Original Research Paper Medicine

RETROSPECTIVE STUDY OF H1N1 POSITIVE PATIENTS (2014-15) IN WESTERN RAJASTHAN

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ABSTRACT

AIM: To study the clinical profile of H1N1 patients during the 2014-2015 epidemic in Western Rajasthan and to study the outcome during treatment at tertiary level healthcare center.

METHODS

Study region: The study is as conducted in Department of medicine, DR. S.N.M.C. & MDM Hospital which is a tertiary care hospital in western part of Rajasthan. This institute provides health services to around 12 million populations residing in Jodhpur and neighbor districts e.g. Barmer, Jaisalmer, Jalore, Pali, Sirohi, Nagaur.

Study Design: It was a retrospective study based on systematic analysis of institute medical records during the epidemic period.

Study size: All patients who were enrolled in institute record system during the study period (2014-15) and were H1N1 positive on RT-PCR were analyzed from their bed head tickets.

SUMMARY and CONCLUSIONS: The study was done on 162 H1N1 positive patients out of which 119(73%) were discharged and 43(26%) succumbed to death.

47% were males and 50% were females. Total number of deaths were 43 out of which 28% were males and 24% were119(73%) were discharged and 43(26%) succumbed to death. 47% were males and 50% were females. Total number of deaths were 43 out of which 28% were males and 24% were females. Most affected age group was 21-40 years in both sexes.

KEYWORDS : H1N1, Swine flu, Rajasthan

INTRODUCTION

The word influenza was first used in England in 1743. Standard influenza nomenclature includes the virus type (A, B or C), geographical origin, strain number, year of isolation, and virus sub-type[1].Influenza A virus is a member of the Orthomyxoviridae family. Influenza A sub-type classification is based on the antigenicity of the 2 major cell surface glycoprotein; hemagglutinin (HA) and neuraminidase (NA). To date 16 HA (H1-H16) and NA (N1-N9) sub-types have been identified. Influenza A virus has the ability to undergo periodic change in antigenic characteristic of cell surface glycoproteins. Major changes in these glycoprotein are referred to as antigenic shift and minor changes are called antigenic drift. Antigenic shift is associated with epidemics and pandemics[2].The incubation period of influenza ranges from 1 to 4 days. Aerosol transmission may occur 1 day before the onset of symptoms; thus, it may be possible for transmission to occur via asymptomatic persons or persons with subclinical disease, who may be unaware that they have been exposed to the disease. [3-5]Three influenza pandemics occurred in the 20th century and killed tens million of peoples[6], with each of these pandemic being cause by the appearance of a new strain of the virus in the human. In April 2009 a novel flu strain evolved that combined genes from human, pig, and bird flu, initially dubbed "swine flu" and also known as influenza A/H1N1, emerged in Mexico, the United States, and several other nations. The 2009 flu pandemic was a global outbreak of a new strain of H1N1 influenza virus, often referred to as "swine flu"[7]. Rajasthan, the largest state in India, reported its first case of H1N1 infection on 23rd July 2009. Soon the disease spread all parts of the state.

Number of Swine Flu Cases and Deaths in Rajasthan (2009 to 2015)

a		Jan, 2010-Dec, 2010		Jan, 2011-Dec, 2011		Jan, 2012-Dec, 2012		1st Jan, 2013-16th June, 2013		Total no. Of cases till Apr 8, 2015	
Cases	Death	Cases	Death	Cases	Death	Cases	Death	Cases	Death	Cases	Death
3032	150	1710	153	36	11	343	60	847	163	6597	406

In 2015 (up to 8th April) a total no of 6597 H1N1 Positive cases and 406 fatal cases reported in rajasthan which was highest in India.[8]

MATERIALS AND METHODS

Study region: The study is as conducted in Department of Medicine, DR. S.N.M.C. & MDM Hospital which is a tertiary care hospital in western part of Rajasthan. This institute provides health services to around 12 million population residing in Jodhpur and neighbouring districts e.g. Barmer, Jaisalmer, Jalore, Pali, Sirohi, Nagaur.

Study Design: It was a retrospective study based on systematic analysis of institute medical records during the epidemic period.

