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EPIZOOTIOLOGY AND CONTROL MEASUREMENTS OF FOOT AND MOUTH DISEASE (FMD) IN SAUDI ARABIA FROM 1999 TO 2004

(With One Table and One Figure)

By

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وبائية مرض الحمى القلاعية وطرق السيطرة عليه بالمملكة العربية السعودية فى الفترة ما بين ١٩٩٩ و ٢٠٠٤ م

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تم تسجيل عدد ستة اندلاعات لمرض الحمى القلاعية بالمملكة العربية السعودية خلال الفترة ما بين يولية ١٩٩٩ إلى يونية ٢٠٠٤م، خمسة منها كانت للفيروس المنتمى للنوع المصلى (O) وواحدة كانت للفيروس المنتمى للنوع المصلى (SAT 2). وان اربع اندلاعات للمرض قد اصابت الابقار فقط وان الاندلاعين الاخريين قد اصابا الابقار والاغنام والماعز، وان اندلاعتان شديدتان كانت للفيروس (O) بمناطق المملكة الخمسة (الوسطى والشرقية والغربية والشمالية والجنوبية) فى الفترات ما بين فبراير إلى أبريل لعام ٢٠٠١م وأغسطس إلى نوفمبر لعام ٢٠٠١م. وأن اندلاعتان محدودتان للفيروس (O) قد سجلت بالمنطقة الوسطى من المملكة في الفترة من اكتوبر إلي نوفمبر لعام ١٩٩٩م ومن مارس إلي أبريل لعام ٢٠٠٠م وأن الاندلاعه المحدودة الأخيرة للفيروس (O) قد حدثت مؤخراً بالمنطقة الجنوبية من المملكة بجازان في شهر يونيه لعام ٢٠٠٤م. وأن الاندلاعه الوحيده للفيروس (SAT 2) قد سجلت لآول مره بالمملكة في مارس وأبريل لعام ٢٠٠٠م بالخرج (المنطقة الوسطي) متزامنة مع اندلاعة الفيروس (O). تم حساب معدلات الإصابة والنفوق إلي العدد الكلي من الحيوانات ومعدلات النفوق إلي العدد المصاب من الحيوانات خلال الاندلاعات الستة. كانت أكثر أعراض المرض شيوعاً في الحيوانات المصابة هى الحمى الشديدة وفقدان الشهية والتهاب الفم الحويصلي والتهاب جلد القدم والضرع والحلمات الحويصلي. تم استخدام اختبار الاليزا الساندوتشي الغير مباشر للكشف عن الفيروس وتحديد نوعه المصلي في عينات الأنسجة المجمعه من الحيوانات المصابة وتم إرسال بعض العينات الإيجابية منها إلي مختبر بيربريت المرجعي (المعمل المرجعي العالمي لمرض الحمى القلاعية) بالمملكة المتحدة وذلك لتحديد العلاقة الانتيجينية بين العترات المعزولة والعترات الداخله في صناعة اللقاح المستخدم

بالمملكة حيث يتم تكبير القطعة 167-bp من الجين VPI وحساب تسلسل النيكلوتيدات 472-639 بها. وقد أظهرت النتائج أن جميع عترات الفيروس (O) المعزولة من المناطق المختلفة بالمملكة أثناء الاندلاعات من يوليو ١٩٩٩م إلي يناير ٢٠٠٢م كانت متماثلة وذات ارتباط وثيق بعترة O1 Manisa القياسية المستخدمة فعلياً في إنتاج لقاح مرض حمى القلاعية (التركيبة السعودية). وقد انتهت الدراسة إلي التشديد على أهمية استمرار برنامج التحصين الوطني لمرض الحمى القلاعية في الإبقار في جميع مناطق المملكة. وتنفيذ تقنين منع انتقال قطعان الإبقار والإغنام والماعز أثناء فترة ظهور المرض في مناطق المملكة المختلفة. وإن عدم تسجيل اندلاعات للمرض بالمملكة في الفترة من مايو ٢٠٠٢م إلي مايو ٢٠٠٤م يمكن اعتباره دليل على نجاح إجراءات السيطرة المطبقة وينصح بإجراء الدراسات الوبائية الجزئية واستمرار مراقبة العلاقة بين عترات الحقل وعترات القاح المستخدم.

