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Foot-and-mouth disease: Current scenario in Asia and Bangladesh

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ABSTRACT

Foot-and-mouth disease virus is a positive stand RNA virus that causes an acute vesicular disease of bovid wild and domesticated ruminants. Foot-and-mouth disease virus (FMDV) comprises of 7 antigenically distinct serotypes (Type O, A, Asia 1, C and SAT1-3) that do not provide cross-protection against one another. Foot-and-mouth disease (FMD) is a pandemic disease, accounting for a global loss of 6.5-21 billion US$ per annum. The present investigation aimed at the comparison of FMDV in Bangladesh with that of circulatory types in Asian continent. Categorization, estimation and demography of FMD in Asia continent are analyzed. Comparative genome and phylogeography of the FMDV in Asia is discussed. Three serotypes of FMDV are circulating in Asian territory, including mainland Southeast Asia, South Asia and Middle East with predominance of type O, whereas Serotype A and Asia1 are found to be confined to certain geographical regions. Cattle are most susceptible to FMD, whereas Pig serves as mixing vessel that may boost the emergence and re-emergence episode of several lineages/genotypes. Whole Genome and phylogeography analysis revealed that the transboundary movement of FMDVs are responsible for spreading of this disease in Asian regions. In 2013-2015, Saudi Arabia experienced the emergence of Ind-2001 lineage under Middle East South Asia (ME-SA) topotype of FMDV type O and Genotype VII of FMDV type A, which is normally endemic in the Indian subcontinent. Intrusion of type SAT1-3 in Arabian Peninsula occurred due to transboundary animal movement from FMDV enzootic African countries. Transboundary movement of FMDV, inappropriate vaccination and inadequate awareness are the main reasons for FMD spread in most of the Asian Countries.

Keywords: Foot-and-mouth disease, progressive control pathway, sustainable control

INTRODUCTION

The etiological agent, Foot-and-Mouth Disease Virus (FMDV), is a member of the genus *Aphthovirus* and family *Picornaviridae*. FMDV is a small non-enveloped virus containing icosahedral capsid having pseudo T3 symmetry. The FMDV has a positive sense single stranded RNA genome having a large single open reading frame (ORF) flanked by highly structured 5'and 3'Un-Translated regions (5'UTR and 3'UTR, respectively) alike other picornaviruses. The genome is encapsidated by sixty copies each of the four structural proteins of which VP1, VP2 and VP3 are exposed outside and VP4 is completely internal (Mittal *et al.*, 2005). The four capsid proteins, 1A, 1B, 1C, and 1D (also known as VP4, VP2, VP3, and VP1, respectively), are encoded by the N-terminal half of the ORF. Nonstructural proteins include Lpro, 2A, 2B, 2C, 3A, 3B, 3C pro, and 3D pol which occupies about two-third of the ORF (Carrillo *et al.*, 2005). Asia experienced outbreaks from serotypes O, A and Asia 1 in recent years (FAO, 2016). Influx of cattle from North-Africa to the Middle-East during the season of sacrifice risks introducing serotypes SAT1, SAT2, SAT3 in Asia, requiring dynamic strategies for prevention and eventually eradication of this disease (FAO/OIE). Demographic analysis of cattle contracting FMDV was carried out at outbreak sites. Serotypes O, A and Asia1 were found to circulate simultaneously within Bangladesh (Ullah *et al.*, 2014; Nandi *et al.*, 2015). Occurrence of Ind-2001 sub-lineage of Middle East-South Asia (ME-SA) topotypes of serotype O, genotype VII of serotype A and genotype C of Asia1 within the same time-frame as India, suggests trans-border movement of cattle. Comparative genome analysis from Bangladesh and those reported from official institutes across the world shows introduction of new genotypes/ sub-lineages and re-emergence of topotypes due to trans-border movement of the FMDV.

IMPACT ON ECONOMY AND AGRICULTURE

The impact of FMDV can be direct loss due to a reduction in production and changes in herd structure, and indirect loss regarding costs of FMD control and management. Global study conducted in 2012 showed that economic loss due to FMDV amounts to US$ 5 billion (Knight-Jones and Rushton, 2013). FMDV causes production loss due to

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disease, disruption of food supply in the market, financial input in prevention and control measures taken, infrastructure and budget that can be afforded by developed nations alone. FAO revealed that the cost of the first phase of the FMDV Progressive Control Program takes 5 years and will cost US$ 820 million to cover 79 endemic countries. Vaccination in the subsequent steps would cost US$ 694 million, excluding rising economies like India and China (Donaldson, 2012). Tens of thousands of animals are slaughtered and incinerated to inhibit a greater epidemic, which adds up to the burden of loss (Saeed *et al.*, 2015). The impact of animal slaughter and production loss is the most severe on small farms, because each outbreak claims at least 10% of the annual income (Knight-Jones *et al.*, 2016). More importantly small farmers close the business and switch to another profession because labor-intensive animal farming added with financial uncertainty is not feasible in the long run. Farmers have been seen to keep the early outbreaks a secret and to sell meat and milk of infected animals to avoid financial loss, which resulted in the spread of FMDV beyond control (Gunarathne *et al.*, 2016). The incursion of FMDV in disease-free Japan in Miayazaki 2010 resulted in culling of approximately 300,000 cattle within a month and changed the occupational census of the area (Muroga *et al.*, 2012). About 23.2 million people in rural Bangladeshi earn their livelihood from livestock, the majority of which is bovid. The total economic loss due to FMD is 60 million US$ per year in Bangladesh and in India it is 4.45 billion per year (Morzaria *et al.*, 2010).