Study size: All patients who were enrolled in institute record system during the study period (2014-15) and were H1N1 positive on RT-PCR were analysed from their bed head tickets.

Inclusion criteria:

1. All laboratory confirmed cases (RT-PCR based) of novel influenza H1N1
2. Age above 15 years
3. Either sex

Exclusion criteria

1. Laboratory confirmed negative for novel influenza H1N1
2. Age less than 15 years
3. Bed head tickets which had incomplete information regarding clinical profile and outcome during treatment.

Tools: The study protocol was be approved by the institutional ethical committee. Patients admitted with fever with chills and rigor, cough, shortness of breath was be selected for the study. The record of the patient were analyzed thoroughly for clinical profile and events and outcomes during hospital stay.

Statistical analysis: Collected data were analyzed with appropriate statistical tests.

OBSERVATIONS

Table 1: Distribution of H1N1 positive male cases according to residence in various age group

Age (in yrs)	MALE				FEMALE			
	Rural		Urban		Rural		Urban	
	Death	Discharge	Death	Discharge	Death	Discharge	Death	Discharge
<20	0	1 (2.63)	0	1 (2.38)	1 (2.08)	4 (8.33)	0	4 (11.76)
21-40	3 (7.89)	11 (28.95)	0	9 (21.43)	10 (20.83)	19 (39.58)	3 (8.82)	10 (38.24)
41-60	10 (26.32)	5 (13.16)	3 (7.14)	18 (42.86)	2 (4.17)	10 (20.83)	2 (5.88)	11 (38.24)
>60	4 (10.53)	4 (10.53)	3 (7.14)	8 (19.05)	0	2 (4.17)	2 (5.88)	2 (11.76)
Total	17 (44.74)	21 (55.26)	6 (14.29)	36 (85.71)	13 (27.08)	35 (72.92)	7 (20.59)	27 (79.41)

Table 2: Distribution of co- morbid condition in male H1N1 positive

Comorbidities	MALE				FEMALE			
	Rural		Urban		Rural		Urban	
	Death	Discharge	Death	Discharge	Death	Discharge	Death	Discharge
Cardiovascular (HT, IHD, RHD)	2 (5.2)	3 (7.8)	2 (4.6)	4 (9.5)	0	7 (20.5)	1(2.9)	3 (8.82)
Respiratory (Asthma, COPD, K Chest)	3 (7.8)	2 (5.2)	2 (4.6)	6 (14.2)	2 (4.17)	4 (11.7)	1 (2.94)	2 (5.88)
DM	1 (2.63)	2 (5.26)	1 (2.38)	5 (11.90)	0	2 (4.17)	0	3 (8.82)
Renal	0	0	0	0	0	0	0	0
GIT	0	0	0	0	0	0	0	0
CNS	0	0	0	0	0	0	0	0

TABLE 3: Showing death distribution in male H1N1 positive patients which have other illness

Cause of death	MALE		FEMALE	
	Rural	Urban	Rural	Urban
B/L pneumonia with ARDS	12	3	11	Tab5
H1N1 Positive with Renal failure	4	1	0	0
H1N1 Positive with Liver failure	5	0	6	2
H1N1 Positive with DM	1	1	0	0
H1N1 Positive with HTN	2	2	0	0
H1N1 Positive with COPD	2	1	2	1
H1N1 Positive with MODS	5	2	2	3
H1N1 Positive with CAD	0	1	0	1

RESULTS:

The Present study aimed to assess the morbidities and mortalities among H1N1 positive patients in terms of demography, clinical profile and cause of death so that high risk groups and clinical features can be identified to help in early intervention. The study was done in 162 H1N1 positive patients who were admitted in MDM hospital, Jodhpur. Out of these 162 patients 119 (73%) were discharged and 43 (26%) succumbed to death.