SUMMARY

Over a period of five years from July 1999 to June 2004, five outbreaks of FMD serotype O and one outbreak of FMD serotype SAT 2 were reported among livestock in Saudi Arabia. Four out of the six outbreaks were limited to cattle, while the other two outbreaks were expanded to all livestock including cattle, sheep and goats. Two extensive outbreaks of FMD virus serotype O were recorded in the five regions of the country (central, eastern, western, northern and southern regions) in February-April/2001 and August/2001-November/2001. While two out of three limited outbreaks of FMDV serotype O were occurred only in the central region in October-November/1999 and in March-April/2000. The last outbreak was reported recently in the southern region (Jizan) in June/2004. Infection with FMDV serotype SAT 2 was reported for the first time in Saudi Arabia during an outbreak of FMDV serotype O in the central region (AL-Karj, Riyadh) on March-April/2000. Morbidity, mortality and case fatality rates during six FMD outbreaks from 1999 to 2004 in Saudi Arabia were calculated. The most common clinical symptoms were high fever, anorexia, vesicular stomatitis, vesicular dermatitis in coronet and cleft of feet, teat and udder. Indirect sandwich-enzyme linked immunesorbent assay (IS)-ELISA was used for detection and typing of FMD virus in the collected tissue specimens. Some selected tissue specimens which given positive result to FMD virus-antigen detection by indirect sandwich-ELISA were submitted to FMD reference world laboratory, Pribright, UK for determination of the antigenic relationship between field and vaccinal strains. Where, A 167-bp fragment, of VP1 gene 472-639, was amplified and sequenced. The results indicated that field strains of FMD virus serotype O isolated from different regions in Saudi Arabia during FMD outbreaks between July

1999 and January 2002 were homolgous and closely related to O1 monisa strain of FMDV serotype O that already incorporated in formulation of Saudi vaccine against FMD. The current study concluded that national vaccination program against FMD in Saudi Arabia should be strictly continue in traditional cattle population in all the kingdom regions. Legalization of the restriction of the animal movement should be practiced for cattle, sheep and goats populations during the risk period of FMD in different localities in SA. Absence of FMD outbreaks in SA between May/2002 and May/2004 may act as an indicator for the success of the applied control measures. Molecular epidemiological studies and monitoring of the relationship between the vaccine and the field viruses should be continued.

Key words: *Control measures - Epizootiology – Foot and mouth disease (FMD) – Gene sequencing - Indirect sandwich-enzyme linked immunesorbent assay (IS)-ELISA - Saudi Arabia (SA) – Serotypes – Vaccine*

INTRODUCTION

Foot-and-mouth disease (FMD) is the most transmissible contagious viral disease of all cloven hoofed animals. Clinically the disease is characterized by high fever, anorexia, acute vesicular stomatitis and vesicular dermatitis in feet and udder, high rate of morbidities, and mortalities in newborns (Radostits, *et. al.* 2000). FMD is caused by a virus of the genus Aphthovirus, family Picornaviridae. There are seven serotypes of FMD virus, namely O, A, C, SAT 1, SAT 2, SAT 3, and Asia 1, that infect cloven hoofed animals. Infection with any one serotype does not confer immunity against another. Within serotypes, many subtypes can be identified by biochemical and immunological tests (OIE, 2000).

FMD is endemically or sporadically infected the most regions in Africa and Asia, particularly countries in the Middle East. In vast majority of the Arabian Peninsula countries, epidemics of different serotypes of FMD virus repeat breaks out; this seems to be due to continuous importation of livestock from many countries in Africa and Asia (Hafez *et. al.* 1994).

In Saudi Arabia (SA), epidemics of FMD were caused by serotype O, A, C, Asia 1 and SAT 1. Outbreaks caused by serotype O were recorded in 1970-73, 1978 and 1980-1998; epidemics caused by serotype A were reported in 1973, 1976, 1984, 1986-1987 and 1991-1993; outbreak caused by serotype C was recorded in 1984; epidemics

caused by serotype Asia I were reported in 1982 and 1992. Epidemic caused by serotype SAT 1 was recorded in 1962-1970 (FAO, 1994; Farag *et. al.* 1998b).

The disease occurs in the form of outbreaks that rapidly spread from herd to herd before it is controlled (Radostits *et. al.* 2000). Outbreaks of FMD repeatedly occur among the population of ruminant animals in various regions of Saudi Arabia (Hafez *et. al.* 1993a).