FMDV IN ASIA

FMDV circulates worldwide, but developed countries have succeeded to stop the FMDV epidemic by means of extensive surveillance, control measures and vaccines to get rid of the outbreaks. However, most of the Asian countries are still suffering from the FMDV outbreaks. FMDVs throughout the world have been sub-divided into seven independent circulating and evolving FMDV genotypes; which are called pools.

Asia has three pools circulating all over it. Pool 1 comprises of serotypes O, A and Asia1 circulating within Malaysia and other Southeast Asia/Central Asia/East Asia. Pool 2 includes serotypes O, A and Asia1 within South Asia, including Bangladesh. Pool 3 comprises of West Eurasia and the Middle-East (Hammond, 2016). Serotype C has not been reported in Asia since 1995. Certain countries share viruses belonging to two different pools. Virus circulation and evolution within these regional virus pools result in changing needs for appropriate vaccine selection. There have been some limited outbreaks due to SAT1 viruses in the Middle East (Saeed *et al.*, 2015). FMDV viruses are divided into seven serotypes, each sharing 50% sequence homology in the whole genome. Each serotype is divided into antigenic subtypes. Each serotype is classified into many distinct lineages which share 85% homology in the VP1 protein sequence (Knowles and Samuel, 2003). The recent lineages in Pool 1 are O/SEA/Mya-98, O/ME-SA/PanAsia, O/CATHAY, O/ME-SA/Ind2001d of serotype O, A/ASIA/Sea-97 and Iran-05SIS1 sublineages belonging to Serotype A. Pool 2 exhibited O/ME-SA/Ind2011 and O/ME-SA/PanAsia-2 of serotype O and A/ASIA/G-VII belonging to serotype A. The Occasional spread of Asia1 has also been reported in this region. Pool 3 is reported to include AFG-07, HER 10, SIS-10/12, FAR-09/11 and BAR-08 sub-lineages within A/ASIA/Iran-05 lineage belonging to serotype A. Recent incursion from South Asia introduced lineages A/Asia/G-VII, A/ASIA/Sea-97, A/ASIA/Sindh-08, A/AFRICA/G-IV of serotype A and O/ME-SA/Ind2001 of Serotype O in Eurasia and Middle-East. Sindh-08 lineage of serotype Asia1, ANT-10 and FAR-09/11 sublineages of O/ME-SA/PanAsia-2 and O/ME-SA/Ind2001 lineage from serotype O had been introduced from Pool 2 to Pool 3. SAT 2/IV/Ken-09, SAT 2/VII/Alx-12 and Ghb-12 sublineages of serotype SAT2 also incur from Pool 4 into Pool 3 (Hammond, 2016). Therefore, Pool 3 has the most frequent incursions from adjacent pools, but unrestricted movement of animals and lack of control measures can introduce more lineages within a pool. Monitoring of lineages within a pool is important because vaccines target exposed viral proteins of a given antigenic subtype. Change of lineage alters antigenicity of circulating virus, rendering marketed vaccines ineffective (Siddique *et al.*, 2014). A field investigation from Bangladesh showed that isolates with the substitution of 8 amino acids in the G-H loop of VP1 protein of FMDV type Asia1 could cause disease in vaccinated cattle from farms in Gazipur (Ullah *et al.*, 2015). This circulating strain of Asia1 in Bangladesh belonged to genetic lineage C, while the vaccine strain was from IND 63/72 belonging to genetic lineage B (Ullah *et al.*, 2015). Such discrepancy in VP1 proteins poses threat of vaccination failure as well as the loss associated with contracting outbreaks despite expensive vaccination.

FAO monitors lineages of circulating viruses from reports of reference laboratories or published official bulletins and articles. FAO, OIE and other monitoring agencies also pointed out the shortage of resources for extended surveillance within Asia. Table 1 summarizes the circulating serotypes of FMDV in Asian countries.

ROUTES OF TRANSMISSION OF FMDV

FMD spreads very fast. FMDV transmits mainly through aerosol, and can spread directly from a sick animal to a susceptible host, through animal products as well as on fomites. The onset of clinical signs occurs 3-4 days' post infection and was associated with high levels of virus in the blood, oro-pharyngeal fluid and nasal fluid. Detection of virus in the air was also significantly associated with transmission (Charleston *et al.*, 2011).

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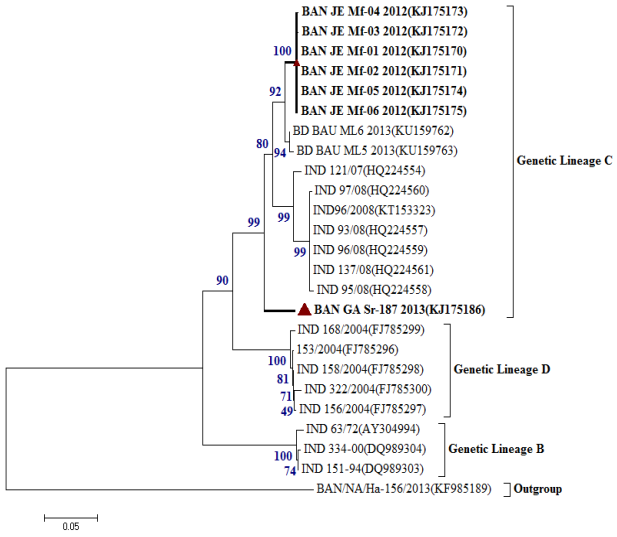

Figure 1: Phylogenetic analysis of VP1 sequences of native Foot-and-Mouth Disease Virus (FMDV) type Asia 1 samples. (Sequences in Bold are of local origin under the flagship of Microbial Genetics and Bioinformatics Laboratory). Foot-and-Mouth Disease Virus prototype sequences from GenBank were included. The evolutionary history was inferred using the neighbour-joining (NJ) method and Kimura 2-parameter + G model of base substitution with 1000 bootstrap replicates value. Phylogeny reconstruction was carried out in MEGA 5.2.

