Rift Valley fever among children and adolescents in southwestern Saudi Arabia

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Infectious diseases; Epidemiology; Emerging diseases

\textbf{Summary}
\textbf{Purpose:} Rift Valley fever (RVF) virus has expanded its geographical range, reaching Asia in 2000. This work investigated RVF seroprevalence among children born after the 2000–2001 outbreak in Saudi Arabia and compared it with the seroprevalence of adolescents born before the outbreak.

\textbf{Design:} In a seroepidemiological study in southwestern Saudi Arabia (Jazan, Aseer, and Al-Qunfuda), a random sample of 389 children and adolescents was investigated. Data were collected regarding the subjects’ sociodemographic status, housing conditions, and animal contact. Blood samples were collected and tested for RVF-specific IgG and IgM.

\textbf{Results:} None of the study samples were found to be seropositive for anti-RVF virus IgM. None of the study subjects aged 1–8 years (born after the outbreak) were positive for RVF-specific IgG. In contrast, 14 subjects (4.8%) aged 9–19 years (born before the outbreak) were positive for RVF-specific IgG. Among adolescents in our study, 4.9% were positive for anti-RVF IgG. This study showed that among adolescents, a history of contact with aborted animals (aOR = 13.361, 95% CI = 5.091–35.072) and transporting aborted animals (aOR = 18.861, 95% CI = 11.125–31.622) were significant risk factors.

\textbf{Conclusions:} Despite the low virus activity recently reported among animals, neither clinically apparent RVF infections nor outbreaks among humans have been documented, indicating that the control measures taken by the Ministry of Agriculture and Ministry of Health are effective.

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Introduction

Rift Valley fever (RVF) is an acute zoonotic viral disease that affects ruminant animals and humans. The disease is named after the Rift Valley of East Africa, where the etiologic virus was first isolated in 1930 during an investigation into an epidemic of infections among sheep on a farm in the Rift Valley in Kenya [1]. On 11 September 2000, the Ministry of Health (MOH) of the Kingdom of Saudi Arabia received reports of unexplained severe hepatitis in 7 patients from the Jazan region near the southwestern border of Saudi Arabia. On 15 September 2000, laboratory tests performed at the CDC confirmed the diagnosis of RVF. By the end of the outbreak (22 September 2001), the total number of hospitalized cases was 884, of which 843 were laboratory confirmed [2]. No RVF outbreaks or human cases have been reported in the Kingdom of Saudi Arabia since then.

The objectives of the present study were to determine the seroprevalence of RVF virus infection among children born after the outbreak and compare it with the seroprevalence of adolescents born before the outbreak in the southwestern regions of Saudi Arabia. This study also aimed to identify potential risk factors leading to RVF virus infection.

Materials and methods

Ethical statements

The protocol for this study was reviewed and approved by the ethical committee of King Khalid University. Written informed consent was obtained from each individual (or his/her guardian for children).

Study area

The study area included the Jazan and Aseer regions and the Al-Qunfuda area in the Makkah region. The Jazan region is located in southwestern Saudi Arabia, bordering the northwestern region of Yemen. The climate is hot and humid most of the year. The majority of the local inhabitants work as farmers and raise domesticated animals for their livelihood. Electricity is not yet available in the vast majority of the remote villages. The Aseer region extends from the high mountains of Sarawat (at an altitude of 3200 m above sea level) to the Red Sea. This region borders Jazan and is located to its northeast. Al-Qunfuda is further northward along this coastal plain in the Makkah region. The social and environmental conditions in the three study areas are similar. The health care facilities in the study areas include 13 hospitals and 134 primary health care centers (PHCCs) in Jazan, 17 hospitals and 253 PHCCs in Aseer, and 1 hospital and 29 PHCCs in Al-Qunfuda [3].

Sampling procedures

Five areas in the Jazan region (Jazan, Baysh, AboArish, Al Ardah, and Samtah), four areas in the Aseer region (Al Birk, Al Gahma, Muhayeel, and Al Majardah) and the Al-Qunfuda area in the Makkah region were selected as target sites for the present study. The selected areas reported Rift Valley fever cases during the 2000—2001 outbreak. In late 2008, a random sample of children and adolescents attending the outpatient clinics of these hospitals for any reason was included in the study.

Questionnaire-based interviews

A comprehensive questionnaire-based interview was offered to all children (or guardians) and adolescents. The questionnaire included questions on sociodemographic data, environmental and housing conditions, and exposures during the previous 6 years.

Blood sampling

Venous blood samples (approximately 5—10 ml) were collected from each participant in plain tubes and allowed to clot at room temperature (range 18—20 °C). The samples were then centrifuged at 10,000 rpm for 10 min, and the separated sera were aliquoted into two portions and stored at −20°C until they were transported in Styrofoam boxes containing dry ice (solid carbon dioxide, −40°C) to the Virus Lab of the Abha College of Medicine. All samples were received in a frozen state and grouped by the area of collection. The samples were stored in labeled boxes in deep freezers at −20°C.