In our study we found that total number of male patient admitted was 80 (47%) out of which 38 (47%) were rural and 42 (52%) were urban. Overall mortality among male was 23(28%). Among rural males 17(44%) succumbed to death while 21(55%) survived. Among urban males 6 (14%) succumbed to death while 36 (85%) survived. In both rural and urban males most affected age group was 41-60. The study also showed that total number of female patient admitted was 82 (50%) out of which 48 (58%) were rural and 34 (41%) were urban. Overall mortality among females was 24%. Among urban females 7(20%) succumbed to death while 27 (79%) survived. Among rural females 13(27%) succumbed to death while 35 (72%) survived. In both rural and urban females the most affected age group was 21-40. In rural females 29 (60%) were in this age group while in urban females 13 (38%) were in this age group. (Table no.1)

The study revealed that most common co morbid condition associated in rural males was disease of the respiratory system and cardiovascular system(13% and 13% respectively) followed by diabetes 7.8% while in urban males its was cardiovascular system and respiratory disease (14% and 19% respectively) followed by diabetes 14%. It also showed the most common co morbid condition in rural females and urban females was disease of the cardiovascular system 21% and 8% respectively, followed by respiratory system 18% and 9% respectively. (Table no.2)

In our study it was concluded that most common cause of death among males was bilateral pneumonia with ARDS with hypoxic respiratory failure (65%). Another 30% death due to septicemia and multi organ dysfunction syndrome with H1N1 infection. 13% death were due to respiratory illness with influenza. It was also found that most cause of death in females was B/L pneumonia with ARDS with respiratory failure 80%. 25% died due to septicemia and multi organ dysfunction syndrome. (Table no 3). (Table 4)

DISCUSSION: The Present study was aimed to assess the mortalities among H1N1 positive patients in terms of demography, clinical profile and cause of death so that high risk groups and clinical features can be identified to help in early intervention.

In both rural and urban females the most affected age group was 21-40. In rural females 29 (60%) were in this age group while in urban females 13 (38%) were in this age group. Maximum number of deaths was also in this age group (20% in rural females and 8% in urban females).

Previous studies show that ROGELIO PEREZ-PADELLA et [9]al in their study in Mexico concluded that more than half of the patients were between 13 and 47 years of age. ANAND KUMAR[10] et al in their study of critical illness concluded that among the 168 patients with confirmed or probable 2009 influenza A(H1N1), the mean (SD) age was 32.3(21.4) year and 113 were female (67.3%). SEEMA JAIN et al[11] in their study of 272 hospitalized patients in U.S found that the median age of patients who died was 26 years. D.B. KADAM et al[12]in their study of H1N1 positive patients in Pune concluded that mean age of survivor's population was 31.4 while that of succumbed patients was 36.23%. MATHUR et al[13]study show that the most affected age group in both male and female patients was 21-40 year. Our study concluded that 87% of rural males and 90% of urban males presented within five days of onset of symptom while 11% of rural males and 10% of urban males presented after five days. We found that male patients which presents within 1-5 days were also significantly associated with high mortality rate (82% and 83% respectively) in both rural and urban but not statically significant. We were also found that 83% of rural females and 94% of urban females presented within 1-5 days onset of symptom while 15% of rural females and 3% of urban females presented after five days. Our study found that female patients which presents within 1-5 days were also significantly associated with high mortality rate (84% and 100% respectively) in both rural and urban female ROGELIO PERAZ-PADELLA et al[9] in their study in the Mexico concluded that one contributing factor for death in the patients may have be delayed admission and delayed initiation of oseltamavir. K.N BHATT et al[14] and D. B. KADAM et al[12] in their study concluded that higher mortality was associated with delayed presentation and late institution of oseltamavir. Mathur et al[13] in their study in Western Rajasthan concluded that patients presentation after five days of onset of symptoms have high mortality.

Our study concluded that rural males and urban males (2% and 2% respectively) had normal respiratory rate at presentation while 97% rural males and 95% urban were tachypneic (respiratory rate >20/min). tachypnea as a significant factor for mortality in both rural and urban but not statistically significant. It also show that 2% of rural female and 8% of urban female had normal respiratory rate at

presentation while 97% rural females and 91% urban females were tachypneic. Tachypnea was a significant risk factor for mortality in both rural female (p value <0.0003) and urban females, but in urban females not statistically significant.

