Hemorrhagic Septicemia Outbreak as a Consequence to SAT_2 FMD Infection in Buffalo and Cattle in Alexandria Province, Egypt

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Abstract: 5630 fattening buffalo and cattle calves aged from 6 to 30 months belonging to 25 farms at Alexandria province, Egypt were included in this study. Morbidity and mortality rates of FMD and H.S were documented. Vesicular fluids were collected for virus isolation and serotyping. Lung, liver and heart blood were collected from died calves for isolation and serotyping of *P. multocida*. Cell mediated immune response was monitored by measuring Phagocytic activity (PA) and Phagocytic index (PI). Also antimicrobial sensitivity on *P. multocida* isolates was performed. FMD SAT_2 and *P. multocida* B_2 serotypes were isolated; PA and PI were 16, 1.5 and 20, 1.9 in FMD infected and non-infected ones respectively. Buffalo calves showed more susceptibility to HS and higher case fatality rates than cattle calves. Mortality rate among *p. multocida* infected fattening calves aged from 12-15 months was higher than older and younger ages. *P. multocida* isolates were highly susceptible to Ceftotaxime sodium and ceftifour sodium than other antimicrobials. It can be concluded that SAT_2 FMD infection played an important role in appearance of HS outbreak in buffalo and cattle in Alexandria province, Egypt causing high mortality rates especially in 6-15 months age buffalo and cattle calves respectively.
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1. Introduction

Foot-and-mouth disease virus (FMDV), member of the *Picornaviridae* family, and the only member of the genus *Aphthovirus*, is the causative agent of the highly contagious disease of cloven-hoofed animals ***(Maddur et al., 2010).*** The effects of FMDV on the immune system of the host have not been widely studied in detail. Analyses during the acute phase of FMDV serotype O infection showed a transient lymphopenia involving T cells, although B cells have not been evaluated. Also, the function of T cells during the acute phase of infection was significantly impaired ***(Golde et al., 2011).*** Foot-and-mouth disease virus has been shown to disrupt the innate response *in vitro* and also interacts directly with antigen-presenting cells and their precursors. This interaction results in suboptimal immune function, favoring viral replication and the delayed onset of specific adaptive T-cell responses ***(Ayebazibwe et al., 2010).***

Haemorrhagic septicaemia (HS) is a major disease of cattle and buffaloes occurring as catastrophic epizootics in many Asian and African countries, characterized by an acute, highly fatal septicaemia with high morbidity and mortality (***Mustafa, et al., 1978 and Singh, et al., 1996).***The disease is caused by *Pasteurella multocida*, a Gram-negative coccobacillus residing mostly as a commensal in the upper respiratory tract of animals. The Asian serotype B:2 and the African serotype E:2 (Carter and Heddleston system), corresponding to 6:B and 6:E (Namioka-carter system), are mainly responsible for the disease. ***(Hopkins et al., 1998).***

The pathogenesis of haemorrhagic septicaemia in buffalo infected with *Pasteurella multocida* is poorly understood but usually occur after decreasing immunity of the animal due to stressful condition or immunosuppression due to intercurrent infection as FMD, However, the characteristic of sudden onset leading to the rapid death of infected animals is similar to that seen in other clinical conditions known to involve endotoxic shock. ***(Radostits et al., 2007)***

The clinical manifestations of the typical disease caused by B:2 or E:2 strains include a rise in temperature, respiratory distress with nasal discharge, and frothing from the mouth, and leads to recumbency and death. Septicemia is the characteristic feature in all the disease conditions. The incubation period varies from 3 to 5 days. In per acute cases, sudden death with observable clinical signs may be observed ***Carter and De Al Wis (1989) and De Al Wis (1992).***

Disease incidence was higher in 6-24 months old animals and groups of less than 10 animals. The disease was seasonal, occurring only in rainy seasons of the year, and victims were only cattle and buffalo. Successful treatment was reported if antibiotics were given at the initial stages of the disease ***(Farooq et al., 2007).***

Buffaloes are generally more susceptible to HS than cattle and show more severe forms of disease with profound clinical signs. Subcutaneous oedema from the mandible to the brisket is one distinctive feature of the disease in endemic areas, most deaths are confined to older calves and young adults. Massive epizootics may occur in endemic as well as non-endemic areas ***(Carter and De Al Wis, 1989 and De Al Wis, 1992).***

The objectives of this study are evaluation of role of FMD in aggravating hemorrhagic septicemia infection in fattening buffalo and cattle calves through analysis of epidemiological data, morbidity and case fatality rates and measuring cell mediated immune response, also evaluation of different medications used in treatment of cases.

