ORIGINAL RESEARCH PAPER

Volume - 11 | Issue - 07 | July - 2022 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

STUDY OF TWO YEARS EPIDEMIOLOGICAL TREND OF SWINE FLU (H1N1) CASES BY CROSS SECTIONAL ANALYSIS IN TERTIARY CARE TEACHING HOSPITAL OF WESTERN INDIA

Medical Science

Shah Meet C — Intern Doctor, Medical College Baroda – The M. S. University of Baroda.

Mistry Chirag B* — Faculty, Medical College Baroda – The M. S. University of Baroda. *Corresponding Author

Javadekar Tanuja B — Professor & Dean, Medical College Baroda – The M. S. University of Baroda.

ABSTRACT

BACKGROUND & OBJECTIVE: To study region-wise monthly incidence, alteration in seasonal trend and geographical distribution of Swine Flu (H1N1) cases in district of western India for two years. **MATERIAL AND METHOD:** After Ethics Committee approval, a cross-sectional study was carried out with analysis of two years' demographic profile, geographical distribution and seasonal variation of real time Reverse Transcription–Polymerase Chain Reaction (RT-PCR) - H1N1 positive cases. Annual change in pattern of positive cases was analyzed by independent sample student's t - test ($P < 0.05$). **RESULT:** Out of 3,524 Seasonal Flu cases investigated by Influenza A (H1N1) RT-PCR, total 1,600 Seasonal Flu–positive cases were analyzed. On looking at Age-wise distribution of patients, during first year, maximum number of Seasonal Flu positive cases was from age group of 1 to 10 years, while during next year, maximum number of cases was from age group of 51 to 60 years. During first year of epidemic, incidence of 836.12 cases per 1,00,000 population per year was detected with peak during winter as compared to 121.49 cases per 1,00,000 population per year with peak during monsoon in second year of epidemic. **INTERPRETATION & CONCLUSION:** During Epidemic of Seasonal Flu, Swine Flu (H1N1) positive cases got reduced annually, and seasonal pattern of H1N1 positive cases changed with peak during monsoon as compared to conventional winter peak. Overall change in seasonal trend, pediatric age distribution suggests need of in depth analysis of development of herd immunity, and risk factors involved for monsoon peak with alarming precaution by epidemic preparedness.

KEYWORDS

Cross-sectional Study, Demographic Profile, Epidemic, Pediatrics, RT-PCR, Seasonal Flu.

INTRODUCTION:

In the midst of various form of Seasonal Influenza, Swine Flu (H1N1) is a highly contagious acute respiratory disease, caused by Influenza A(H1N1) virus. In humans, the clinical picture of Swine Flu remains similar to those of influenza having fever, chills, sore throat, muscle pains, severe headache, coughing, weakness, and general discomfort[1].

Currently, as per updates of World Health Organization (WHO), there is overall increase in the number of infections globally. National Influenza Centres (NICs) and other national influenza laboratories from 102 countries, have identified that majority of cases were typed as Influenza A (93.8%) as compared to influenza B (6.2%)[1].

Moreover, as per WHO reports, "all age groups can be affected due to Swine Flu (H1N1) but pregnant women, children under 5 years, the elderly, individuals with chronic medical conditions (such as chronic cardiac, pulmonary, renal, metabolic, neuro-developmental, liver or hematologic diseases) and individuals with immunosuppressive conditions (such as HIV/AIDS, receiving chemotherapy or steroids, or malignancy) and healthcare workers can be more at risk of serious outcome than others"[2].

On the other hand, pattern of age distribution of patients and seasonal trend is changing due to antigenic shift and drift in influenza virus, due to re-assortment by transfers of genes among strains crossing swine, avian, and human species [3,4,5].

On looking at challenges for Influenza A (H1N1) treatment and prevention, still more study is needed for better understanding in changing nature of influenza illness relating to the distribution of cases and deaths by age, gender, and the associated risk factors, including the possible impact of climate change[6].

A uniform mechanism to collect, analyze and disseminate clinical, epidemiological and virology-related data could help public health policy and action. Monitoring of the genetic character of the virus and surveillance for drug resistance in the context of Swine Flu (H1N1) and other influenza viruses remain a high priority[6].

In India, the epidemic is evolving rapidly, and number of laboratory confirmed cases may be just a tip of iceberg[7]. So this study was planned to identify current epidemiological pattern of Swine Flu cases with respect to seasonal, monthly, age, gender and geographical variation over a period of two years.