In Previous study show D.B.KADAM et al[12] of H1N1 positive patient in Pune concluded that tachypnea was significantly associated with death in H1N1 positive patients. MATHUR et al[13] in their study of H1N1 patients in western Rajasthan, in both male and female patients tachypnea was significantly associated with fatal outcome. The study concluded that 5% of rural males were in shock (systolic BP 90 mm of Hg) at presentation and all of them succumbed to death. So shock was invariably associated with fatal outcome. It also showed that 4% of rural female were in shock at presentation and all of them succumbed to death. So shock was invariably associated with fatal outcome in female also (p value <0.048).

The study concluded that 45% of total rural males and 62% of urban males had normal arterial oxygen saturation at presentation. 39% of rural male patients with low saturation (<90%) succumbed to death, while 11% of urban females with low saturation died. Thus low saturation was significantly associated with high mortality (p value < 0.002 in rural, p value < 0.014 in urban). It also showed that 47% of total rural females and 61% of urban females had normal arterial oxygen saturation at presentation. 27% of rural female patients with low saturation (90%) succumbed to death while 18% of urban female with low saturation died. It was revealed that low oxygen saturation is significantly associated to high mortality in both rural or urban females (p value <0.0003).

This view was supported by ANAND KUMAR et al[10] in their study who found that low saturation was associated with ICU admission and increase mortality.

Another conclusion derived was that 47% of rural males and 31% of urban males had high pCO^2 (> 40) at presentation. It was also found that 27% of rural and 26% of urban females had high pCO^2 at presentation. There was no statistical significant difference rural and urban males but in urban female mortalities associated with high pCO^2 (p value 0.0004).

The study also revealed that 21% of rural male and 16% of urban males had acidosis pH(<7.35) at the time of presentation. 19% rural males with acidosis succumbed to death while 7% of urban males with acidosis died. Acidosis was significantly associated with mortality in rural males (p value 0.013) while this was not so with urban males. It was also found that 15% of rural females and 18% of urban females had acidosis at the time of presentation. 8% of rural with acidosis succumbed to death while 14% of urban female with acidosis died. Acidosis was significantly associated with mortality in rural female (p value 0.006) as well as with urban females (p value 0.0001). This was supported by ROGELIO PEREZ-PADELLA et al[9] in their study in Mexico and by D.B.KADAM et al[12] in their study of H1N1 positive patients in Pune who concluded that hyperlactatemia and acidosis was associated with poor prognosis. Mathur et al[13] in their study in western Rajasthan revealed that acidosis have statistically significant value for fatal outcome.

It was found that 74% of rural males and 86% of urban males had normal Total Leukocyte Counts at presentation. Thus normal TLC was significantly associated with H1N1 infection. It was found that 79% of rural female and 74% of urban female had normal TLC at presentation. Thus normal TLC was significantly associated with H1N1 infection. This was supported by ROGELIO PEREZ-PADELLA et al[9] in their study in Mexico who found that one of the most consistent laboratory characteristic in H1N1 infection was a TLC within normal limits. There was no significant association between TLC and death in both males and females.

Our study revealed that 47% of rural males and 42% urban males had increased blood urea at presentation. Increased blood urea was associated with more deaths in rural males that was statistically significant (p value 0.002). It also showed that 25% of rural females and 59% of urban females had increased blood urea at presentation. Increased blood urea was associated with more death in both rural female and urban female.

In our study it was found that 34% of rural males and 14% of urban males had increased serum creatinine at presentation. Increased serum creatinine was statistically significant associated with more death in rural males (p value 0.042) and urban males (p value 0.029). It also also show that 8% of rural females of 12% of urban females had increased serum creatinine at presentation. Increased serum creatinine was associated with more death in both rural female and urban female but not statistically significant.

Previous study by Mathur et al[13] in Western Rajasthan concluded that patients with raised serum creatinine level at presentation have significantly association with high mortality.

The study revealed that 50% of rural male and 45% urban male had increased SGOT at presentation. Increased SGOT was not associated with higher H1N1 infection and not significant association with mortality. It was also found that 33% of rural female and 47% of urban females had increased SGOT at presentation. In our study it was seen at 47% of rural male and 35% of urban males had increased SGPT at presentation. Increased SGPT was not associated with H1N1 infection and not significant association with mortality. It also shows that 21% of rural female and 35% of urban female had increased SGPT at presentation. Increased SGPT was not associated with H1N1 infection and not significant association with mortality.