Air-borne transmission of FMDV is the major cause of epidemics throughout continents, 44% of FMDV transmission are airborne or environmental. Infected animals shed virus from secretory fluids. The maximum distance travelled by infectious virus over water is estimated to be 250 kms. Sick bovid and carriers spread the virus to susceptible healthy animals. Species of the sick animal and the susceptible host animal determine the intensity of the disease. Sheep are usually less susceptible to FMDV than cattle. Dose of virus inhaled by the susceptible host determines if the host will catch the disease (Chase-Topping *et al.*, 2013).

Humans, ticks, birds, rodents and pets may carry and spread FMDV through short distances. Animal products and fomites are the routes of transmission depending on duration of survival of FMDV in or on the product; and intended use of the fomite in animals. FMDV has been infectious to humans for 28 h (World Organization for Animal Health/OIE, 2008).

The knowledge of the route of transmission within and between farms is necessary to control the disease. Aerosol transmission of viral particles both from infected farms and during transportation across a certain distance is the major risk factors. Two mathematical models are described for explaining and predicting routes of transmission of FMDV. One model, called stratified model, includes parameters that influence the spread of virus in a farm. Distance of the susceptible farms from an infected farm, relative susceptibility of farmed animals, species content, mixing patterns of animals, spatial kernel are the parameters of stratified model. Non-stratified model takes transmission routes, between-farm contact rates, corresponding transmission probabilities per contact into account to explain how FMDV spreads from one farm to another (Cottam *et al.*, 2008). FMDV has a high mutation rate, resulting in rapid evolution, therefore complete genome sequences from isolates collected within 24-48 h from symptomatic animals can be used to track FMDV movement from farm to farm in real time and to predict if the outbreaks are linked to single or multiple releases from the source, and predicted the existence of undetected intermediate infected premises that were subsequently identified. Studies on risk factors for FMD in cattle indicated risk factors for FMDV in cattle or ruminants, including farm management, feed source, animal trades, husbandry, and geographical factors. The majority of farmers, small holders in particular, have limited knowledge of farm management especially biosecurity systems. They believe that vaccination provides perfect disease protection then they do not have a disinfection system at the farm gate (de Rueda *et al.*, 2014).

The beef cattle and buffalo herds are in free range and can cross into the neighboring village. Therefore, the frequency of a village that had outbreaks was associated with neighboring villages sharing these common resources (Seneque, 2011).

SUCCESS AND LIMITATIONS OF ERADICATING FMDV

The Progressive Control Pathway for Foot and Mouth Disease (PCP-FMD Principles and Applications, 2011) is a strategy developed by Food and Agriculture Organization (FAO) from the United Nations to assist and facilitate countries where FMD is still endemic to progressively reduce the impact of FMDV. The PCP depicts eradication of FMDV in 4 stages. Countries where the disease is endemic with no reliable information on the disease status are classified as stage 0. A comprehensive study of the epidemiology of FMD is required to move from stage 0 to 1 (PCP-FMD Principles and Applications, 2011). Stage 1 assists in identifying appropriate control options. Countries in stage 1 are in the process of developing their control strategies in at least one animal production sector based on a comprehensive assessment of the epidemiology and control options. Progression from stage 1 to 2 requires a risk based FMD control plan. Stage 2 involves the implementation of the chosen policy. Countries in stage 2 implement risk-based FMD control strategy that aims to reduce disease in at least one animal production sector. In order to move from stage 2 to 3, an aggressive strategy to eliminate FMD needs to be developed. Countries in stage 3 should adopt a control plan to progressively reduce/eliminate virus circulation in at least one region/production system (PCP-FMD Principles and Applications, 2011).

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Table 1: Distribution of FMDV in Asian countries.

Zone	Countries	Circulating Serotypes	Report in	Reference
Central Asia	Kazakhstan	O, A, Asia1	2015	WRLFDM (2016)
	Uzbekistan	O, A, Asia1		
	Tajikistan	O, A, Asia1		
	Turkmenistan	O, A, Asia1		
	Kyrgyzstan	O, A, Asia1		
	Afghanistan	O, A, Asia1		
	Pakistan	O, A, Asia1		
South Asia	India	O, A	2013	
	Bhutan	O, A	2013	
	Sri Lanka	O	2014	
	Bangladesh	O, A, Asia1	2015	
	Nepal	O	2016	
East Asia	Japan	FMDV free	2010	SEAFMD 2020 (2007)
	Singapore	FMDV free		
	Philippines	O, A	2014	
	Vietnam	O, A, Asia1	2014	
	China	O, A	2015	
	Hong Kong	O	2015	
	Taiwan	A	2015	
	Mongolia	O, A	2015	
	Cambodia	O, A	2015	
	Indonesia	O, A, Untyped	2015	
	Laos	O, A	2015	
	Myanmar	O, A, Asia1	2015	
	Thailand	O, A	2015	
	North Korea	O	2016	
	South Korea	O	2016	
	Malaysia	O, A	2016	
Western Asia and Middle East	Georgia	Free	2001	WRLFMD (2016)
	Jordan	O, A	2006	
	Azerbaijan	O, Asia1	2013	
	Iraq	A, O	2013	
	Qatar	O	2013	
	Armenia	O, A, Asia1	2014	
	Bahrain	O, A, Asia1, SAT2	2015	
	Iran	A	2015	
	Lebanon	O, A, Asia1, SAT1	2015	
	Oman	O,SAT2	2015	
	Turkey	O, A, Asia1, SAT1	2015	
	Saudi Arabia	O, A, SAT1, SAT2	2016	
	Syria	O, A, Asia1, SAT1	2016	
	Israel	O	2016	
	Gaza Strip	O	2016	
	Kuwait	O	2016	
	United Arab Emirates	O	2016	
	Yemen	O, A	2016	