Testing for serum anti-RVF IgG and IgM antibodies

RVF kits were provided as bulk reagents to be further processed prior to testing. The RVF IgG ELISA kit (batch # 2007) was manufactured, standardized and provided by the National Institute of Communicable Diseases, Special Pathogens Unit, Johannesburg, South Africa. All relevant reagents, including the controls, were supplied with the kits. RVF-IgM assays were performed using these kits.
Table 1 Seroprevalence of RVF IgG by age group and location.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Seroprevalence of RVF IgG</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
</tr>
<tr>
<td>Age group related to outbreak of 2000</td>
<td></td>
</tr>
<tr>
<td>1—less than 9 years (born after the outbreak)</td>
<td>0/98</td>
</tr>
<tr>
<td>9—19 years (born before the outbreak)</td>
<td>14/291</td>
</tr>
<tr>
<td>Chronological age group</td>
<td></td>
</tr>
<tr>
<td>Preschool age (1—less than 6 years)</td>
<td>0/62</td>
</tr>
<tr>
<td>Pre-adolescent age (6—less than 10 years)</td>
<td>0/43</td>
</tr>
<tr>
<td>Adolescents (10—19 years)</td>
<td>14/284</td>
</tr>
<tr>
<td>Location</td>
<td></td>
</tr>
<tr>
<td>Aseer region</td>
<td>6/103</td>
</tr>
<tr>
<td>Jazan region</td>
<td>8/274</td>
</tr>
<tr>
<td>Al-Qunfuda</td>
<td>0/12</td>
</tr>
</tbody>
</table>

according to the manufacturer protocols, and the results were evaluated accordingly.

Statistical analysis

The data were coded, validated, and analyzed using the SPSS PC+ version 13 software package. The frequency, percentage, arithmetic mean, median and mode were used to characterize the data. The Chi-square test was used to assess significance at the 5% level. Binary logistic multivariate analysis, adjusted odds ratios and 95% confidence intervals were used to identify potential risk factors for exposure among adolescents.

Results

Description of the study sample

The present study included 389 children and adolescents. There were 62 preschool children (less than 6 years), 43 pre-adolescents (6—less than 10 years) and 284 adolescents (10—19 years). There were 98 children aged 1—8 years who were born after the outbreak in 2000, and 291 persons aged 9—19 years who were born before the outbreak. The study sample included 256 males and 133 females. The subjects were from Aseer (103), Jazan (274) and Al-Qunfuda (12). Regarding occupation, 62.8% (27) of pre-adolescent children were students, and the rest were not in school. The majority of adolescent females were non-working housewives (58, 62.8%), whereas the majority of male adolescents were students (141, 73.8%), followed by shepherds and manual workers (39, 20.4%). The rate of school attendance for female adolescents (69, 74.2%) was similar to that for males.

Housing conditions

The majority of the participants lived in traditional non-concrete houses (249, 64.0%). Only 39.0% of the subjects lived in houses with electricity. Fifty-one percent (200) kept sheep in their houses (alone or with other animals, such as goats). Cows were present in the houses of 7.5% (29) of participants. In contrast, camels were only present in the houses of 3.6% (14) of the participants. Forty percent of subjects (156) lived in houses equipped with water basins for animals.

History of contact with animals in the past 6 years

Seventeen percent (49) of the adolescents had a history of participating in the slaughter of animals in the past 6 years, 7.4% (21) of adolescents had a history of contact with aborted animals, and 4.2% (12) of adolescents had a history of transporting aborted animals.

Seroprevalence of Rift Valley fever virus infection

None of the study samples were seropositive for anti-Rift Valley fever IgM. In contrast, 14 (3.6%) of the study samples were positive for anti-Rift Valley fever IgG. None of the samples from preschool and pre-adolescent children were IgG seropositive. Table 1 shows that none of the samples from children aged 1—less than 9 years (born after the outbreak) had RVF-specific IgG. In contrast, 14 subjects (4.8%) aged 9—19 years (born before the outbreak) were positive for RVF-specific IgG. Among adolescents, 4.9% were positive for anti-Rift Valley fever IgG. The highest seroprevalence was
Table 2  Multivariate analysis, adjusted Odds ratio (aOR) and antecedent 95% confidence intervals (CI) of potential risk factors determining seropositive RVF IgG among adolescents in southwestern Saudi Arabia.

<table>
<thead>
<tr>
<th>Variable</th>
<th>aOR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Lower Upper</td>
</tr>
<tr>
<td>Gender: females vs. males</td>
<td>3.711</td>
<td>0.604 12.803</td>
</tr>
<tr>
<td>Housing condition: traditional vs. concrete</td>
<td>3.527</td>
<td>0.308 14.383</td>
</tr>
<tr>
<td>Housing electricity: yes vs. no</td>
<td>2.516</td>
<td>0.236 8.835</td>
</tr>
<tr>
<td>Having animals in house: yes vs. no</td>
<td>2.378</td>
<td>0.243 12.240</td>
</tr>
<tr>
<td>Having animal water basins in house: yes vs. no</td>
<td>2.797</td>
<td>0.471 9.137</td>
</tr>
<tr>
<td>History of slaughtering animals: yes vs. no</td>
<td>1.004</td>
<td>0.045 3.311</td>
</tr>
<tr>
<td>Contact with aborted animals*: yes vs. no</td>
<td>13.361</td>
<td>5.091 35.072</td>
</tr>
<tr>
<td>Transporting aborted animals*: yes vs. no</td>
<td>18.861</td>
<td>11.125 31.622</td>
</tr>
</tbody>
</table>

* Significant (P < 0.05).

observed in the Aseer region (6.6%, 6.4%), followed by the Jazan region (8.5%, 4.5%). The highest seroprevalence in different hospitals was observed in Al Birk in the Aseer region and Al Ardah in the Jazan region (18.3% for each).

