia Governorate, in the northeast of Nile Delta, were ear tagged and monitored for acquisition of RVFV antibodies. Sheep were bled at

approximately 3 month intervals and sera were tested for hemagglutination inhibition (HI) antibodies to RVFV. HI reactors were tested for RVFV specific IgM antibody by ELISA and neutrallizing antibody to RVFV by plaque reduction neutralization (PRN) tests. Base line results showed 1.2% prevalence of HI antibody to RVFV with titers from 1:20 to 1:320. All HI positive sera were PRN positive through PRN titers were generally higher than HI titers. No RVFV specific IgM antibody was detected in the HI and PRN positive sera. Throughout the study, no initially sero-negative sheep became positive and no HI positive sheep showed an appreciable increase above initial antibody titre. These data indicate absence of RVFV transmission to sheep in Dakahlia Governorate during the study period.

Gad *et al*. (1989) evaluated the vector competence of parental *Cx. pipiens* populations for RVF virus and investigated variations in the vector competence among different geographic strains of this mosquito in Egypt. *Cx. pipiens* females were fed on viremic hamsters circulating 9.4-10.5 log10 SMICLD50 of virus. Mosquitoes were freezed at different intervals extending between 0-12 days of extrinsic incubation (EI). Transmission experiments started at day 5 of EI when individual females were allowed to re-feed on normal hamsters. The infection rates for the geographic strains tested ranged between 85% and 100% and the transmission rates ranged between 6% and 35%. The transmission of RVF virus to normal hamsters took place at days 9, 12, 15 and 18 of EI by the different tested *Cx. pipiens* strains. Transmitter females contained significantly more virus than the non-transmitters except for the strain of Giza. Most of the infected *Cx. pipiens* individuals were of the non-transmitting type even those with high titers. Barriers at the salivary gland level competing RVF virus transmission are probably present in Egyptian *Cx. pipiens*. RVFV infection was observed to adversely affect *Cx. pipiens*. They found no geographic variations in the vector competence of Egyptian *Cx. pipiens* for RVF virus.

Corwin *et al*. (1992) carried out a sero-survey during October and November 1989 to estimate the prevalence of selected arboviral, rickettsial, and Hantaan viral antibody among schoolchildren samples of from 4 villages in the Bilbeis district, Sharkia G. Blood specimens were obtained from subjects aged 8 to 14 years. ELISA of the sera indicated that the prevalence of antibody was 9% (21/223) for Sicilian sand fly fever, 4% (8/223) for the Rift Valley fever, 3% (15/437) for the West Nile virus and 9% (28/315) for Hantaan (HTN) virus. Antibody was found among 22% (93/418) of the same study subjects against *Coxiella burnetti*, 53% (199/373) against *Rickettsia typhi*, and 37% (137/371) against *R. conorii*.

Corwin *et al*. (1993) found a prevalence of RVF in the Nile Delta 13 years after the major outbreak there.

Arthur *et al.* (1993) mentioned that RVF human infections were first noted in the Aswan Governorate in late May, 1993. Only cases of ocular disease, an

infrequent and late manifestation, were reported. Of 41 cases, 35 were tested serologically and 27 (77%) had RVFV-specific IgM antibodies. The estimated 600-1500 infections occurred in the region. Abortions in cattle and buffalo were seen concurrently and antibodies to RVFV were present in 39% of the domestic livestock, presumably unvaccinated. The virus was isolated from an aborted water buffalo fetus.

CDC (1994) reported that in June 1993, several Egyptians in Aswan G. (1993 population: 952,000) in southern Egypt sought medical care for acute loss of vision following an illness characterized by fever, headache, retro-orbital pain, and myalgias. The ophthalmologists who examined them reported paramacular retinal hemorrhages and edema, and RVF was suspected; serologic studies of these patients confirmed diagnosis of acute RVF (1,2). In August 1993, serologic surveys were conducted in two villages to estimate the prevalence of RVFV-antibody among persons residing in selected rural communities in Aswan Governorate. This report summarizes the findings of the sero-surveys and two nested epidemiologic studies done in the same villages 2 weeks later.