MATERIAL AND METHODS:

In this cross sectional study, analysis of two years' investigation report of real time Reverse Transcription–Polymerase Chain Reaction (RT-PCR) for Swine Flu - Influenza A (H1N1) virus for patients of acute respiratory illness in tertiary care teaching hospital of Vadodara district and surrounding sub district was done.

Permission of Ethics Committee:

Before starting this study, approval of the Institutional Ethics Committee was taken (Registration No. IECHR- PGR/22-19/22.04.2019).Permission of Hospital Superintendent and Institute head was taken for collection of data of Laboratory reports and profile of patient. Identity of patient is kept confidential during submission of report and publication phase.

Study Design:

A cross-sectional study was carried out for analysis of investigation case reports of two years duration (1st January 2017 to 31st December 2018). Case details of reports of Seasonal Influenza and Swine Flu (H1N1) Investigations were entered and data was analyzed to identify positive result of patient by RT-PCR Diagnostic Technique with their demographic profile i.e. age, gender, geographical distribution and seasonal variation.

Comparative analysis of yearly trend of Swine Flu cases was carried out with reference to previous year to identify change from epidemic to endemic state. Annual pattern of positive cases of Swine Flu was analyzed with reference to geographical distribution and demographic profile.

Sample Size Calculation:

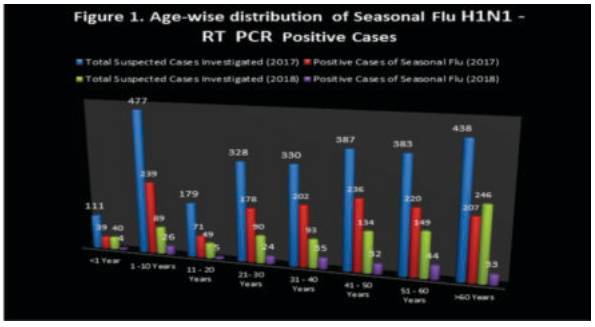
All cases investigated at RT- PCR Lab of tertiary care teaching hospital of Vadodara for Swine Flu (H1N1) for two years e.g. from 1st January 2017 to 31st December 2018 were analyzed. Considering above study period, to know seasonal trend, all total 3,524 investigation case reports of two years were analyzed irrespective of RT- PCR for H1N1 positive status.

Statistical Analysis:

Incidence Rate of Swine Flu (H1N1) Case was calculated with consideration of Month wise distribution in year 2017 and 2018. Data was entered in excel sheet and statistical significance of difference between age wise distribution, monthly cases of different year 2017 & 2018 was analyzed by independent sample student's t - test ($P < 0.05$).

RESULTS:

In this study involving two years investigation case report of year 2017 and 2018, total 3,524 investigation case reports of Seasonal Flu were analyzed and among them 1,600 cases were identified as Influenza A - Swine Flu (H1N1) positive as per investigation done by RT-PCR.



On looking at Age-wise distribution of patients, during year 2017, maximum number of Swine Flu positive cases was from age group of 1 to 10 years followed by 41 to 50 years. On the other hand, during year 2018, maximum number of cases was from age group of 51 to 60 years followed by 31 to 40 years. Difference between positive cases of Swine Flu detected during year 2017 & 2018 was highly significant as per independent sample student's t - test ($P < 0.001$) as shown in **Table 1. and Figure 1.**

Table 1. Age-wise distribution of Swine Flu (H1N1) - RT PCR Positive Cases

	Year 2017			Year 2018		
Age Group (years)	Total Suspected Cases Investigated	H1N1 - RT PCR Positive Cases *	Positive Cases (%) (N=1397)	Total Suspected Cases Investigated	H1N1 - RT PCR Positive Cases*	Positive Cases (%) (N=203)
<1	111	39	2.79	40	4	1.97
1 -10	477	239	17.11	89	26	12.81
11 – 20	179	71	5.08	49	5	2.46
21- 30	328	178	12.74	90	24	11.82
31 – 40	330	202	14.46	93	35	17.24
41 – 50	387	236	16.89	134	32	15.76
51 – 60	383	220	15.75	149	44	21.67
>60	438	207	14.82	246	33	16.26
Total	2634	1397	100.00	890	203	100.00