In the univariate analysis, the seroprevalence of anti-RVF IgG among male adolescents was 3.1%. In contrast, the prevalence among female adolescents was 8.6%. The observed difference in prevalence by sex was statistically significant ($\chi^2 = 3.98, P = 0.048$).

Risk factors for Rift Valley fever IgG seropositivity among adolescents

After adjusting for other potential risk factors, the study showed that a history of contact with aborted animals (aOR = 13.361, 95% CI = 5.091–35.072) and a history of transporting aborted animals (aOR = 18.861, 95% CI = 11.125–31.622) were significant risk factors (Table 2) among adolescents. In contrast, sex, housing conditions (concrete or traditional) and having water basins for animals inside the house were not significant with respect to the seroprevalence of anti-Rift Valley fever IgG among adolescents.

Discussion

It is speculated that the RVF virus was introduced to the Arabian Peninsula in 1997–1998 during the RVF epidemic in East Africa via the introduction of infected livestock or windborne infected mosquitoes. It is also hypothesized that climatic conditions have contributed to sufficient vector populations to support transmission in Saudi Arabia [4].

The present study documented that none of the children born after the outbreak of 2000–2001 had any evidence of previous exposure to or a recent infection with RVF virus, as documented by the lack of RVF-specific IgG and IgM. In humans, RVF virus infection generates a primary antibody response of the IgM class that lasts for three months, whereas lifelong immunity is mediated by the IgG class [1].

Among adolescents, an overall seroprevalence of 4.9% was found in the study regions following the RVF outbreak of 2000–2001. Human studies conducted during RVF outbreaks have documented higher rates in Egypt [5,6], Sudan [7,8], the Central African Republic, Cameroon [9,10], Nigeria, and Kenya [11].

The highest seroprevalence of anti-Rift Valley fever IgG among adolescents was observed in Al Birk in the Aseer region and Al Ardah in the Jazan region. These areas were the initial sites of the 2000 outbreak. RVF virus transmission is largely governed by the habits of the locals in relation to living with, handling, and slaughtering animals. The disease was notably uncommon in children younger than 10 years of age, an observation that has been noted elsewhere [11].

Recent studies using ELISAs similar to our study documented a similar variation in the prevalence of RVF-specific IgG during an interepidemic period in Kenya, with an overall seroprevalence of 10.8% (among all age groups) [12–14]. The higher rate in Kenya is most likely due to the cumulative effects of previous exposures to RVF virus. In our study, the lower seroprevalence documented in areas far from the initial site of the outbreak could be attributed to the restriction of animal movement to and from the affected areas during the outbreak in addition to health education and the massive vector control measures that were immediately implemented [6].

Among the adolescents included in the present study, the rate of seroprevalence among females was higher than among males (8.6% and 3.1%, respectively). In addition to handling meat during
cooking, females milk domestic animals and assist in their deliveries. Some females also butcher and skin animals for the local markets. In contrast, in a cohort of 834 laboratory-confirmed cases among 884 cases reported to the Saudi Ministry of Health during the outbreak, Madani et al. [2], documented a male-to-female ratio of 4:1. This apparent discrepancy may be because the present study was conducted during the post-outbreak period and detected individuals who had been subclinically infected and were thus not reported to the Ministry of Health during the outbreak. Furthermore, because no younger children exhibited signs of RVF virus exposure and no older children were IgM positive, the results of the present study suggest that the recent RVF virus activity in the study area was low or nonexistent among humans.

The present study showed that a history of contact with aborted animals and a history of transporting aborted animals were significant risk factors among adolescents. Adolescents in the study area usually help family members to handle animal tissues during the slaughtering, butchering, or skinning of animals; assist with animal births; perform veterinary procedures; and/or dispose of carcasses or fetuses. The identification of risk factors related to animals is not a unique finding, and similar risk factors have been documented by others [12,15,16].

Despite the low RVF activity recently reported among animals [17,18], the present study appears to indicate that measures undertaken by the Ministry of Agriculture have been able to effectively control RVF outbreaks among humans in southwestern Saudi Arabia. The inherent bias-related limitation of the present study was the use of a convenience sample of individuals attending the outpatient clinics of the region for any reason.

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Competing interests

None declared.

Ethical approval

The protocol for this study was reviewed and approved by the ethical committee of King Khalid University. Written informed consent was obtained from each individual (or his/her guardian for children).

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