Gad *et al*. (1995) stated that host-selection patterns of mosquitoes were determined over a 1-yr period at Abu Heif, a village in Sharkia Governorate, and has had a history of RVFV transmission. *Cx. pipiens* and *Cx. antennatus* were the most common mosquito species collected, and 8,252 blood meals from both species were analyzed by the precipitin technique. The host availability was estimated by a monthly census of the human and animal populations. Both the mosquito species exhibited opportunistic endophagic behavior. In the bedrooms, 79% of *Cx. pipiens* fed on humans, compared with 53% of the *Cx. antennatus*. In animal sheds, 35% of *Cx. pipiens* and 68% of *Cx. antennatus* fed on sheep or goats. *Cx. pipiens* was primarily anthropophilic (forage ratio=2.7) whereas *Cx. antennatus* was mainly an ovine feeder (forage ratio=2.4). These data denoted that two *Cx*. species probably were involved in the transmission of RVFV in Sharkia G. during the epidemics of 1977 and 1978, *Cx. pipiens* being main responsible for humans transmission, and *Cx. antennatus* for domestic animals. The persistent custom of keeping sheep and goats inside the human dwellings, combined with the opportunistic host selection by the local mosquitoes, continues to make this area receptive to RVFV transmission.

Abu-Elyazeed *et al*. (1996) reported that in the early summer of 1993, an outbreak of RVF was reported among both humans and animals in Aswan G, Upper Egypt. To determine whether RVF infection had spread to the Nile delta region of the country, we carried out a cross-sectional survey of 1181 occupationally exposed abattoir workers (97% male; age 10-72 years) in 15 governorates of Egypt in November 1993. The overall prevalence of anti-RVFV IgM antibody was 2% (in 7 governorates ranged from 0% to 10%). The highest prevalence was in Ismailia (10%) and Sharkia (8%) governorates. But, none of the seropositive subjects

reported having experienced an episode of fever in the 2 months prior to the study. The prevalence of antibody was significantly higher ($P < 0.05$) among workers employed in high-risk jobs as cutting animals' throats (relative risk (RR=2.24)) and handling animal parts (RR=2.37). They stated that abattoir workers represented a useful sentinel population for surveillance of RVF.

Gad *et al*. (1999) stated that in 1993, RVFV reappeared and determined the prevalence and feeding patterns of mosquitoes in five villages where the virus was active. Of the ten species recovered, were *Ae. caspius*, *Cx. pipiens*, *Cx. antennatus*, and *Cx. perexiguus* constituted 99% of >35,000 mosquitoes captured in dry ice-baited CDC light traps. *Ae. caspius* was commonest except at Nag' El Hagar where it was replaced by *Cx. perexiguus*. *Cx. pipiens* ranked 2nd, except at Nag' El Ghuneimiya, where it was replaced by *Cx. antennatus*. Most blood meals analyzed by an ELISA reacted to > or=1 antiserum. *Cx. pipiens* was mainly anthropophagic, and therefore considered the main vector of RVFV among humans. *Ae.caspius* feeds were chiefly from humans, bovines, and equines. *Cx. antennatus* and *Cx. perexiguus* that fed generally on bovines. Mixed blood meals from humans and RVF virus susceptible animals were identified in predominant mosquitoes. Prevalence and host selection, as well as predicted probability for a blood meal being interrupted, indicated that *Ae. caspius* may have served as a bridge vector between humans and bovines in 4 of the villages. *Cx. perexiguus* may have played this role at Nag' El Hagar. Because potential vectors are abundant, the susceptible domestic animals were closely associated with humans, and surveillance of imported livestock was not systematic, they added that RVF sporadically would recur in Egypt.

Abd el-Rahman *et al*. (1999) reported that an epizootic of RVF occurred in Egypt between April and August 1997. The signs among infected cattle and sheep were high fever, icterus, bloody diarrhoea and abortion. Aborted sheep foetuses and sera from the affected herds were collected in the Aswan and AssiutGs, Upper Egypt, for virological and serological examination. A cytopathic effect was detected in Vero cell cultures 48 h after inoculation with the fetal liver and spleen suspensions. The same suspensions caused paralysis and mortalities two to three days post intracerebral injection in mice. The isolated virus was identified using an agar gel precipitation test (AGPT) and a direct fluorescent antibody technique. Seroexamination revealed that all tested sheep (57) and cattle (93) gave positive results to serological tests by using a complement fixation (CF), serum neutralization (SN) and indirect immunofluorescence assay; only 48 (84.2%) of 57 sheep sera and 69 (74.2%) of 93 cattle sera gave positive results using an AGPT. Titrations indicated that SN was more sensitive than CF. Importation of infected ruminants, especially camels from Sudan, was the principal source of infection. Aswan is the nearest Egyptian governorate to the Sudan, was the focus of RVFV infection in Egypt. As a result of high insect

populations, the epizootics of RVF have usually occurred during summer season in Egypt. The reoccurrence of epizootics from time to time indicates failure of the applied RVF vaccination program in Egypt.

