



REDUCING MORTALITY & HOSPITAL STAY IN SWINE FLU PATIENTS WITH EARLY DIAGNOSIS AND TREATMENT WITH OSELTAMIVIR AND IV VITAMIN C- A DETAILED CLINICAL PERSPECTIVE

Dr Deepa Sunil Banjan*

MD, Associate. Professor Department of Medicine RGM & CSMH. Kalwa

*Corresponding Author

Dr Amitanshu Hazare

Senior Resident Medicine. Department of Medicine RGM & CSMH

ABSTRACT

-H1N1 INFECTION also known as Swine flu, is a viral illness seen in Humans. 2009 WHO declared a Pandemic as many people suffered worldwide. The clinical picture in severe cases of pandemic (H1N1) 2009 influenza is markedly different from the disease pattern seen during epidemics of seasonal influenza. [1] The dominant strain flu strain in India this year was the A/Michigan/7/2009 (H1N1) pdm09 virus, which replaced in 2016. A/California/7/2009 (H1N1) pdm09 virus as the predominant virus around the world. As per ICMR reports.

A cross-sectional study on patients coming with flu like symptoms was carried out over a period of 12 months in a public hospital. Total 300 Patients were tested, 71 cases were admitted. 43 were positive for H1N1. The Patients were categorised into A, B, C as per National guidelines of WHO on H1N1 epidemics, they were divided in 2 Random groups. Group 1 was treated with Oseltamivir 75 mg Bid and Vitamin C 1500 mg IV/day. A reduced rate of complications of PCR POSITIVE H1N1 Michigan/7/2009/pdm09 H1N1, was observed. The average hospital stays remained 4 days as compared to 10 days in patients not given Vitamin C iv. No death was reported after discharge. Early administration of Vitamin C administration as adjuvant therapy with Oseltamivir, helped to reduce hospital stay, complications and Mortality

KEYWORDS : H1N1, Oseltamivir, Vitamin C. Hospital Stay

Introduction:

H1N1 or Swine flu, is a deadly disease-causing influenza in humans. H1N1 influenza virus is an orthomyxovirus and produces virions that are 80 to 120 nm in diameter, with an RNA genome size of approximately 13.5 kb. The swine influenza genome has 8 different regions which are segmented and encode 11 different proteins: 1] Envelope proteins hemagglutinin (HA) and neuraminidase (NA) 2] Viral RNA polymerases which include PB2, PB1, PB1-F2, PA, and PB3] Matrix proteins M1 and M2 [3] Non-structural proteins NS1 and NS2 (NEP), which are crucial for efficient pathogenesis and viral replication [5]

The dominant strain flu strain in India this year is the A/Michigan/7/2009 (H1N1) pdm09 virus, which replaced last year A/California/7/2009 (H1N1) pdm09 virus as the predominant virus around the world. As per ICMR reports, The A/Michigan/7/2009 (H1N1) pdm09 virus has been isolated in the Indian population for the first time, so the outcome is unknown. [1*] National statistics from Union Ministry data show that there have been 8,648 confirmed cases and 345 deaths in Month of May compared to 1,786 cases and 265 deaths between January and December months [2*]. The symptoms of H1N1 influenza infection are cough, coryza, breathlessness, fever, Malaise, body ache. Severe infections result in Pneumonia and Pleural effusions. Deaths have been reported mainly due to Type 1 respiratory failure... Swine influenza spreads from person to person, either by inhaling the virus or by touching surfaces contaminated with the virus, then touching the mouth or nose. Symptoms occurring in infected human by H1N1 are like any other flu symptoms. Treatment is largely supportive and consists of bed rest, increased fluid consumption, cough suppressants, antipyretics and analgesics for fever and myalgia. Management largely includes the potential use of antiviral agents for patients presenting with illness due to influenza virus infection. If the illness is known or suspected to be due to a zoonotic influenza A virus, oseltamivir or zanamivir are treatment options. For known or suspected infection with avian influenza H5N1 virus, antiviral treatment should follow the World Health Organization (WHO) rapid advice guidelines on pharmacological management of humans infected with highly pathogenic avian influenza A (H5N1) virus. WHO also recommends vaccination of the high-risk group with seasonal influenza vaccine. Vaccination is recommended for health care workers working in close proximity to influenza patients are at higher risk of acquiring the disease. [3*]. In Our study, we also studied the effects of IV vitamin C as a therapeutic adjuvant in H1N1 cases.