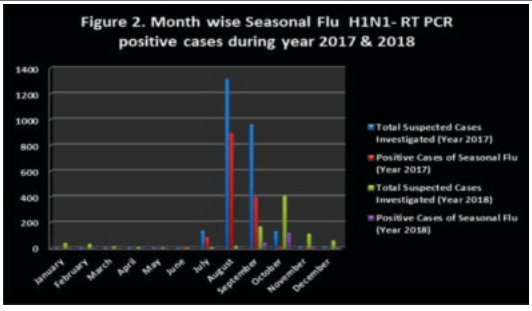
*Significant as per independent sample student's t- test ($P < 0.001$)

Among all investigated suspected cases of Seasonal Flu, H1N1 – RT PCR case positivity rate was more among 31 to 40 years age group during year 2017 and 2018 as shown in **Table 1.**

During year 2017, incidence rate of new cases of Swine Flu(H1N1) was 836.12 cases per 1,00,000 population per year, while it was 121.49 Cases per 1,00,000 Population per year. Overall, during Swine Flu Epidemic year 2017, there was 7(seven) times more incidence of H1N1 cases as compared to year 2018 as shown in **Table 2.**

Table 2. Annual Incidence Rate of Swine Flu (H1N1) RT-PCR Positive Cases

Year	2017	2018
Incidence Rate of H1N1 - RT PCR Positive Cases	836.12 Cases per 1,00,000 Population per year	121.49 Cases per 1,00,000 Population per year



As shown in **Figure 2 And Table 3**, on looking at monthly Incidence Rate per 1,00,000 people, during year 2017, Flu cases started showing positive result of RT- PCR for H1N1 from July to October. On the other hand, during year 2018, Flu cases were showing positive result of RT-PCR for H1N1 positive from September to December with few cases during January.Difference in month-wise number of cases of year 2017 & 2018 was highly significant as per unpaired t test $P < 0.001$. On the other hand, difference in month-wise positive cases of Swine Flu during year 2017 & 2018 was statistically not significant as per independent sample student's t - test ($P > 0.05$)

Table 3. Month-wise Incidence and distribution of Swine Flu (H1N1) - RT PCR Positive Cases

	Year 2017				Year 2018			
Month	Total Suspected Cases Investigated**	H1N1 - RT PCR Positive Cases ***	Positive Cases (%)	Monthly Incidence	Total Suspected Cases Investigated**	H1N1 - RT PCR Positive Cases ***	Positive Cases (%)	Monthly Incidence Rate per 1,00,000 people
January	9	0	0	0.00	42	3	7.14	0.18
February	13	0	0	0.00	34	0	0	0.00
March	9	0	0	0.00	15	2	13.33	0.12
April	9	0	0	0.00	11	1	9.09	0.06
May	10	2	20	1.20	6	0	0	0.00
June	13	5	38.46	2.30	5	0	0	0.00
July	138	87	63.04	3.77	9	0	0	0.00
August	1314	893	67.96	4.07	18	0	0	0.00
September	961	396	41.21	2.47	169	46	27.22	2.75
October	134	14	10.45	0.63	408	121	29.66	7.24
November	17	0	0	0.00	113	17	15.04	1.02
December	16	0	0	0.00	60	13	21.67	0.78
Total	2463	1397	56.72		890	203	22.81	

** Not significant as per independent sample student's t- test ($P = 0.285$)
*** Not significant as per independent sample student's t- test ($P = 0.23$)

Table 4. Gender-wise distribution of Swine Flu (H1N1) - RT PCR Positive Cases

	Year 2017			Year 2018		
Gender	Total Suspected Cases Investigated (A)	H1N1 - RT PCR Positive Cases** (B)	Positive Cases (B /A x 100)	Total Suspected Cases Investigated (A)	H1N1 - RT PCR Positive Cases** (B)	Positive Cases (B /A x 100)
Male	1376	729	52.98 %	493	118	23.94 %
Female	1266	667	52.69 %	397	85	21.41 %
Transgender	1	1	100.00 %	0	0	0.00 %

** Not significant as per independent sample student's t- test ($P = 0.228$)

On analysis of month wise Swine Flu positive cases, more number of cases was diagnosed positive during August and September Month during year 2017. On the other hand, more number of cases was diagnosed positive during September and October Month during year 2018 as shown in **Figure 2.**

As shown in Table 4, on looking at gender-wise distribution of Swine Flu(H1N1) cases, both male and female are almost equally affected and this gender - wise difference was found statistically not significant as per independent sample student's t - test ($P > 0.05$).