Youssef (2001) used RT-PCR to detect RVFV in *Cx. pipiens* mosquito pools collected from Alexandria and Behira governorates o (50 pools each). All mosquito pools were subjected to double sandwich ELISA technique to detect RVFV antigen. Of 100 mosquito pools, only 18 (18%) were positive by ELISA, 10 (20%) out of 50 pools were positive in Behira G. and 8 (16%) were positive in Alexandria G. All positive samples (18) in addition to two negative ones (one was used as a negative control and the other was used as a positive control after addition of 1.0 ml. of 103 inactivated RVF virus) were subjected to RT-PCR. Out of these 18 ELISA positive samples, only seven (38.89%) were positive for RVFV by RT-PCR. The results suggested the possibilities of existence of other phleboviruses that cross react with RVFV.

El-Esnawy (2001) determined arboviral etiology in those workers, 264 serum samples were obtained from the workers in four sewage treatment plants (STPs) during January and October 1999. ELISA-IgG and IgM detected WestNile (54.14%), Sindbis (21.97%), RVF (7.95%), Sand-fly Naples (SFN) and Sand-fly Sicilian (SFS) viruses, while, only one recent infection for each of RVF, SFS and SFN (1/264, 0.38%) and 3 persons for SIN viruses. Helwan workers' exhibitted the highest infection rate for most of the studied arboviruses WN, SFN, SIN and SFS. Yoiussef and Donia (2001) examined blood samples of 300 *R. rattus* were trapped from 3 different governorates of Egypt (one hundred each), blood samples were withdrawal and subjected for detection of anti-RVF antibodies by both ELISA and ID techniques. The prevalence rate of antibodies by ELISA were 88 (29.33%) positive out of 300 blood samples, the highest rate was in Behira G. 36 (36%) and the lowest one was in Alexandria G. 22 (22%) while it was 30 (30%) in Minia G. But when ID technique was applied, it gave only 18 (6%) positive samples out of 300 tested blood samples with highest rate in Behira and Minia governorates (8%) and it was only (2%) in Alexandria G. They stated that *R. rattus* make possible candidate as intermediate host in maintenance cycle of RVF in Egypt.

Youssef and Donia (2002) applied A reverse transcriptase (RT-PCR) was to detect Rift Valley Fever Virus (RVF-V) in blood samples of *Rattus rattus* collected from Alexandria, Behira and Minia governorates (100 each). Out of 300 blood samples 29(9.67%) were positive for RVF-Virus by RT-PCR with higher percent in Behira G. rural areas (16%), followed by Minia G. rural areas (13.85%) while the lowest percent was in Alexandria G. urban areas (0.00%). The overall percent in rural areas were (13.5%) while it was only (2.0%) in urban areas. They suggested that *Rattus rattus* plays an important role in the maintenance cycle of RVFV in Egyptian rural areas.

Turell *et al*. (2002) evaluated the potential vectors of arboviruses during the RVF outbreak in the Nile Valley, August, 1993 and collected mosquitoes in villages with known RVFV activity. Mosquitoes were sorted to species, pooled, and processed for the virus isolation by intracerebral inoculation into suckling mice and by inoculation into cell culture. A total of 33 virus isolates was obtained from 36,024 mosquitoes. Viruses were identified by indirect fluorescent antibody testing and consisted of 30 flaviviruses (all members of the Japanese encephalitis complex, most probably West Nile virus (WN) and three alphaviruses (all members of western equine encephalitis complex, most probably Sindbis). The identity of selected viruses was confirmed by reverse transcriptase-PCR and sequencing. *Cx. antennatus* and *Cx. perexiguus* accounted for five (17%) and 23 (77%) of the WNV isolations, respectively. Despite isolation of viruses from 32 pools of mosquitoes (both WN and Sindbis viruses were isolated from a single pool), RVF virus was not isolated from the mosquitoes, even though most of them are known competent vectors collected during an ongoing RVF outbreak. Thus, it should be remembered, that even during a known arbovirus outbreak, other arboviruses might still be circulating and causing disease.