Materials and Methods

A cross-sectional Random control study was done over a period of 12 months in a public institute from June 2017 – June 2018. After Ethical

committee approval, 300 patients presenting with cough, coryza, fever and breathlessness were randomly screened for H1N1 virus in the Throat swabs with informed consents. Standard Real Time PCR Tests were used to detect presence of virus and infection in throat swabs collected following the national guidelines [10*] Adults of all ages were included without any specific gender selection. Patients of already established disease other than H1N1 were excluded from the study. The patients were divided into 3 categories. A, B & C. Category A did not require hospitalisation, treatment with Oseltamivir. Mild symptoms and history less than 48 hrs onset. Patients who had all symptoms of A plus a High-risk condition were classified into Category B. Category C included all patients with High risk symptoms that included breathlessness, cough, ARDS, Cyanosis, pleural effusion, Pneumonia, and other high risks conditions like pregnancy, Diabetes, Malignancy, Hiv/ Aids, Kidney disease. [10*] All 300 patients were treated with Vitamin C orally dose 300-1500 mgs/ day as per severity of symptoms. Category A were given Vit C Orally. Category B & C were given Oral Oseltamivir 75 MG bid for 7-14 days plus Vitamin C 1500 mg Intravenously. Complicated cases were treated for respective complications with antibiotics and supportive care. Fever was treated with paracetamol orally. All positive patients were isolated and category C were treated in isolated Intensive care. Exposed immediate family members were given PEP and treating personals were offered Voluntary vaccination against prevailing strain. N95 masks and isolation kits were provided for sample collectors and contacts. All cases were admitted in isolation wards as per National guidelines. [10*]. The admitted cases were divided into 2 groups. Group 1 was given Oseltamivir and iv Vitamin C 1500 mgs/day. 43 patients were given Vitamin C. Group 2 was not given Vitamin C.

Observations and Conclusions:

300 patients had been screened for symptoms, 71 required admission to the hospital. [23.66%] 43 patients among the 71 admitted, were tested positive for H1N1.virus. [60.56%]. 16 positive patients developed complications. 10 females and 06 males [62.5%, 37.5%]. Age group range was from 21- 75 years Total duration of hospital stay was in the range of 2-14 days. No deaths were observed in admitted patients in our study. No complications were reported in category A patients. No patient progressed from B to C category after starting treatment. The maximum number of cases were recorded in the month of June till December. The intensity showed seasonal trends. Cough & rhinorrhoea were the most common presentation, followed by fever and then breathlessness. Cyanosis was observed in 17 patients. Cough was the most predominant symptom first to appear and last to go in all admitted positive patients. Fever was the second most prominent symptom and seen in 234 cases. Average duration of fever post admission was from 0-4 days. Rhinorrhoea did not persist beyond 3

days. 10 patients had complicated disease 2 had secondary bacterial pneumonia. 3 patients with pleural effusion. 3 with uncontrolled diabetes and sepsis and 2 patients had ARDS. 7 males and 3 females had complications. All complicated patients were PCR positive for H1N1. Patients who were treated with Oseltamivir and Vitamin C iv 1500 mg per day showed reduction in hospital stay by No deaths were reported or observed during the study. 39.43 % not given Vitamin C .60.56% Given Vit C. Hospital stay in group A= 10 days in group B= 4 days. 14.33 % showed reduction in symptoms with Vitamin C as compared to 9.33 % in Group not administered iv Vitamin C. Average Hospital stay of patients who were given Vitamin C along with Oseltamivir was 4 days as compared to 10 days of the group who was only given Oseltamivir.

Table 1

Symptoms	Total	Admitted	H1N1 Swab +ve	Male +ve	Female +ve	Complications	Days Of Hospita / stay/ +duration Of Symptom
1]Cough, cold fever less than 48 hrs,	300	71	43	23	20	10 - 3.33%	2-14 days
complications	16	43	43	06	10		6-14 days
fever	234	71	43	23	20		0-3 days
cough	300	71	43	23	20		0-14 days
Rhinorrhoea	300	71	43	23	20		0-3 days
breathlessness	119	71	43	23	20		0-14 days
cyanosis	17	71	43	13	04		0-10 days
Diarrhoea/ abd discomfort	nil	nil	nil	nil	nil		nil
Pneumonia / Pleural effusion/ ARDS	10	71	43	7	03	10- 3.33%	14 days.