This requires very significant national capacity and ongoing investment, including the ability to ensure maintenance of sufficient herd immunity in critical populations to prevent FMDV circulation. Moving to stage 4 requires that FMD is controlled to an extent that it is not endemic in domestic livestock. If a country decides to continue along the FMD-PCP to stage 4 and beyond, it may ask the OIE for endorsement of its national FMD eradication program. Progression to stage 4 would thus indicate attaining officially recognized FMD free status with vaccination by the OIE for the whole or part of the country. Countries in stage 4 maintain zero circulation with no incursions of FMDV (PCP-FMD Principles and Applications, 2011). Countries usually free of FMD that detect an incursion of the disease would normally not enter the Pathway, but rather would act to eradicate the disease and re-apply directly to the OIE for re-instatement of an officially recognizved FMD-free status as soon as

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possible. The possibility that OIE could implement a country's national FMD control program in the higher stages of the PCP is foreseen (Hammond, 2016). Table 2 summarizes the current state of PCP-FMD in Asian countries.

Control of FMD is difficult due to variations in viral serotype and consistency, effectiveness of control measures, and emergence of new subtypes. FMD outbreaks originate from transportation of carrier animals to susceptible populations or disease-free regions. FMD increases due to seasonal or periodic cycling, host susceptibility, and predisposal to epizootic risk. Asian countries suffering from FMD outbreaks often lack coordinated or serious mandatory measures for control of this disease. Further, movement and exchange of animals and animal products across neighboring countries are very common. The amount of FMD vaccines produced locally is insufficient to fulfill the demands of large populations of animals in Asia (Saeed *et al.*, 2015).

In South East Asia (SEA) countries like Brunei, Indonesia, East Malaysia and Singapore are recognized internationally free of the disease without vaccination while China, Philippine, Thailand are very prone to FMD outbreaks (Gleeson *et al*., 2003). In the year 2005, FMDV Asia1 reemerged in China (Mardones *et al*., 2010). In the year 2010, report of FMD was recorded in Southern Cambodia, Iran, and Republic of Korea (Rashtibaf *et al.*, 2012; Yoon *et al.*, 2012; Young *et al.*, 2013). Gurumurthy *et al.* (2002) compared the sequences of FMDV Asia1 isolates from different outbreaks in India between 1985 and 1999 against two strains used for vaccine production and deduced the synonymous nucleotide substitution rate to be 2.7×10^{-2} per nucleotide per year. Studies from Pakistan revealed an increase in serotype A causing more severe outbreaks between 2005 to 2009 (Abubakar et *al.*, 2012). Serotype A from Pakistan showed a nucleotide substitution rate of 1.2×10^{-2} per nucleotide per year in lineage A-Iran05 between 2002 to 2009 (Jamal *et al.*, 2011).

Accoding to PCP-FMD road map for SAARC countries 2011-2020, Bangladesh is supposed to achieve stage 2 in 2016, provided that epidemiological studies, risk identification, and fixed risk-based control plan are completed as shown in Table 2. (PCP-FMD Report, 2013). Unfortunately, due to poor/no reporting system by the appropriate authorities of FMD to the OIE, inappropriate vaccination, and poor veterinary service care, Bangladesh is placed at stage 0 (non-reporting stage).

The success of PCP in South and Southeast Asia is challenged due to following reasons

- Basic knowledge of circulating strains is scarce, making management and tracking of the source difficult. Therefore, risk-based control options are not possible.
- Uncontrolled animal movement during religious festivals leads to the incursion of carrier animals and contaminated animal products from neighboring countries which might be PCP stage 0. This problem is difficult to tackle because imposing bans on animal import causes severe deficiency in the market. Border control and surveillance of the incoming cattle could be an option, but absence of cost-effective point-of-care diagnosis and intervention techniques pose a big threat in maintaining Stage 2 status of the PCP.
- Lack of routine surveillance and laws after achieving stage 2 is often difficult because it needs active participation of local, national and regional veterinarians, policy-makers and farm owners. Local producers often don't want to reveal outbreaks fearing loss and closure of business. This problem cannot be alleviated without agriculture insurance and demurrage from the national level.
- Lack of trained individuals in the field to curb epidemic is one problem that challenges promotion from stage 3 to stage 4. Massive culling and incineration of infected cattle according to biosecurity and environment-friendly protocols need a large number of professionals in the field, which might take years of work to develop.