Botros *et al*. (2006) vaccinated318 European cows and 115 buffaloes were vaccinated with the locally prepared Smithburn vaccine, of which, 100 cows and 20 buffaloes were pregnant. The twenty-eight cows aborted within 72 days post-vaccination, buffaloes did not abort. Blood samples collected 77 days post-vaccination from aborted cows, 17 pregnant cows, five pregnant buffaloes, and 32 non-pregnant cows. Sera were tested by ELISA for anti-RVF IgM and IgG. All aborted cows were strongly positive for IgG. Five of 17 cows and two of five buffaloes that did not abort were IgG positive. The percentage of IgM positives in aborted cows was 25% and 0% in non-aborted cows. The percentage of IgG positives in pregnant non-aborted cows was lower than in non-pregnant cows. The percentage of IgG positives of non-pregnant cows was lower than pregnant aborted cows. Virus was isolated from one aborted fetus. Nucleotide sequence of fetus virus was compared to Smithburn of Onderstepoort, local Smithburn and virus isolates from 1993 to 1994 and 1977 RVF outbreaks. Nucleotide sequences of Onderstepoort and Egyptian Smithburn vaccines were almost identical. The sequences of 1993-1994 isolates were identical to 1977 outbreak virus. Virus from the fetus had two mutations; it is apparently a variant that is genetically distant from local Smithburn and Onderstepoort vaccines. The fetus virus was genetically distant from virus of 1993/1994 and 1977 outbreaks. They concluded that antibody response to vaccination with local Smithburn had occurred in some, but not all the cows and buffaloes. The virus isolation from the fetus suggests in utero transmission of used vaccine virus, which resulted in high abortions in European cows.

Kamal (2009) evaluated RVF live attenuated vaccine (Smithburn strain) by using goats as experimental animal. The results indicate that this vaccine cause severe deleterious pathological changes in liver especially in kids and causing abortion in pregnant does. The virus was seen to be propagated inside the hepatic cells forming intranuclear inclusions also seen by E.M. The viral antigens were detected in hepatic cells, gall bladder, endothelial lining of blood vessels, leukocytes, kidneys and heart by using immunoflourescent technique. They concluded that the use of live attenuated vaccine of RVF (Smithburn strain) for immunization of livestock is not safe in Egypt as it considered an endemic area.

Youssef (2009) examined 245 pig blood samples and forty three blood samples of human contacts to the pigs (Veterinarian and assistants, butchers and Abattoir workers) were collected from pigs' abattoir at Alexandria G. Blood samples were subjected to the detection of RVF antibodies by ELISA and HAI techniques. The detection rate of RVF antibodies in pig sera was 37 positive (15.1%) out of 245 tested sera samples. The highest detection rate of positive samples was in winter season (12/58, (20.69%) and lowest detection rate was at summer (7/70, (10.0%), while it was 9 (15.79%) and 9 (15.0%) positive out of 57 and 60 samples in spring and autumn respectively with no significant differences between them. When HAI technique was applied to detect the RVF antibodies in pig sera, it gave only 20 positive samples out of 245 (8.16%) with highest detection rate was also in winter 7 (12.07%) while it was only 1 (1.43%) in summer season with significant differences between the results obtained in the summer season and those of autumn and winter seasons. The history from all human contacts excluded the possibilities of taking neither vaccination nor infection from other sources. The detection rates of antibodies against RVF virus in human contacts were 6 (13.95%) and 3 (6.98%) by ELISA and HAI techniques respectively. They did not exclude the pig's act as a possible intermediate host in the maintenance cycle of RVFV.