2. Materials and Methods

2.1. Animals: 5630 (3038 buffalo and 2592 cattle) fattening calves aged from 6 to 30 months belonging to 25 farms at Alexandria - Cairo desert road, Egypt were included in this study.

2.2. Clinical examination: fattening calves were examined clinically, Clinical picture, morbidity and mortality rates of FMD and H.S were documented.

2.3. Collection of samples: **a. For assessment of FMD virus**, vesicular fluid from tongue vesicles of infected calves was collected and kept on ice before storage in the laboratory.

b. For assessment of H.S, lung, liver and heart blood samples were collected from died calves and kept on ice before storage in the laboratory.

2.4. Isolation and identification of FMD: Vesicular fluids were sent to animal health research institute (AHRI), Dokki, Giza, Egypt for FMD virus isolation and serotyping.

2.5. Isolation and identification of *P. multocida:* It was performed according to ***Rimler and Rhoades, (1994)***.

2.6. Serotyping of *P. multocida* isolates: Isolates were analyzed by using rapid slide agglutination test using capsular type B antiserum according to ***(Heddleston et al., 1972; Rimler and Rhoades, 1994).*** Serotyping was performed in the Department of Clinical Microbiology, Central Health Laboratories, Ministry of Health, Cairo, Egypt.

2.7. The cellular immune response: monitored by Phagocytic activity and Phagocytic index in peripheral blood mononuclear cell cultures acc. to ***Kawahara et al., (1991).*** Also differential leukocytic count was performed acc. to ***Schalm (1986).***

Phagocytic activity (PA) = percentage of phagocytic cells containing yeast cells.

$$\text{Phagocytic index (PI)} = \frac{\text{Number of yeast cells phagocytozed}}{\text{Number of phagocytic cells}}$$

2.8. Antimicrobial sensitivity test:

Assessment of antimicrobial sensitivity on *P. multocida* isolates was performed as previously described by ***(Quinn et al., 1994)***. Results were interpreted according to ***Koneman et al., 1992.***

2.9. Trials for treatment of H.S:

Table (1): Number of animals subjected to different antimicrobial treatments:

Group	Number of animals (2600)
Group 1 Ceftifour sodium	470
Group 2 Lincspectin and gentamycin.	350
Group 3 Cefotaxime sodium.	905
Group 4 Tylosine and gentamycin	150
Group 5 Tultrathromycin.	170
Group 6 Sulphadimethoxin + Trimethoprim	70
Group 7 Oxytetracycline LA 20%	200
Group 8 Amoxycillin 15% LA.	75
Group 9 Florfenicol 15%	210

3. Results

3.1. Morbidity and mortality rate of FMD in fattening calves:

As shown in (Table 2): 4616 out of 5630 (81.9%) fattening calves showed one or more of clinical signs of FMD - SAT2 serotype as confirmed by animal health research institute (AHRI), Dokki, Giza, Egypt**.** The clinical signs observed include fever, salivation, decrease appetite, presence of vesicles in tongue, gum and interdigital space and/or lameness. Also 13 (0.23%) out of 5630 animals examined died after sever illness of FMD.

Table (2): Morbidity and mortality rates of FMD in fattening calves

No. of animals		Morbidity rate		Mortality rate	
5630		No.	%	No.	%
		4616	81.9	13	0.23
2592 cattle	3038 buffaloes				

3.2. Isolation & Serotyping of *Pasteurella multocida*:

Isolation and identification of *P. multocida* in the present study revealed that, Gram-negative, bipolar-staining short bacilli. *P. multocida* organisms produce oxidase, catalase and indol, and will reduce nitrates. They do not produce hydrogen sulphide or urease, and fail to use citrate or liquefy gelatin. Glucose and sucrose are always fermented with the production of acid only. Serotyping identification of *P. multocida* isolates by using rapid slide agglutination test using capsular type B antiserum indicate *P. multocida* type B2.