COMPARATIVE GENOMICS OF FMDV

Comparative genomics of FMDV allows us to see how the virus mutates over time and locations and more importantly to trace the origin of the incurring FMDV strain. Genome sequencing provides excellent insight into the evolutionary and epidemiological dynamics of such viruses. To allow better, more targeted interventions, sequencing data from different outbreaks, need to be analyzed in a timely fashion to maximize their value for animal health. Many lineages circulate over Asia and spread from one part to another. For example, lineage O/ME-SA/Ind2001 is normally restricted to India, Bangladesh, Nepal and Bhutan, but this strain was also reported in Saudi Arabia, Libya in 2013 and in Tunisia and Algeria in 2014-2015. FMDV Asia1/Sindh-08 in the Middle East incurred in South Asia (Brito *et al.*, 2015). Saudi Arabia could also trace its outbreak of serotype A with strain A/SAU/1/2015 from A/Asia/G-VII lineage to BAN/GA/Sa-197/2013 from Bangladesh (Ullah *et al.*, 2014.). Such findings are surprising due to the geographic distance and limited export of animal products (Bachanek-Bankowska *et al.*, 2016).

In India, 7 sub-lineages of the serotype O were categorized by molecular analysis, namely Branch A, B and C-I, C-II, Pan Asia I, Pan Asia II and 'Ind2001' under Middle East-South Asia (ME-SA) topotype. The Pan Asia II lineage emerged in 2003. O/Ind2001 re-merged in 2008 and is causing devastating epidemics along with Pan Asia lineages in India till now (Biswal *et al.*, 2012).

China documented the changing pattern of FMDV over the last decade. The predominant type of FMDV was a pathogenic strain Asia 1/JS/WX/05 during 2005-06, which spread over 11 provinces in India. In 2009, a new lineage Asia1/XJATS/09 broke out to 9 more provinces despite vaccination and containment measures. New mutations enhanced virulence, immune evasion and persistence in host. FMDV type A was introduced to China from Southeast Asia because the etiology of the

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epidemic A/WH/09 and ASH/09 related closely to A/MAY/02, A/Tai/97 and A/Lao/8/06 from Malaysia, Taiwan and Laos respectively. China is experiencing incursion of FMDV Type O after 2011 (Zengjun and Youjun, 2014).

Table 2: Attainment of Progressive Control Pathway for Eradication of FMDV in Asia (According to FAO).

Zone	Countries	Current Stage of PCP	Expected Year of Eradication
Central Asia	Kazakhstan	4	2020
	Uzbekistan	3	-
	Tajikistan	2	-
	Turkmenistan	3	-
	Kyrgyzstan	3	2020
South Asia	Afghanistan	3	-
	Pakistan	2	-
	India	4	-
	Sri Lanka	3	2020
	Nepal	2	-
	Bhutan	2	-
	Bangladesh	2 (In reality '0')	-
East Asia	China	3	2020
	North Korea	3	2020
	South Korea	3	2020
	Japan	FMD free	FMD free
	Taiwan		2020
	Mongolia		2020
	Cambodia		2020
	Indonesia		-
	Laos		2020
	Malaysia	4	-
	Myanmar	3	-
	Singapore	FMD free	FMD free
	Thailand	4	-
	Vietnam	3	-
Western Asia	Armenia	3	-
	Azerbaijan	3	-
	Georgia	3	2023
	Iran	3	-
	Iraq	3	-
	Israel	3	-
	Jordan	Provisional 3	-
	Kuwait	Provisional 3	-
	Lebanon	Provisional 2	-
	Qatar	Provisional 3	-
	Saudi Arabia	2	-
	Syria	3	2021
	Turkey	2	-
	United Arab Emirates	3	-

A number of complete genome sequences of FMDV isolates have been reported from Bangladesh. One isolate of type A strain (BAN/GA/Sa-197/2013) from Gazipur in Bangladesh, revealed a 84-nucleotide insertion within the 5'-untranslated region (UTR), a lengthened poly(C) tract, and amino acid substitutions at the VP1 region compared to the available genome sequence of the vaccine strain (Ullah *et al.*, 2014).This genome is 8,220 nucleotides in length and contains a 1,100-nt 5′-untranslated region (UTR) with a 17-residue poly(C) tract, a 6,999-nt single open reading frame coding for a polyprotein containing four structural proteins (VP4, VP2, VP3, and VP1) and eight nonstructural proteins (L, 2A, 2B, 2C, 3A, 3B, 3C, and 3D), and a 121-nt 3′-UTR with a 28-nt poly(A) tail. Phylogenetically, the isolated FMDV type A strain (BAN/GA/Sa-197/2013) clustered within genotype VII of the Asia topotype. BAN/GA/Sa-197/2013 shares 94% nucleotide homology (in relation to the complete genome) with IND 245/2007. Neighboring countries showed 10% variation at the nucleotide sequence level and 5% variation at the deduced amino acids of the VP region. Specifically, there are 15

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substitutions in the VP1 region, including 4 amino acids (T44N, T45A, N46S, and T48I) in the B-C loop (residues 40 to 60) and 2 amino acids (T143V and I154V) in the G-H loop (residues 138 to 154), which indicates antigenic heterogeneity. Furthermore, there is an 84-nt insertion at positions 394 to 477 within a region of the 5′-UTR and a 2-nt insertion at the 3′-UTR in comparison to the vaccine strain (Ullah *et al.*, 2014).