Table 5.1. H1N1 - RT PCR Positive Cases in Vadodara District during Year 2017 and 2018

Name of Area	H1N1 - RT PCR Positive Cases (Year 2017)	H1N1 - RT PCR Positive Cases (Year 2018)
Ajwa	2	3
Akota	13	2
Alkapuri	2	4
Atladra	34	3
Bajwa	11	3
Chhani	14	15
Fatehgunj	0	3
Gorwa	36	8
Gotri	47	7
Harni Road	44	10
Jambuva	1	0
Karelibaug	59	10
Makarpura	32	6
Maneja	8	2
Manjalpur	63	5
Nizampura	95	1
Padra	0	3
Pratapnagar	14	1
Ranoli	2	0
Raopura	75	9
Sama	72	11
Savli	17	1
Sayajigunj	6	0
Sokhada	12	0
Subhanpura	22	7
Tandalja	31	5
Tarsali	56	5
Vadsar	5	3
Vasna	50	5
Waghodia	101	9
Warasiya	11	3
Total	935	144

In Vadodara District, during year 2017, more number of cases was diagnosed positive for Swine Flu chronologically in Waghodia, Nizampura, and Raopura region. On the other hand, during year 2018, more number of cases was diagnosed positive in Chhani, Sama, Karelibag, and Harni region as shown in Table 5.1.

Table 5.2. H1N1 - RT PCR Positive Cases from Periphery of Vadodara District and Migrant Population during Year 2017 and 2018

Area	H1N1 - RT PCR Positive Cases (Year 2017)	H1N1 - RT PCR Positive cases (Year 2018)
Ahmedabad	1	1
Anand	35	4
Bharuch	45	3
Borsad	1	0
Chhota Udepur	20	3
Dahod	55	5
Gandhinagar	2	0
Dabhoi	19	1
Jambusar	1	0
Karjan	24	0
Karnataka	1	0
Kheda	1	0
Madhya Pradesh	29	3
Mahisagar	30	2
Nadiad	0	2
Narmada	15	1
Padra	53	0
Panchmahal	66	9
Rajasthan	10	0
Sinor	5	4
Surat	1	0
Vasad	1	0
Total	415	38

On looking at geographical distribution, there were more number of Swine Flu (H1N1) Positive Cases from Panchmahal, Dahod and Padara Sub District surrounding Vadodara during last two years as shown in Table 5.2. Conversely, difference in number of positive cases was detected as per geographical distribution during year 2017 & 2018.

DISCUSSION:

Influenza (flu) is highly contagious respiratory illness caused by influenza viruses having potential to cause mild to severe form of disease. Moreover, Influenza viruses are highly unstable having tendency of showing seasonal epidemic trend and capable of causing pandemics [3].

Indian population is at risk of various epidemic time to time and among viral respiratory illnesses, Swine Flu (H1N1) Virus is a single stranded RNA virus - continues to be a major public health threat worldwide [6]. World Health Organization (WHO) has raised the level of Influenza pandemic alert from phase 5 to 6 on 11th June 2009 [8].

As per WHO assessment, the overall severity of Influenza pandemic was moderate implying that most people recover from infection without the need for hospitalization. Globally, influenza virus infects about three to five million individuals annually, leading to approximately 650,000 deaths[9]. The first influenza pandemic of the 21st century broke in Mexico in 2009, as a result of re-assortment between avian, human, and swine influenza viruses to develop a new strain of Influenza A (H1N1) [6],[10].

Influenza A (H1N1) continues to be a major public health threat due to possible emergence of more virulent H1N1 strain resulting from dynamic changes in virus adaptability consequent to functional mutations and antigenic drift in the Hemagglutinin (H) and Neuraminidase (N) surface proteins. Swine Flu - Influenza A (H1N1), acquired mutations could be associated to an improved adaptability of the virus for efficient human transmissibility [6].

In this study, total 3,524 investigation report of sample collected from oropharyngeal swabs of patients hospitalized for acute respiratory illness in hospitals of Vadodara district and surrounding sub district. All received sample were tested with real time Reverse Transcription–Polymerase Chain Reaction (RT-PCR) based investigation and total 1600 (45.40%) positive cases for Swine Flu - Influenza A (H1N1) virus were detected. In another study, analyzing clinically suspected cases of influenza-like illness received in the Virus Research and Diagnostic Laboratory, Department of Microbiology, Sri Venkateswara Institute of Medical Sciences (SVIMS), Tirupati, from January 2017 to May 2018, samples were tested for influenza A, influenza A (H1N1) pdm09, influenza A (H3N2), influenza B, influenza B/Yamagata and influenza B/Victoria detected that 522 (40.59%) case were positive out of 1,286 investigated samples [11].