The demonstration of FMD viral antigen is sufficient for a positive diagnosis. Complement fixation (CF) has been the traditional test for diagnosis, but it has been replaced in many laboratories by the enzyme-linked immunosorbent assay (ELISA), as this is more specific and sensitive and is not affected by pro- or anti-complementary factors (OIE, 2000). It was suggested that nucleotide sequence analysis should be used as a standard method of diagnosis, because when compared with other techniques it more clearly reveals the origin and course of epizootics and offers the possibility of preventing further outbreaks. It is also necessary for determination of the suitability of the current vaccine formulation throughout a genetic comparison between the recent isolates and number of standard strains of FMD virus, belonging to the same serotype (Beck & Strohmaier 1987).

The eradication of FMD in infected countries by the implementation of slaughtering-out is impractical for various reasons, but vaccination with good quality FMD vaccines can help prevent losses in stock production and reduce the overall incidence of the disease (Hunter, 1998). In the country in which control of FMD relies predominantly on vaccination, the stability of the currently used vaccine in high potency is the only way to protect the animals against FMD outbreaks (Farag *et. al.* 1998b).

In implementation of FMD control in SA, by the beginning of 2002, authorities legalized the policy of prevention of livestock transportation between different areas or regions. They applied a national vaccination regime of all the traditional herds of cattle with a polyvalent vaccine of FMD and herds of sheep and goats in vicinity of dairy cattle farms with serotype O vaccine of FMD.

Planning an adequate control program against FMD requires a thorough understanding of the current epizootiological status of the disease (Hafez *et. al.* 1994). The present study was initiated to analyze the obtained epizootiological data of FMD in Saudi Arabia (SA) throughout the last five years, from October 1999 to June 2004, for

purpose of discussing the epizootiological behavior of the disease and efficiency of the undertaken strategies for control of FMD.

MATERIALS and METHODS

Epizootiological data

Epizootiological data, morbidity, mortality and case fatality rates, and clinical signs of FMD in cattle, sheep and goat populations, as well as history of livestock vaccination against FMD were recorded in different localities of Saudi Arabia during the last five years between July 1999 and June 2004.

Specimens for laboratory diagnosis

Specimens of detached tongue epithelium, vesicular fluid and scraped vesicles of the mouth, feet or teat were collected from infected animals on 50% glycerin in 0.04 M phosphate buffer saline PBS pH 7.2-7.6 in special container, and sent in ice box to the section of virology, veterinary diagnostic laboratories, Riyadh.

Laboratory investigations

Indirect sandwich-enzyme linked immunesorbent assay (IS)-ELISA

Commercial IS-ELISA kit for detection and typing of FMD virus in tissue specimens produced by reference world laboratory of FMD, Pirbright, UK was used according to manufacturer's recommendation. The test was developed and validated by Roeder and Le Blanc Smith (1987); Ferris and Dawson (1988). IS-ELISA was carried out in the section of virology, veterinary diagnostic laboratories, ministry of agriculture, Riyadh. It based on sandwich formation in which the polystrine plates are coated with rabbit antisera specific for the different seven serotypes of FMD virus. With the addition of the test sample, antigen (if present) is trapped by the coated rabbit antibodies. Specific Guinea pig-anti-FMD virus detecting antibodies are then added which react with the trapped antigen. The bound Guinea pig antibodies are detected by means of the rabbit anti-guinea pig IgG conjugated with horse radish peroxidase (HRPO) and addition of OPD substrate|chromgen solution. A mean corrected optical density (OD) value of > 0.1 above background indicates a positive result and the serotype of FMD virus can be read.