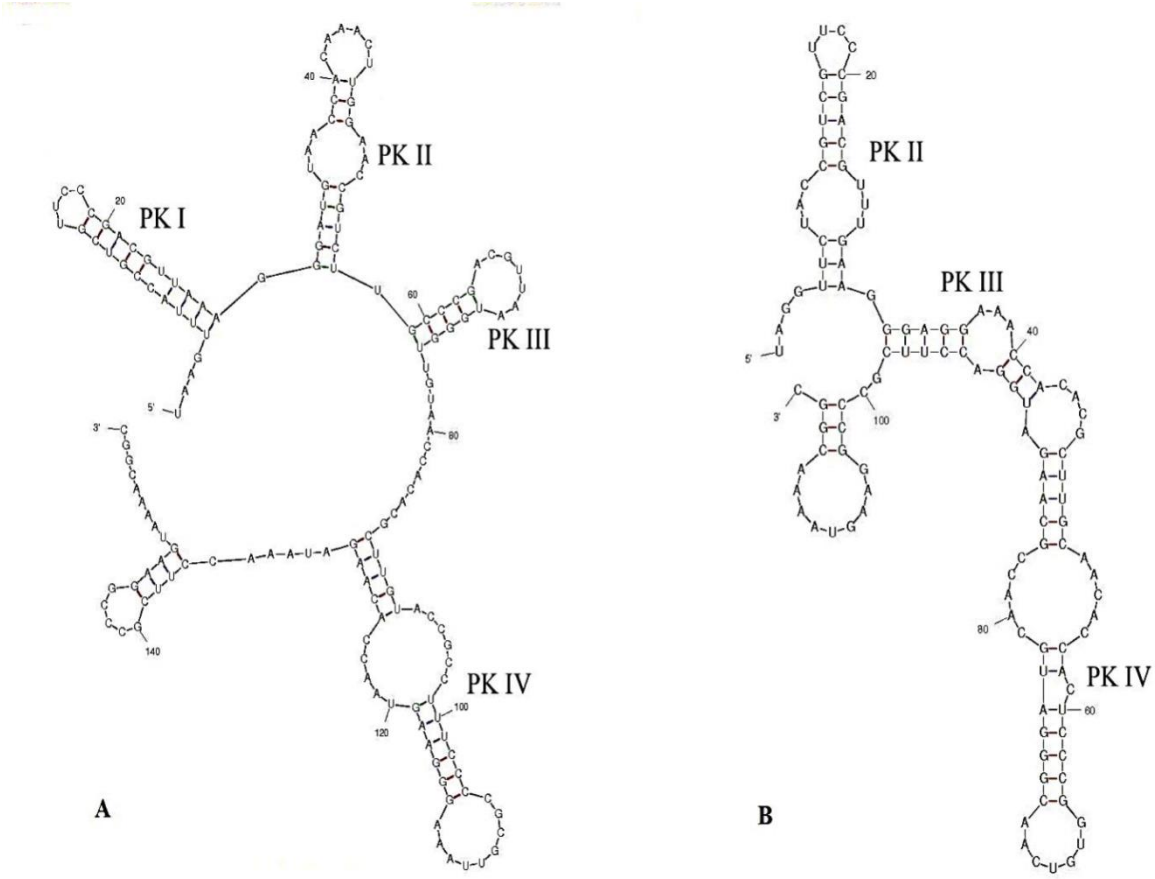

Figure 2: Predicted Secondary Structure of Pseudoknot of BAN/NA/Ha-156/2013 (A) and NCBI RefSeq (B). In the local isolate, a total of 4 pseudoknot loop structures are evident (PKI, PKII, PKIII and PKIV) whereas PKI loop structure is missing in NCBI RefSeq (Accession No. NC004004).

The complete genome sequence of another circulatory FMDV serotype O (BAN/NA/Ha-156/2013) isolated from Natore, Bangladesh revealed antigenic heterogeneity within the VP1 region, a fragment deletion and insertions at the 5' untranslated region (UTR) and 3A region (Sultana *et al.*, 2014).This complete genome of strain is 8,131 nucleotides (nt) in length, including a 1,020-nt 5′ untranslated region (5′-UTR) with a 15-nt poly(C) tract, a 6,999-nt open reading frame (ORF), and a 112-nt 3′-UTR with a ≥21-nt poly(A) tail. The homologous comparison and phylogenetic analysis of the nucleotide and deduced amino acid (aa) sequences between strain BAN/NA/Ha-156/2013 and other FMDV strains available in the database revealed that the strain is clustered within the Ind2001 linage of the ME-SA topotype of FMDV serotype O. Strain BAN/NA/Ha-156/2013 shares 88% nucleotide homology (in relation to the VP region) with the currently available vaccine strain (FMDV O strain India/R2/75). Compared to the vaccine serotype, critical amino acid substitutions were determined at the VP1 GH loop (positions 136–150): D138E, S140A, and I144V, which are responsible for antigenic heterogeneity. Moreover, an insertion of 11 amino acid residues in the 3A segment and the deletion of a total of 81 base stretches at the S-fragment along with a 43-nt insertion within the 5′ UTR immediately following the Poly(C) tract results in one extra PK loop (Fig. 2) were found in comparison to the NCBI FMDV type O. The predicted secondary structure of S-fragment of BAN/NA/Ha-156/2013 shows characteristic stem loop structure similar to the NCBI RefSeq.

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A total of 47 VP1 sequences showed only a few mutations at several antigenic sites. Five antigenic peptides have been identified as the least variable epitopes, with just fewer amino acid substitutions. Only a limited number of serotype Asia1 antigenic variants were found to be circulated within the South Asian region. This emphasizes a possibility of formulating synthetic vaccines for controlling foot-and-mouth disease by Asia1 serotypes (Alam *et al.,* 2013).

CONCLUSION

Cross-border cattle movements are possibly one of the main reasons for spreading of different serotypes between countries. So prevention of cross-border cattle movements, national or regional FMD policy and successful FMD control program were the essential prerequisite to control the FMDV in endemic countries.