In previous study MATHUR et al[13] study in western Rajasthan show that H1N1 positive patients had raised SGOT and SGPT were significant association with influenza infection.

The study concluded that 18% of rural male and 10% of urban males had hyponatremia while 31% of rural male and 35% of urban male had hypernatremia. 26% of rural males patient with deranged sodium level expired while 10% of urban males who had deranged sodium level succumbed to death. It was also found that 25% of rural females and 18% urban females had hyponatremia while 50% of rural female and 41% of urban female had hypernatremia. 18% of rural female patient with deranged sodium level expired while 11% of urban female who had deranged sodium level succumbed to death.

The study reveal that 47% rural males and 55% of urban males had hypokalemia while 18% of rural males and 14% of urban males had hyperkalemia. 26% of rural patients with deranged potassium level expired While 14% urban male who had deranged potassium level succumbed to death. Hence deranged potassium level was significantly associated with death. It also shows that 52% of rural female and 41% of urban female had hypokalemia while 19% of rural female and 18% of urban female had hyperkalemia. 16% of patient with deranged potassium level expired among rural female while 15% of urban female who had deranged potassium level succumbed to death. Hence deranged potassium level in urban female statistically significant associate with death (p value 0.007)

The study revealed that most common co morbid condition associated in rural males was disease of the respiratory system and cardiovascular system (13% and 13% respectively) followed by diabetes 7.8% while in urban males its was cardiovascular system and respiratory disease (14% and 19% respectively) followed by diabetes 14%. It also showed the most common co morbid condition in rural females and urban females was disease of the cardiovascular system 21% and 8% respectively, followed by respiratory system 18% and 9% respectively. SEEMA JAIN et al[11] in their study of 272 hospitalized patient in US found that 13 patients who dead 68% had an underlying medical condition, including neurological disease 21% asthma or COPD 16%. D B KADAM et al[12] their study of H1N1 patient in Pune found that co morbidities were present in 46% of the study population of which 31% had a single

while 15% had more than one co morbidities.

In our study it was found that out of total 82 admitted female 19 (23%) were pregnant. Out of the 19 pregnant female (33%) were rural and (9%) were urban. Out of 31 rural female 7 (15%) expired and 9 (19%) survived. Thus pregnancy was a factor associated with increased mortality in female (mortality rate 42%) as against non pregnant female (mortality rate 12%). This was also seen by SEEMA JAIN et al[11] and MATHUR et al[13] in their study of H1N1 positive patient who concluded that pregnancy was a risk factor associated with increased mortality.

In our study it was concluded that most common cause of death among males was bilateral pneumonia with ARDS with hypoxic respiratory failure 65%. Another 30% death due to septicemia and multi organ dysfunction syndrome with H1N1 infection. 13% death were due to respiratory illness with influenza. It was also found that most cause of death in females was B/L pneumonia with ARDS with respiratory failure 80%. 25% died due to septicemia and multi organ dysfunction syndrome.

This fact was supported by various studies. LOUIE J K et al[15] their study of H1N1 influenza in california found that the most common cause of death were viral pneumonia and acute respiratory distress syndrome. D B KADAM et al[12] in their study of H1N1 positive patients in Pune concluded that patients who developed pneumonia and respiratory failure succumbed to death in more number. A PUVANALINGAM et al[16] in their case study of the clinical profile of H1N1 swine flu influenza found that most common cause of death in patients was due to pneumonia and respiratory failure.

In our study concluded that total death in rural male was 17(74%) out of which 13 (76%) were on mechanical ventilation and total death in urban male 6 (26%) out of which 5(83%) were on mechanical ventilation. It was found in our study that total mortality in rural female was 13(65%) out of which 10 (77%) was on mechanical ventilation, while in urban female total mortality was 7 (35%) out of which 5 (71%) on mechanical ventilation. In Previous study show A PUVANALINGAM et al[16] concluded that requirement of mechanical ventilation was associated with poor prognosis in H1N1 positive patients

CONCLUSIONS:

The study was done on 162 H1N1 positive patients out of which 119(73%) were discharged and 43(26%) succumbed to death.