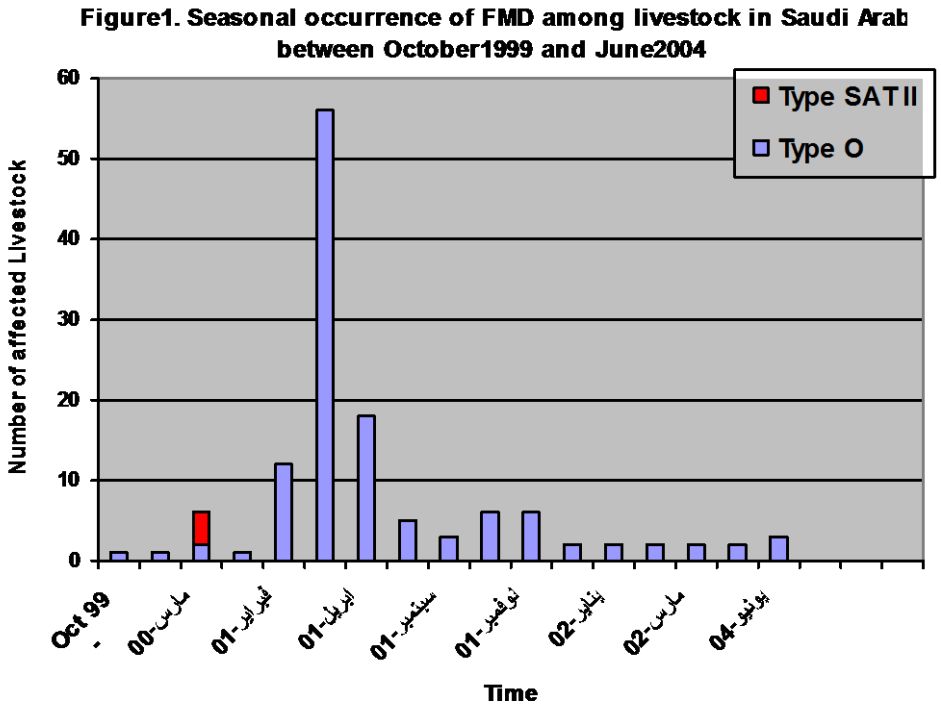
Direct complmentry DNA (cDNA) sequencing

Between 1999 and 2002, selected tissue specimens which given positive result to FMD virus-antigen detection by indirect sandwich-ELISA were sent to FMD reference world laboratory, Pribright, UK for

determination of the percentage of nucleotide difference between field isolates and battery of known strains of the same serotype of FMD virus including strains that incorporated in Saudi vaccine formulation. Where a 167-bp fragment of VP1 gene (472-639) was amplified and sequenced. A value of 15% nucleotide difference was used as a cut-off (Beck & Strohmaier 1987; Samuel & Knowles, 2001a).

RESULTS

Table 1: Represents the prevalence of FMDV in Saudi Arabia between 1999 and 2004. While the seasonal occurrence of FMD in livestock in Saudi Arabia within the period from July 1999 to June 2004 is shown in figure (1).



DISCUSSION

Foot-and-mouth disease (FMD) virus is the most economically important veterinary pathogen due to its highly infectious nature, ability to cause persistent infections and long term effects on the condition and productivity of the many animal species it affects (Knowles & Samuel 2003). Over a period of five years, between July 1999 and June 2004, five outbreaks of FMD serotype O and one outbreak of FMD serotype SAT 2 were recorded among livestock in Saudi Arabia (SA). Four out of the six outbreaks were limited to cattle, while the other two outbreaks were expanded to all livestock including cattle, sheep and goats. Serotype O is the most prevalent of the seven serotypes of FMDV and occurs in many parts of the world (Samuel & Knowles, 2001a).

In all affected regions of Saudi Arabia, a regular manner of typical clinical signs of FMD. including high fever, anorexia, vesicular stomatitis, vesicular dermatitis in coronet and cleft of feet, teat and udder, and mortalities in newborns with variation of its frequency in cattle sheep and goats were observed. A relative high frequency of lameness and mortalities in newborn lambs and kids was recorded in infected sheep and goats flocks. High mortality rate among lambs and kids due to FMD virus infection was previously observed by Hafez, *et. al.* (1995). Lameness, pyrexia and anorexia were the most common clinical signs of FMD in the affected sheep and goats flocks (Farag, *et. al.* 1998a). Typical cases of FMD are characterized by a vesicular condition of the feet, buccal mucosa and, in females, the mammary glands. Clinical signs can vary from mild to severe and fatalities may occur, especially in young animals (OIE, 2000). Clinically, the onset of the disease is heralded by a precipitate fall in milk yield and a high fever accompanied by severe dejection and anorexia, followed by the appearance of an acute painful stomatitis with abundant salivation. Vesicles and bullae appear on the buccal mucosa, dental pad, tongue, on the feet and the coronet. Rupture of the vesicles causes acute discomfort and the animal is grossly lame (Radostits *et. al.* 2000).