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REFERENCES

Abubakar, M., Kanwal, S. and Saeed, A. (2012). Persistence, emergence and distribution of foot and mouth disease virus (FMDV); Global and Pakistan perspectives. *Pakistan Journal of Life and Social Sciences* **10, 84-90.**

Alam, S. S., Amin, R., Rahman, M. Z., Hossain, M. A. and Sultana, M. (2013). Antigenic heterogeneity of capsid protein VP1 in foot-and-mouth disease virus (FMDV) serotype Asia1. *Advances and Applications in Bioinformatics and Chemistry* **6, 37-46.**

Bachanek-Bankowska, K., Wadsworth, J., Thapa, B., King, D. P. and Knowles, N. J. (2016). Complete genome sequence of a serotype a foot-and-mouth disease virus from an outbreak in Saudi Arabia during 2015. *Genome Announcements* **4, e1591-15.**

Biswal, J. K., Sanyal, A., Rodriguez, L. L., Subramaniam, S., Arzt, J., Sharma, G. K., Hammond, J. M., Parida, S., Mohapatra, J. K., Mathapati, B. S. Dash, B. B., Ranjan1, R., Rout, M., Venketaramanan, R., Misri, J., Krishna, L., Prasad, G., Pathak, K. M. and Pattnaik, B. (2012). Foot-and-mouth disease: Global status and Indian perspective. *The Indian Journal of Animal Sciences* **82, 109-131.**

Brito, B. P., Rodriguez L. L., Hammond, J. M., Pinto, J. and Perez, A. M. (2015). Review of the global distribution of foot-and-mouth disease virus from 2007 to 2014. *Transboundary and Emerging Diseases* **1865-1882.**

Carrillo, C., Tulman, E. R., Delhon, G., Lu, Z., Carreno, A., Vagnozzi, A., Kutish, G. F. and Rock, D. L. (2005). Comparative genomics of foot-and-mouth disease virus. *Journal of Virology* **79, 6487-6504.**

Charleston, B., Bankowski, B. M., Gubbins, S., Chase-Topping, M. E., Schley, D., Howey, R., Barnett, P. V., Gibson, D., Juleff, N. D., Woolhouse, M. E. J. (2011). Relationship between clinical signs and transmission of an infectious disease and the implications for control. *Science* **332, 726-729.**

Chase-Topping, M. E., Handel, I., Bankowski, B. M., Juleff, N. D., Gibson, D., Cox, S. J., Windsor, M. A., Reid, E., Doel, C., Howey, R., Barnett, P.V., Woolhouse, M. E. J. and Charleston, D. (2013). Understanding foot-and-mouth disease virus transmission biology: identification of the indicators of infectiousness. *Veterinary Research* **44(46).**

Cottam, E. M., Wadsworth, J., Shaw, A. E., Rowlands, R. J., Goatley, L., Maan, S., Maan, N. S., Mertens, P. P. C., Ebert, K., Li, Y., Ryan, E. D., Juleff, N., Ferris, N. P., Wilesmith, J. W., Haydon, D. T., King, D. P., Paton, D. J. and Knowles, N J. (2008). Transmission pathways of foot-and-mouth disease virus in the United Kingdom in 2007. *PLoS Pathogens* **4(4), e1000050.**

de Rueda, C. B., de Jong, M. C., Eblé, P. L. and Dekker, A. (2014). Estimation of the transmission of foot-and-mouth disease virus from infected sheep to cattle. *Veterinary Research* **45, 58.**

Donaldson, A. I. (2012). Vaccines: Types, quality control, matching and supply. Proceedings of the FAO/OIE Global Conference on Foot and Mouth Disease Control, Bangkok, Thailand **pp. 95-102.**

FAO (2016). Foot-and-Mouth Disease Situation. Monthly Report January 2016. Link: http://www.fao.org/fileadmin/user_upload/eufmd/docs/FMD_monthly_reports/2016/Monthly_Report_January_2016.pdf [Retrieved on 28 November 2016]

Gleeson, L. J., Bauer, K. and Aidaros, H. A. (2003). A review of the status of FMD in South East Asia and approach to control and eradication. *Science and Technology Review* **21, 465-475.**

Gunarathne, A., Kubota, S., Kumarawadu, P., Karunagoda, K. and Kon, H. (2016). Is hiding foot-and-mouth disease sensitive behavior for farmers? A survey study in Sri Lanka. *Asian-Australasian Journal of Animal Sciences* **29, 280-287.**

Gurumurthy, C. B., Sanyal, A., Venkataramanan, R., Tosh, C., George, M. and Hemadri, D. (2002). Genetic diversity in the VP1 gene of foot-and-mouth disease virus serotype Asia 1. *Archieve of Virology* **147,85-102.**

Jamal, S. M., Ferrari, G., Ahmed, S., Normann, P., Curry, S. and Belsham, G. J. (2011). Evolutionary analysis of serotype A foot-and-mouth disease viruses circulating in Pakistan and Afghanistan during 2002–2009. *Journal of General Virology* **92,2849–2864.**

Knight-Jones, T. J. D. and Rushton, J. (2013). The economic impacts of foot and mouth disease – What are they, how big are they and where do they occur? *Preventive Veterinary Medicine* **112, 161-173.**

Knight-Jones, T. J., Robinson, L., Charleston, B., Rodriguez, L. L., Gay, C. G., Sumption, K. J.