Mikhail *et al*. (2009) and Morsy (2012) reported many species of mosquitoes mainly *Culex* all over the Egyptian governorates

Kamal (2011) reported that RVFV caused marked morbidity and mortality in animals and humans. RVFV was introduced for the first time in Egypt in 1977. In the endemic areas, the vector control and vaccination is considering appropriate measures if feasibly done and the used vaccine was completely safe and the vaccination programs covered all susceptible animals. They added that Egypt imported livestock and camels from the African Horn and the Sudan for human consumption. The imported livestock and camels were usually not vaccinated against RVFV. But, in rare occasions, the imported livestock were vaccinated but with unknown date of vaccination and the unvaccinated control contacts were unavailable for laboratory evaluations. Also, large number of the imported livestock and camels are often escaped slaughtering for breeding which led to

the spread of new strains of FMD and the introduction of RVFV from the enzootic African countries. The article gave general picture on the Egyptian situation of RVF to help in control.

Ali *et al*. (2011) stated that the abortion rates on beef and dairy cattle farms usually did not exceed 10% significant economic losses because of abortion storms could be encountered. The determining the cause of abortions was usually a challenge and it generally remains obscure in more than 50% of the necropsy submitted fetuses. Bovine viral diarrhea and bovine herpesvirus-1 are the most common viruses causally associated with bovine abortions in farmed cattle globally. RVFV and the bluetongue virus are important insect-transmitted abort-genic viruses. The geographic distribution of these two viruses is primarily dependent on the distribution of the insect vector, but direct transmission is possible. No doubt, global warming and subsequent insect vector expansion, coupled with the increase in international trade of animals and animal products, have been important factors in the update viruses'geographic advances. Bovine herpesviruses-4 and 5 in cattle, as well as other less frequent vector-borne viruses including epizootic hemorrhagic disease virus, Aino virus, Wesselsbron virus and lumpy skin disease virus were evaluated.

Hanafi *et al*. (2011) mentioned that in June, 2003, an Egyptian hospital-based electronic disease surveillance system recorded increased cases of the acute febrile illness from governorates in the Nile Delta. In response to a request for assistance from the Egyptian MOH and the WHO, the NAMRU-3 provided a assistance in identifying the cause and extent of this outbreak. Testing of human clinical samples (n=375) from nine governorates identified 29 cases of the RVF viremia that spanned the period of June to October, and a particular focus of disease in Kafr el-Sheikh G. (7.7% RVF rate of infection). The veterinary blood samples (n=101) in Ka-fr el-Sheikh were screened by the immunoassay for RVFV-specific IgM identified probable the recent cattle (10.4%) and sheep (5%) infections. The entomologic investigations focused in rural, rice growing villages in the Sidi-Salim district of Kafr el-Sheikh during the August-September, 2003, were tested host-seeking female mosquitoes for pathogenic viruses. Three isolates of RVFV were obtained from 297 tested pools of the female mosquitoes and all the three RVFV isolates came from *Cx. antennatus*. While *Cx. pipiens* was the primary vector of RVFV in Egypt and was often the most common man-biting species found, *Cx. antennatus* was the dominant species captured at the 2003 outbreak location in Kafr el-Sheikh G. This was the first time to find Egyptian *Cx. antennatus* naturally infected with RVFV.

In Sudan

Hassanain *et al*. (2010) stated that since the first isolation of the RVFV in 1930s, there were several epizootics outbreaks in the tropic mainly in Africa including Sudan. They reported RVFV hospitalized feverish patients (New Halfa hospital) ELISA-IgG in 122

(81.8%) of the sera from these 149 patients with fever of unknown origin. Hassan *et al*. (2011) reported that during 2007 a large RVF outbreak occurred with a total of 747 confirmed human cases including 230 deaths (case fatality 30.8%); although it has been estimated 75,000 were infected. It was most severe in White Nile, El Gezira, and Sennar states near to the White Nile and the Blue Nile Rivers. Notably, RVF was not demonstrated in livestock until after the human cases appeared and unfortunately, there are no records or reports of the number of affected animals or deaths. Ideally, animals should serve as sentinels to prevent loss of human life, but the situation here was reversed. An animal contact seemed to be the most risky dominant factor followed by animal products and mosquito bites. Outbreak followed an unusually heavy rainfall with severe flooding and previous studies on RVF suggested that RVFV is endemic in parts of Sudan.