Morbidity, mortality and case fatality rates during the six FMD outbreaks between 1999 and 2004 in livestock in Saudi Arabia were variable. During five outbreaks of FMDV serotype O, a wide range of morbidities (13.6%-100%), mortalities (0%-0.9%) and case fatalities (0%-5%) was reported among traditional cattle herds with no data of vaccination against FMD and no history of previous exposure to FMDV infection. This means that high percentage of the traditional cattle

populations in Saudi Arabia were susceptible to infection with field virus of FMD as result of irregular vaccination or complete neglection of vaccination against the disease by the animals' owners. The very low mortality rates in these animals were expected because the traditional cattle herds in SA are mostly not raised as breeding cattle stock.

On the other hand, narrow range of morbidities (2.6%-3.4%) without mortalities were recorded in five vaccinated dairy cattle herds during 3 out of five FMD serotype O outbreaks. This is due to strict vaccination of dairy cattle farms every three or four months, since 1990 and until now, with a gel adjuvant polyvalent FMD vaccine containing strains OBFS and O1manisa/03039 of serotype O which has always been closely related or homologus to the local strains of FMD virus serotype O (Samuel *et. al.* 1997; Farag *et. al.* 1998b).

Presence of very low morbidity rates due to FMDV serotype O infection in the vaccinated dairy cattle herds are reflect the vaccination breaks which occur periodically in Saudi Arabia. Such FMD vaccination breaks can be explained by the presence of non- or partially-immune cattle due to individual animal variation in the immune response particularly to primary vaccination of yearling's heifers or first lactation cows, which exposed to strong challenge virus evoluted mostly from FMD epidemics outside the dairy farm or sometimes from a carrier foci inside the farm itself as a result of previous exposure to FMD virus infection as reported by Hafez *et. al.* (1993b). Pay (1984) stated that immune cattle in dairy farms may be infected with FMD when exposed to strong challenge virus during outbreaks. Again, absence of moratalities in newborn calves in dairy cattle herds during outbreaks of FMDV serotype O is confirm the excellent immune status of the vaccinated dams. Also, newborn calves in dairy cattle farm are mostly received a pooled colostrum of vaccinated dams (personal communication)

During the most extensive outbreak of FMDV serotype O that occurred between February and April 2001, one herd of vaccinated feedlot cattle was infected. The morbidity and mortality rates were 17.9% and 1.9% respectively. This result has proved that such fattening bulls might not adequately fed colostrum from their immunized dams or improperly vaccinated against FMD.

Therefore, two out of the six FMD outbreaks in SA were serious among small ruminants; where 36 sheep and 11 goats flocks were clinically affected with FMDV serotype O in periods of 2-4/2001 and 8/2001 to 4/2002. The rates of morbidity, mortality and case fatality

were ranged from 13.4% to 66.4%, from 0.0% to 7.8% and from 0% to 17.5% respectively in sheep, and from 9.7% to 53.8%, from 0.0% to 6.6% and from 0% to 12.3% respectively in goats. It is clear that infectivity of Saudi strains of FMD virus serotype O was relatively similar in both sheep and goats. Previously, morbidity rates among small ruminants were ranged from 10% to 40% during a serious FMD outbreak in Saudi Arabia (Farag *et. al.* 1998a).

During a limited outbreak of FMDV serotype O between February and April 2000 in central region (Riyadh area), an outbreak of FMDV serotype SAT 2 was reported for the first time in four dairy cattle farms in Saudi Arabia (in Al-Kharj province) in March 2000. The obtained data revealed that the new virus was challenged the animal causing morbidity, mortality and case fatality rates of 18.1%, 0.1% and 0.6% respectively. Whereas no previous contact between the animals and FMD virus serotype SAT 2 due to vaccination or infection. The questionable low rates of morbidity, mortality and case fatality in Saudi during 2000 outbreak of FMDV serotype SAT 2 in dairy cattle farms could be relatively due to the low virulence of the virus, or could be absolutely due to the presence of a partial immunity to the new strain as a result of immunization against umbrella of several strains of FMDV, serotypes O, A, C and Asia 1 which incorporated in the formulation of the currently used polyvalent vaccine against FMD in SA at that time. Yes, there is a considerable explanation by Xie *et. al.* 1987; Crowther *et. al.* 1993 who found that, from the amino acid sequence alignments, the VP1 gene of SAT 2 serotype viruses has features in common with serotype O. In both serotypes, there is a conserved cysteine residue at the base of the G-H loop that may account for the presence of the conformational neutralizing epitopes of these serotypes. The virus (SAT 2 strain) was not reported outside the locality of the infected farms, although it disappeared rapidly whereas the vaccine of FMDV serotype SAT 2 was imported and used at that time, then added to the polyvalent FMD vaccine formulation replacing to serotype C.