 ISSN (print): 1823-8262, ISSN (online): 2231-7538

and Vosloo, W. (2016). Global foot-and-mouth disease research update and gap analysis: 1- Overview of global status and research needs. *Transboundary Emerging Disease* **63, 3-13.**

Knowles, N. J. and Samuel, A. R. (2003). Molecular epidemiology of foot-and-mouth disease virus. *Virus Research* **91, 65-80.**

Mardones, F., Perez, A., Sanchez, J., Alkhamis, M. and Carpenter, T. (2010). Parameterization of the duration of infection stages of serotype O foot-and-mouth disease virus: An analytical review and meta-analysis with application to simulation models. *Veterinary Research* **41, 45.**

Mittal, M., Tosh, C., Hemadri, D. Sanyal, A. and Bandyopadhyay, S. K. (2005). Phylogeny, genome evolution, and antigenic variability among endemic foot-and-mouth disease virus type A isolates from India. *Archives of virology* **150, 911-928.**

Morzaria, S. (2010). Investments for resilience against vulnerability: Transboundary animal disease control, **July 7-9.**

Muroga, N., Hayama, Y., Yamamoto, T., Kurogi, A., Tsuda, T. and Tsutsui, T. (2012). The 2010 foot-and-mouth disease epidemic in Japan. *Journal of Veterinary Medical Science* **74, 399-404.**

Nandi, S. P., Rahman, M. Z., Momtaz, S., Sultana, M. and Hossain, M. A. (2015). Emergence and Distribution of Foot-and-Mouth Disease Virus Serotype A and O in Bangladesh. *Transboundary and Emerging Diseases* **62, 328-331.**

PCP-FMD Principles and Applications (2011). Official Declaration of Progressive Control Pathway from Food and Agriculture Organization (FAO). Available from: http://www.oie.int/eng/A_FMD2012/docs/Background_papers_PCP_FMD.pdf [Retrieved on 11 November 2016]

PCP-FMD Report (2013). Second Regional Workshop on Progressive Control Pathway for Foot and Mouth Disease (PCP-FMD) for South Asian Countries. Available from: http://www.rsu-saarc.org/content/reports/2013-10-02_2nd-PCP-FMD-Agra-India.pdf [Retrieved on 11 November 2016]

Rashtibaf, M., Sharifi, K., Zibaee, S. and Dehghani, H. (2012). A survey on the frequency of foot-and-mouth disease virus carriers in cattle in North-east of Iran by RT-PCR: Implications for revising disease control strategy. *Transboundary and Emerging Diseases* **59, 482-489.**

Saeed, A., Kanwal, S., Arshad, M., Ali, M., Shaikh, R. S. and Abubakar, M. (2015). Foot-and-mouth disease: overview of motives of disease spread and efficacy of available vaccines. *Journal of Animal Science and Technology* **57, 10.**

SEAFMD 2020 (2007). A roadmap for foot-and-mouth disease freedom with vaccination by 2020 in South-East Asia. Available from: http://www.seafmd-rcu.oie.int/documents/SEAFMD%202020%20WEB%20Version.pdf [Retrieved on 28 November 2016]

Seneque, S. (2011). Foot-and-Mouth Disease Control in Asia. Meeting Unique Challenges.in Proceedings of the Proceedings of 5th Asian Pig Veterinary Society Congress Pattaya, Thailand.

Siddique, M. A., Ullah, H., Nandi, S. P., Chakma, D., Sultana, M. and Hossain, M. A. (2014). Molecular characterization of foot-and-mouth disease virus type O from wild pig in Bangladesh. *Bangladesh Journal of Microbiology* **31, 41-45.**

Sultana, M., Siddique, M. A., Momtaz, S., Rahman, A., Ullah, H., Nandi, S. P. and Hossain M. A. (2014). Complete genome sequence of foot-and-mouth disease virus serotype O isolated from Bangladesh. *Genome Announcements.* **2, e01253-13.**

Ullah, H., Siddique, M. A., Sultana, M. and Hossain, M. A. (2014). Complete genome sequence of foot-and-mouth disease virus type A circulating in Bangladesh. *Genome Announcements* **2, e01253-13.**

Ullah, H., Siddique, M. A., Al Amin, M., Das, B. C., Sultana, M. and Hossain, M. A. (2015). Re-emergence of circulatory foot-and-mouth disease virus serotypes Asia1 in Bangladesh and VP1 protein heterogeneity with vaccine strain IND 63/72. *Letters in Applied Microbiology* **60, 168-173.**

World Organization for Animal Health/OIE (2008). Foot-and-mouth Disease. Manual of diagnostic tests and vaccines for terrestrial animals (mammals, birds and bees) Paris, France. Available from: http://www.oie.int/doc/ged/D7709.PDF [Retrieved on 27 November 2016]

WRLFMD, World Reference Laboratory for FMD (2016). Molecular Epidemiology Reports. Available from http://www.wrlfmd.org/fmd_genotyping/ [Retrieved on 11 November 2016]

Young, J. R., Suon, S., Andrews, C. J., Henry, L. A. and Windsor, P. A. (2013). Assessment of financial impact of foot and mouth disease on small holder cattle farmers in Southern Cambodia. *Transboundary and Emerging Diseases* **60, 166-174.**

Yoon, H., Yoon, S. S., Wee, S. H., Kim, Y. J. and Kim, B. (2012). Clinical manifestations of foot-and-mouth disease during the 2010/2011 epidemic in the FRepublic of Korea. *Transboundary Emerging Diseases* **59, 517-525.**

Zengjun, L. and Youjun, S. (2014). Foot and mouth disease situation and control strategies in the People's Republic of China – the current situation. National Foot-and-Mouth Disease Reference Laboratory, Lanzhou Veterinary Research Institute of CAAS.

 ISSN (print): 1823-8262, ISSN (online): 2231-7538