In Saudi Arabia

Al-Afaleq and Hussein (2010) found that August-September 2000, an overwhelming outbreak of RVF struck the southwestern part of Saudi Arabia and adjoining Yemeni territories. During the outbreak, which was the first ever to be recorded outside Africa, around 40,000 animals, mostly sheep and goats, died or aborted and 883 cases, with 124 deaths, were recorded among humans in Saudi Arabia. An additional 1328 human cases, with 166 deaths, were recorded in northwestern Yemen. Vector studies in Saudi Arabia showed *Ae. vexans arabiensis* and *Cx.* (*Culex*) *triteniorynchus* as main vectors of RVF in the region. Both of these species and several others, which could be potential vectors of the virus, occur throughout the Kingdom. Al-Afaleq *et al*. (2012) studied prevalence of IgG antibodies against RVFV in 22 major localities in five ecologically different regions of Saudi Arabia where vaccination against RVF virus was not practiced. The total of 3,480 sheep, goats, cattle and camels with no previous history of vaccination against RVFV was randomly tested. All tested animals were negative for ELISA-IgG antibodies against the virus except 4/1,508 sheep and 3/ 913 goats. All animals were clinically normal and they concluded that the detected cases were either false positive or vaccinates smuggled from the outbreak zone.

Nfon *et al*. (2012) stated that RVF, a re-emerging mosquito-borne disease of ruminants and man, was endemic in Africa but spread to Saudi Arabia and Yemen, meaning it could spread even further.

Al-Azraqi *et al*. (2012) examined a random samples of the general population (patients and their relatives) attending the outpatients' clinics for any reasons in Jizan, Aseer and Al-Qunfuda, Out of 2322 persons only 139 were positive for RVF-specific IgG (6.0%), but none were sero-positive to specific IgM. They revealed zero prevalence of specific IgM and IgG among pre-school children born after the 2000-2001 outbreaks. Using multivariate binary logistic regression analysis to identify the risk factors associated with sero-positive RVF IgG, the following significant risk factors

were identified: lack of electricity, having animals in the house, history of slaughtering animals, contact with or transporting aborted animals.

Generally, Hotez *et al*. (2012) reported that the neglected tropical diseases (NTDs) are highly endemic but patchily distributed among 20 countries and almost 400 million people of the Middle East and North Africa (MENA) region, and the disproportionately affect an estimated 65 million people living on less than US$2 per day. The NTDs, including the soil-transmitted nematodes, filariasis, schistosomiasis, fascioliasis, leprosy, trachoma, leishmaniasis (*L. major*) and (*L. tropica*), fascioliasis, cystic echinococcosis, brucellosis, dengue, DHF, RVF and Alkhurma hemorrhagic fever have being also emerged. The conflict and human and animal migrations are the social key determinants in preventing the control or elimination of NTDs in the MENA.

Indran and Ikegami (2012) stated that Rift Valley fever (RVF) is endemic to sub-Saharan Africa, and was spread into Madagascar, Egypt, Saudi Arabia, and Yemen, causes hemorrhagic fever, neurological disorders or blindness in humans, and high rate abortion and fetal malformation in ruminants. It is classified as a Category A Priority pathogen and overlap select agent by CDC/USDA due to its potential impact on public health and agriculture, with a gap in the safety and immunogenicity in traditional RVF vaccines; formalin-inactivated RVFV vaccine TSI-GSD-200 requires three doses for protection, and the live-attenuated Smithburn vaccine has a risk to cause abortion and/or fetal malformation in pregnant ruminants. They concluded that next generation vaccines would probably superior to traditional ones in safety or immunogenicity, and data of safety and immunogenicity still limited to specific animal models and how the variety of assay done by different laboratories affects the interpretation of results.

Conclusion

Generally speaking, Rift Valley fever is a disaster zoonotic mosquito-borne infectious disease. Outbreak always emphasizes the need for collaboration between public health veterinary and authorities, the entomologists, environ mental specialists, and biologists, as the best strategy towards prevention and control of RVF. An RVF outbreak results in human disease, but also large economic loss with an impact beyond the immediate influence on the directly affected agricultural producers. While local political will, strengthened the international and intersect co-operative efforts for surveillance, the mass drug administration, the vaccination, animal immunization and mosquitoes control are essential for elimination of RVF.

The vaccination is a must for persons at high risk of infection as the research laboratory members, veterinarians and nurses dealing with RFV-patients.

Undoubtedly, all the febrile travelers should be investigated to identify the cause of fever including Dengue fever, Congo hemorrhagic fever, malaria and RFV.

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