The identification of SAT 2 in Saudi Arabia during March 2000 was of great concern because this strain is usually found only in Africa. It is not known with certainly how the FMD, SAT 2 virus was introduced into the affected farms. Tracing the origin of FMD outbreak is an essential part of disease control (Samuel & Knowles, 2001b). SAT 2 is the serotype most often associated with outbreaks of FMD in livestock in southern and western Africa and is the only SAT serotype to

have been recorded outside the African continent in the last decade (Bastos *et. al.* 2003).

Concerning the geographical distribution and seasonal occurrence of FMD outbreaks in livestock in Saudi Arabia between July 1999 and June 2004, two extensive outbreaks of FMD virus serotype O were recorded in the five regions of the country (central, eastern, western, northern and southern) between 2-4/2001 and 8/2001-11/2002. While two out of three limited outbreaks of FMDV serotype O were occurred only in the central regions in 10-11/1999 and in 3-4/2000, and the rest one was reported recently in the southern region (Jizan area) on 6/2004. These results are point out, (1) FMD virus serotype O is mostly endemic in Saudi Arabia particularly in the central region of the country where the majority of dairy cattle farms are centralized in Al-Kharj province, Riyadh and (2) the frequency occurrence of FMD in the kingdom is relatively high on months of spring (March/April) and autumn (October/November).

The continued monitoring of the relationship between the vaccine and the field viruses will maintain the suitability of vaccine strains to provide enough protectability to the exiting field viruses (Farag *et. al.* 1998b). Field strains of FMD virus serotype O isolated from different regions in Saudi Arabia during FMD outbreaks between July 1999 and April 2002 were homolgous and closely related to O1 Manisa strain of FMDV serotype O that already incorporated in formulation of Saudi vaccine against FMD (Advices of FMD-world reference laboratory, Pirbright, UK), it is universally accepted that countries in which FMD is enzootic or which are adjacent to severely infected countries have no alterations other than restriction of animals movement and vaccination of livestock. In Saudi Arabia, vaccination program against FMD was mainly applied in dairy cattle farms, while most of the individual breeding cattle were not vaccinated. Such non-vaccinated cattle play an important role in the dissemination of FMD virus as they excrete large quantities of air-borne virus and they consider the source of reoccurrence of FMD outbreaks in SA. The maintenance of FMD virus depends on a number of factors, including the duration of infectivity and the size of the available host population (Condy *et. al.* 1985).

At the beginning of 2002, The Saudi Arabian Authorities has been engaged in an important process of fighting of FMD for the first time. This process has incorporated both of legalization of the restriction of the animal movement between different areas of the country and application of strict vaccination program. They organized a national park

of FMD vaccination of all traditional cattle population with polyvalent vaccine that contains one strain of serotype Asia 1, one strain of serotype SAT 2, three strains of serotype A (A22 Iraq 24/64, ASA4 23/86/A 4/65 and ASA4 41/91) and two strains of serotype O (O manias/O 3035 and OBFS), vaccination of sheep and goats flocks in vicinities of dairy and feedlot cattle farms with a monovalent vaccine of FMDV serotype O, and ring vaccination of all indigenous livestock during emergency of FMD (strategic emergency ring vaccination).

Absence of FMD outbreaks in SA between May/2002 and May/2004 is the main indicator of the success of the applied control measures. The epidemiological questioner about the last FMD outbreak in Jizan (Southern region) on June/2004 declared that the regime of FMD vaccination in indigenous cattle population has not well practiced in Jizan area and this outbreak was associated with the occurrence of FMD-clinical cases in Yemen (Personal communication). This means that the illegal introduction of livestock from Yemen into Saudi Arabia should be strictly prevented.

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