3.3. The role of FMD in aggravating the hemorrhagic septicemia infection in fattening calves.

3.3.1.Clinical observations:

As shown in (Table 3) 56.32% out of 4616 animals infected with FMD showed signs of H.S. with 13.92% case fatality rate. Signs of HS included, Sudden death without previous signs, sudden dyspnea followed by death within few minutes, bloody diarrhea and/or edema in neck and mandibular area associated with coughing, while Postmortem findings included, consolidation and hepatization of lung, hydropericardium, congested heart, peitecheal hemorrhages on coronary fat, congested liver and/or hemorrhagic enteritis.

Table (3): Morbidity & case fatality of H.S and its relation to FMD infection.

Animals infected with FMD	Morbidity of H.S (2600)		Case fatality of H.S (362)	
4616	No.	%	No.	%
	2600	56.32	362	13.92

3.3.2. Cell mediated immune response:

3.3.2.1. Phagocytic activity and Phagocytic index:

As shown in table (4), FMD infected animals showed lower Phagocytic power than those non infected ones.

Table(4): Results of Phagocytic activity and Phagocytic index.

Samples	Mean Phagocytic activity(PA)	Mean Phagocytic index(PI)
FMD infected (8 animals)	16	1.5
Non infected (4 animals)	20	1.9

3.3.2.2. Differential leukocytic count:

As shown in table (5), FMD infected animals showed lower WBCs count than those non infected ones.

Table (5): Mean WBCs count of FMD infected and non-infected animals.

Samples	Lymphocytes	Monocytes	Basophils	Eosinophils	Heterocytes
FMD infected (8 animals)	38	9	0.75	12	20
Non infected (4 animals)	46	11	0.75	10	23

3.4. Species difference in hemorrhagic septicemia infection in fattening calves.

As shown in (Table 6), buffalo calves showed more susceptibility to infection with H.S and higher case fatality rate than cattle calves.

Table (6): Species difference in hemorrhagic septicemia infection in fattening calves.

Animals infected with FMD		Morbidity of H.S (2600)				Case fatality of H.S (362)			
4616		Cattle		Buffalo		Cattle		Buffalo	
2056 cattle	2560 buffaloes	No.	%	No.	%	No.	%	No.	%
		710	34.3	1890	73.8	27	3.8	335	17.7

3.5. Mortality rate of H.S related to age of fattening calves:

As shown in (Table 7) Mortality rate among *p. multocida* infected fattening calves aged from 12-15 months is higher than older and younger ages.

Table (7): Mortality rate of H.S related to age of fattening calves:

Mortality in fattening calves aged from 6 to 11 months (no= 850 animals)		Mortality in fattening calves aged from 12 to 15 months (no= 950 animals)		Mortality in fattening calves aged from 16 to 30 months (no= 800 animals)	
No.	%	No.	%	No.	%
62	7.29	250	26.31	50	6.25

3.6. Antimicrobial sensitivity on H.S samples.

Antimicrobial sensitivity testing on *p. multocida isolates* showed that cefotaxime sodium, Ceftifour sodium, Marbofloxacin, gentamycin and enrofloxacin are the most effective antimicrobials as shown in table 8.

Table (8): Antimicrobial sensitivity on H.S samples.

Antimicrobial agent	Susceptible (S)		Moderately susceptible (M)		Resistant (R)	
	No. of samples	% of total	No. of samples	% of total	No. of samples	% of total
Cefotaxime	45	90	5	10	0	0
Cefifour sodium	45	90	5	10	0	0
Marbofloxacin	43	86	7	14	0	0
Enrofloxacin	36	72	8	16	6	12
Gentamycin	42	84	6	12	2	4
Erythromycin	14	28	20	40	16	32
Amoxicillin	22	44	19	38	9	18
Penicillin G sodium	-	-	-	-	-	-
Tetracycline	13	26	10	36	19	38
Chloramphenicol	24	48	11	32	10	20
Streptomycin	6	12	12	36	26	32
Trimeth/sulfa	17	34	10	32	17	34
Lincomycin-spectinomycin	39	78	8	16	3	6
Neomycin	8	16	12	24	30	60

3.7. Cure rate after different field treatment trials of H.S cases

As shown in (Table 9) the most effective antimicrobials on infected animals was ceftifour sodium, cefotaxime sodium, gentamycin and lincospectin.