1. 47% were males and 50% were females. Total number of deaths were 43 out of which 28% were males and 24% were females. Most affected age group was 21-40 years in both sexes.
2. Cardiovascular and respiratory system comorbidity was significantly associated with mortality in males whereas it is only cardiovascular in females
3. Day of presentation from onset of symptoms within one to five days was significantly associated with high mortality.
4. Tachypnea and low arterial oxygen saturation were associated with high mortality.
5. Shock and Acidosis were invariability associated with high mortality.
6. Most common cause of death was hypoxemic respiratory failure(65%) and MODS and septicemia in 30%.

In the present study it is concluded that swine flu predominantly affected young age group who were previously healthy. The neglected section of the society that comprises of females particularly of rural background developed more severe form of disease and succumbed to death. Stress is to be given at strengthening health delivery and referral system at periphery level. Primary prevention in the form of vaccination will also help.

Table No. 4 Clinical profile and outcome of H1N1 patient in western Rajasthan.

Sex		MALE				FEMALE			
Residence		Rural		Urban		Rural		Urban	
Outcome		Death	Discharge	Death	Discharge	Death	Discharge	Death	Discharge
respiratory rate	≤20	0	1 (2.63)	0	1 (2.38)	0	1 (2.08)	0	3 (8.82)
	21-30	7 (18.4)	14 (36.84)	3 (7.14)	29 (69.05)	2 (4.17)	27 (56.25)	2 (5.88)	19 (55.88)
	31-40	9 (23.7)	6 (15.78)	3 (7.14)	6 (14.29)	9 (18.75)	7 (14.58)	5 (14.71)	5 (14.71)
	41-50	1 (2.63)	0	0	0	2 (4.17)	0	0	0
	51-60	0	0	0	0	0	0	0	0
sPO2	≤70	6 (15.79)	2 (5.26)	1 (2.38)	0	4 (8.33)	4 (8.33)	2 (5.88)	0
	71-80	5 (13.16)	3 (7.89)	2 (4.76)	4 (9.52)	5 (10.42)	2 (4.17)	2 (5.88)	0
	81-90	4 (10.53)	1 (2.63)	2 (4.76)	7 (16.67)	4 (8.33)	6 (12.50)	2 (5.88)	7 (20.59)
	>90	2 (5.26)	15 (39.47)	1 (2.38)	25 (59.52)	0	23 (47.92)	1 (2.94)	20 (58.82)
pCO2	≤40	4 (10.53)	16 (42.11)	2 (4.76)	27 (64.29)	9 (18.75)	26 (54.17)	1 (2.94)	24 (70.59)
	>40	13 (34.21)	5 (13.16)	4 (9.52)	9 (21.43)	4 (8.33)	9 (18.75)	6 (17.65)	3 (8.82)
TLC	≤11000	10 (26.32)	18 (47.37)	4 (9.52)	32 (76.19)	8 (16.67)	30 (62.50)	4 (11.76)	21 (61.76)
	>11000	7 (18.42)	3 (7.89)	2 (4.76)	4 (9.52)	5 (10.42)	5 (10.42)	3 (8.82)	6 (17.65)
Symptoms	Fever	17 (44.73)	21 (55.26)	6 (14.29)	36 (85.71)	13 (27.08)	35 (72.92)	7 (20.59)	27 (79.41)
	Cough	17 (44.73)	21 (55.26)	6 (14.29)	36 (85.71)	13 (27.08)	35 (72.92)	7 (20.59)	27 (79.41)
	SOB	17 (44.73)	21 (55.26)	6 (14.29)	36 (85.71)	13 (27.08)	35 (72.92)	7 (20.59)	27 (79.41)
	Coryza	0	0	0	0	3 (6.25)	0	2 (5.88)	1 (2.94)
	Myalgia	8 (21.05)	7 (18.42)	2 (4.76)	13 (30.95)	7 (14.58)	8 (16.67)	1 (2.94)	4 (11.76)
	Headache	4 (10.53)	3 (7.89)	3 (7.14)	7 (16.67)	0	11 (22.92)	3 (8.82)	5 (14.71)
	Bodyache	3 (7.89)	7 (18.42)	0	5 (11.90)	4 (8.33)	7 (14.58)	2 (5.88)	7 (20.59)

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