Among the Swine Flu (H1N1) positive cases, during year 2017, there were 729 (52.18%) males and 667 (47.74%) were females. Similarly, during year 2018, there were 118 (58.13%) were male cases and 85 (41.87%) were female cases. In one study of Andra Pradesh, it was observed that there was no significant difference in positivity between genders with 260 (49.81%) females and 262 (50.19%) males being positive [12]. Similar finding was observed in another study saying equal tendency of H1N1 positive cases among both gender, showing 743 (48.88%) were males and 777 (51.12%) were females [6].

The age-wise analysis has shown that all age groups were affected. However, during year 2017, maximum number of cases was from age group of 1 to 10 years followed by 41 to 50 years, while during year

2018, maximum number of cases was from age group of 51 to 60 years followed by 31 to 40 years. Similar finding was observed showing predominance towards age group of 18–35 years (43.22%) and minimum positivity in <1 year group (0.92%) [6]. On the other hand, as per study conducted at Andra Pradesh, the age-specific positivity (data not shown) did not vary significantly across the ages I, II and III; however, it was significantly low in age Group >60 years [11].

It's clinically difficult to judge Swine Flu (H1N1) case Positive status. However, in this study, among all investigated suspected cases of H1N1, case positivity rate was more among 31 to 40 years age group during year 2017 and 2018. Moreover, H1N1 negative status by RT – PCR can be due to various reasons like improper sample collection or failure to maintain cold chain while transferring sample. There can be other strain positive (e.g. H3N2) but all are not tested routinely. In India, as per study conducted at Andra Pradesh, the positive samples were influenza A unsubtypable (109), influenza A (H1N1) pdm09 (356), influenza A (H3N2) (38) and influenza B (19; Victoria - 2, Yamagata - 17) [11].

During year 2017, Incidence rate of new cases of Swine Flu(H1N1) was 836.12 cases per 1,00,000 population per year, while it was 121.49 Cases per 1,00,000 Population per year. Overall, during Swine Flu Epidemic year 2017, there was 7(seven) times more incidence of H1N1 cases as compared to year 2018 [6],[11].

On looking at monthly Incidence Rate per 1,00,000 people, during year 2017, Flu cases started showing positive result of H1N1 RT- PCR from July to October. On the other hand, during year 2018, Flu cases were showing positive result of H1N1 RT- PCR positive from September to December with few cases during January. Similar findings of outbreak peak during monsoon were reported as per studies by Gurav et al. from Panchgani (Maharashtra) and Biswas et al. from Kolkata (West Bengal). They had reported that the outbreaks of Influenza A H1N1 pdm09 were common in monsoon season [13].

As per another study in the state of Andhra Pradesh, the positive cases started increasing in August, peaked for second time in September and declined thereafter with no positive case in November. Hence, there were two peaks for 2017 outbreak; one in summer and another at the start of the winter. Studies from England and Vietnam have also reported two peaks; one in summer and another one in winter for seasonal influenza as well as Influenza A(H1N1) [14],[15].

However, other studies from India did not report dual peaks for influenza, but change in influenza patterns was indicated by Arbat et al. A study by Lin et al. from Guangdong, China reported two peaks for influenza infection; one in July caused by seasonal influenza and another in November by pandemic 2009 strain[16]. The temperate regions reported higher incidences of the human influenza viral infection during the winter season (December – March), while tropical and subtropical areas displayed a year round circulation and biannual peaks [9],[10].

In comparison to previous years when increase in cases was observed in February-March, two peaks of influenza activity were observed in 2017: one during the winter months from February to April (peak in March) and then again more pronounced during summer months from August to October (peak in September). Most influenza activity in northern India was seen during the summer months, but in southern and western India, cases occurred mostly during winter months [17].

Similarly, reports from Kerala the southern state of India, often shows two distinct peaks of influenza infections during the north-east monsoon months of September – November and during the summer months of May – July [18].

As per findings of this study of Vadodara District, during year 2017, more number of cases was diagnosed positive chronologically in Waghodia, Nizampura, and Raopura region. On the other hand, during year 2018, more number of cases was diagnosed positive in Chhani, Sama, Karelibag, and Harni region.