Table (9): Cure rate after different field trials treatment of H.S cases

Group	Number of animals	Cure rate from H.S	
		No.	%
Group 1 Ceftifur sodium	470	423	90
Group 2 Lincspectin and gentamycin.	350	280	80
Group 3 Cefotaxime sodium.	905	815	90.05
Group 4 Tylosine and gentamycin	150	105	70
Group 5 Tultrathromycin	170	85	50
Group 6 Sulpha + Trimeth	70	14	20
Group 7 Oxytetracyclin LA	200	40	20
Group 8 Amoxycillin.	75	Zero	Zero
Group 9 Florfenicol	210	Zero	Zero

4. Discussion

Foot-and-mouth disease virus (FMDV) is the causative agent of a highly contagious vesicular disease of cloven-hoofed animals. Serologically, FMDV can be classified into seven antigenically distinct serotypes, O, A, C, SAT1, SAT2, SAT3, and Asia 1, and innumerable subtypes. Immunologically, there is no cross protection between serotypes. ***(Mohan et al., 2009).***

In the present study as shown in table (2), 4616 out of 5630 fattening calves aged from 6 months to 30 months previously vaccinated by inactivated FMD vaccine serotype A and O showed clinical signs for FMD new strain SAT_2 as confirmed by animal health research institute (AHRI), Dokki, Giza, Egypt. 13 fattening calves died from FMD infection without complication (negative isolation of bacteria and blood parasites).

Early infection of T cells by FMDV may be the main cause of the observed T-cell depletion. Importantly, this lack of T cells is reflected in a reduced response to mitogen activation, which in many cases is totally eliminated. These data suggest a mechanism by which the virus causes a transient immunosuppression, subvert the immune systems, and spreads. These results have important implications for our understanding of early events in the development of a robust immune response against FMDV ***(Fayna Díaz et al., 2006).***

HS is an acute, fatal, septicaemic disease of cattle and buffaloes caused by the gram-negative bacterium *Pasteurella multocida.* The disease has a major impact on the livestock industry where it causes severe economic losses and is ranked as the most important contagious disease of cattle and buffaloes**.** Serotypes B: 2 and E: 2 are two common serotypes of *P. multocida* associated with disease in animals in Asia and Africa, respectively ***(Farooq et al., 2007).***

Our results revealed that *Pasteurella multocida* serotype B:2 was isolated from infected animals. *Pasteurella multocida* serotype B:2 was the most common causative agent of Hemorrhagic septicemia in Buffaloes manifested by a highly fatal septicemia with the causative agent being ***Wijewardana, (1992), Hopkins et al. (1998) and Shivachandra et al. (2011).*** Serotypes B: 2 and E: 2 are two common serotypes of *P. multocida* associated with disease in animals in Asia and Africa, respectively ***(Benkirane and De Alwis, 2002).*** *Pasteurella multocida* remains as commensal in bronchi, terminal bronchioles, and alveoli. This pathogen cannot invade lungs due to defense mechanism but stresses as climatic change, malnutrition, transport, etc. trigger the organism and lungs are unable to clear the pathogens ***(Harper et al., 2006).***

Table (3) explained the role of FMD in aggravating the hemorrhagic septicemia infection in fattening calves, out of 4616 fattening calves infected by FMD, 2600 (56.32%) fattening calves were infected with *Pasteurella multocida* causing H.S disease. 362 (13.92%) fattening calves died from H.S.