TABLE 2

Observed frequencies						Calculations				Data	
Admitted patients	H1N1 +ve	HOSPITAL STAY	COMPLICATIONS	Total		fo - fe		Level of Sig.			
Vitamin C GIVEN	43	4	0	47		7.8737	-2.9263	-4.947368	Number of	2	
VITAMIN C NOT GIVEN	28	10	10	48		-7.8737	2.9263	4.947368	Number of	3	
Total	71	14	10	95					Degrees of	2	
Expected frequencies											
Admitted patients	H1N1 +ve	HOSPITAL STAY	COMPLICATIONS	Total		(fo - fe)/2/fe		Critical Value		Results	
Vitamin C GIVEN	35.1263	6.9263	4.947368421	47		1.7649	1.2363	4.9474	Chi-Square	15.7317	
VITAMIN C NOT GIVEN	35.8737	7.0737	5.052631579	48		1.7281	1.2106	4.8443	p-Value	0.0004	
Total	71	14	10	95							

level of significance =0.05/ no of rows 2/ no of columns=3/ degree of freedom 2

Critical value -5.9915 Chi Square=15.7317 P value 0.0004

Discussion:

Non-seasonal influenza infections have specific clinical manifestations. Pneumonia related to the 2009 H1N1 influenza A pandemic was also found in many cases to be rapidly progressive, leading to respiratory failure and ARDS [7*,8*]. In our study, the most prominent symptoms were cough & fever. The average hospital stay was reduced in patients who were given Vitamin C along with oral Oseltamivir from day 1 of admission. Only 2 cases with complications like secondary bacterial pneumonia were recorded. The reasons could be better diagnostic and ICU facilities, timely intervention and early suspicion with immediate therapy. The A/Michigan/7/2009 (H1N1) pdm09 virus, strain has a lesser attack rate than the California and Early administration of Oseltamivir along with iv Vitamin C, helped in recovery. Oseltamivir has been proved of significance in the cure of H1N1. The role of Vitamin C IV has been helpful in curing Viral infections [11*12*] In our study, the Expected frequency assumption was met hence we concluded that the null hypothesis about Vitamin C making no difference to stay and preventing complications, was rejected. The study showed statistical significance with a P value of 0.0004.. We did not find any contacts suffering from H1N1, emphasising the value of isolation and prophylaxis to be given to contacts. The secondary bacterial pneumonias in 2 patients, responded well without advancing to septicemia. Role of high dose Vitamin C in sepsis has also been proved beneficial in severe sepsis. [13*]

Observations in our study concur with the same

Pleural effusions showed transudate and resolved on X-rays and follow up sonography within 14 days. Pre-existing morbid conditions did not show any significant deterioration due to concomitant H1N1 presence. Hence the study emphasises on early diagnosis, hospitalisation, isolation and treatment with Oral Oseltamivir and IV vitamin C 1000-1500 mg/ day in category B & C patients of H1N1 patients to reduce hospital stay and prevent mortality and morbidity.

Scope of the study & Limitations

The scope of this study helps to contribute to health policies and highlight the need for multidisciplinary actions at various levels to halt spread of H1N1. The reduction in hospital stay as compared to the cost of medication given early, seems far more important where public expenditure is concerned. Limitations were 1] our Sample size was less to compare statistically and advocate therapy as a general recommendation. 2] Being a public hospital, only Oseltamivir effects could be studied as per availability. Zanamavir has been shown to be equally effective therapeutic agent. 3] Follow up of complicated patients and high-resolution CT scans could not be done to rule out long term complications of H1N1 pneumonia or Effusions. 4] Only Oral Therapy could be given hence iv complications or Adverse drug reactions to Oseltamivir could not be studied. Since Multiple strains of H1N1 exist and attack rates are high it is very difficult to predict & isolate which strain causes epidemic in seasonal influenza.

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