P. multocida was the most secondary complication in cattle and buffalos following outbreaks of foot and mouth disease ***(Radostastis et. al., 2007)***. The previous observations were supported by our findings which revealed lower phagocytic power & WBCS count in FMD infected calves than those non infected ones (Tables 4,5), as FMD virus causes a transient immunosuppression as it causes lymphopnea and decreases lymphocyte proliferative response ***(Mohan et al., 2009).***

In the present study, 56.32% morbidity and 13.92% case fatality due to HS has been recorded in fattening calves and the high mortality could be attributed to its acute and sometimes per acute clinical nature which does not allow treating the animals. In the recent past, H.S has been identified as a secondary complication in cattle and buffaloes following outbreaks of FMD ***(Carter and De Al Wis, 1989)***. Case fatality approaches 100% if treatment is not followed at the initial stage of infection ***(De Al Wis, 1992).***

As shown in Table (6), Out of 2056 and 2560 fattening cattle and buffalo calves infected by FMD, 710 (34.3%) and 1890 (73.8%) fattening cattle and buffalo calves infected by *Pasteurella multocida* causing H.S disease respectively. Case fatality rates were 27 (3.8%) and 335 (17.7%) of fattening cattle and buffalo calves respectively. From the previous results, buffaloes showed more susceptibility to the disease than cattle as the overall mean case fatality for buffaloes is nearly three times as high as in cattle ***(Radostits et al., 2007).***

The morbidity, mortality and case fatality rates of hemorrhagic septicemia (HS) in Punjab, Pakistan were 57.58, 8.63; 52.30, 5.27 and 90.83, 61.11% in buffalo and cattle calves respectively ***(Farooq et al., 2011).*** Also, ***De Alwis (1981),*** documented overall mortality rate of 45.2 and 15.8% for buffaloes and cattle, respectively. Similarly, ***Sheikh et al. (1996)*** documented 9% mortality and 78% case fatality rates of HS in buffaloes, whereas these values were 2.5 and 62% in cattle.

Table (7) showed that the mortality rate due to HS was greater in calves (12-15 months) than younger and older ones. The stock of younger both buffaloes and cattle have higher morbidity, mortality and case fatality rates as compared to older ones

(Khan et al., 2011). Animals of all ages are susceptible to Hemorrhagic septicemia but the most susceptible age group is 6 months to 2 years of age **(*Radostastis et. al., 2007*).**

The susceptibility of *P. mulTocida* isolates, expressed in terms of minimum inhibitory concentration (MIC), to antibacterial agents. showed that *P. mulTocida* isolates were sensitive to some antimicrobial agents as shown in table (8). *P. mulTocida* were sensitive to cefotaxime sodium (90%), Ceftifour sodium (90%), marbofloxacin (86%), gentamycin (84%), lincomycin-spectinomycin (78%) and enrofloxacin (72%), while *P. mulTocida* isolates were resistant to penicillin, neomycin, erythromycin, streptomycin, tetracycline, Trimeth/sulfa, amoxicillin and chloramphenicol (Table 8).

52 strains of *P.multocida* isolated from pigs were sensitive to cephalexin (100%) followed by norfloxacin (96.15%), gentamicin (88.46%) ***(Sharma, 2004)***. In addition, most *P. multocida* are resistance to streptomycin, tetracycline, oxacillin and trimethoprim ***(Wassenaar and Silley, 2008).*** Also 67% of isolates resistant to cephalexin **(*Gupta, 1996*)**. The majority of *P.multocida* isolates were sensitive to enrofloxacin, gentamicin and choramphenicol but moderately sensitive to pefloxacin and ciprofloxacin and resistant to sulphadimidine, oxytetracycline, streptomycin, amoxycillin and tetracycline ***(Verma et al., 2004).***

Table (9) showed that 90% of HS cases responded to treatment with Ceftifour sodium and Cefotaxime sodium followed by Lincspectin and gentamycin (80%), Tylosine and gentamycin (70%), Draxxin (50%), Borgal (20%), Alamycin (20%) while Amoxycillin and Nuflor (0%). To achieve effective, drugs must be administered during the early stage of the disease, before appearance of specific clinical signs***(Prescott and Baggot, 1988 & De Alwis, 1999).***

It can be concluded that SAT $_2$ FMD infections played an important role in appearance of HS outbreak in buffalo and cattle in Alexandria province; Egypt causing high mortality rates especially in 12-15 months age buffalo and cattle calves respectively. Treatment of the affected cases is only effective when treated as early as possible with Ceftifour sodium or Cefotaxime sodium.

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