On looking at geographical distribution of patients around Vadodara district, there were more number of Swine Flu (H1N1) Positive Cases from Panchmahal, Dahod and Padara Sub District surrounding Vadodara during last two years. As per online information, no such study showing pattern of distribution of Swine Flu was carried out in past but distribution of disease at area near airport, or area having frequent large gathering of people due to various social occasion or festivals require cautious attention.

CONCLUSIONS:

Seasonal Flu is reported as disease of winter but epidemiology of Seasonal Flu Influenza A (H1N1) is changing in terms of geographical distribution, age and seasonality. During first year of epidemic, H1N1 cases were showing pediatric population predominance with monsoon peak as compared to geriatric predominance with winter peak during second year.

Over a period of time, decrease in number of cases after one year points towards development of herd immunity while such change in seasonal, age and geographical trend suggests need of more study to identify risk factors involved for in monsoon peak with alarming precaution by prophylaxis with epidemic preparedness.

Limitations:

- Considering H1N1 being major prevalent Seasonal Flu in India, RT PCR System of Diagnosis was able to diagnose H1N1 cases only at this set up so other types (e.g. H5N3) may be missed.
- People with good immunity who were infected with Influenza A (H1N1) might not have developed symptoms, while others with mild illness may not have sought medical care.
- The actual number of cases can be more as compare to reported cases of H1N1 - RT PCR positive cases due to iceberg phenomenon of curable disease.

Conflicts of Interest: None

REFERENCES:

[1]. WHO: (2019, Jan 07). Influenza Update 332. Available from: https: //www.who.int /influenza/surveillance_monitoring/updates/ latest_update_GIP_surveillance/en/
[2]. WHO: (2020, May 22). Update about Influenza (Seasonal) Available from: https://www.who.int/en/news-room/fact-sheets/detail/influenza-(seasonal)
[3]. WHO (2020, May 22). "Influenza A (H1N1) frequently asked questions" Available from: http://www.who.int/csr/ disease/ swineflu/faq/en/index.html Who.int.
[4]. International Committee on Taxonomy of Viruses. (2020, May 22) "The Universal Virus Database, version4: Influenza A". Available from: http:// www.ncbi.nlm.nih.gov /ICTVdb/ICTVdB /00.046.0.01.htm
[5]. Heinen PP. (2020, May 22). "Swine influenza: a zoonosis. Available from: http://www.vetscite.org/publish/articles/000041/print.html
[6]. Jones S, Nelson-Sathi S, Wang Y, Prasad R et. al. (2019). Evolutionary, genetic, structural characterization and its functional implications for the infuenza A (H1N1) infection outbreak in India from 2009 to 2017. Scientific Reports. Nature (2019) 9:14690. Available from:https:// www.nature.com/articles /s41598-019-51097-w
[7]. David R. Hillyard. (2009). Novel swine-origin influenza A (H1N1) virus investigation team. N Engl J Med. 360:25.
[8]. MOHFW (2019, October 21). Clinical management Protocol and Infection Control Guidelines-Pandemic Influenza A (H1N1) Available from:https: //mohfw.gov.in /sites/default/files /2366426352.pdf
[9]. Viboud, C., Alonso, W. J. & Simonsen, L. (2006). Influenza in tropical regions. PLoS Med. (3): e89.
[10]. Tamerius, J. D. et al. (2013). Environmental predictors of seasonal influenza epidemics across temperate and tropical climates. PLoS Pathog. (9): 11-18.
[11] Mudhigeti N, Racherla RG, Mahaakshmi PA, Pamireddy ML, et al. (2018). A study of influenza 2017-2018 outbreak in Andhra Pradesh, India. Indian J Med Microbiol. (36): 526-31.
[12]. Gurav YK, Pawar SD, Chadha MS, Potdar VA, Deshpande AS, Koratkar SS, et al. (2010). Pandemic influenza A(H1N1) 2009 outbreak in a residential school at Panchgani, Maharashtra, India. Indian J Med Res. (132): 67-71.
[13]. Biswas DK, Kaur P, Murhekar M, Bhunia R. (2012). An outbreak of pandemic influenza A(H1N1) in Kolkata, West Bengal, India, 2010. Indian J Med Res. (135): 529-33.
[14]. Nguyen HL, Saito R, Ngiem HK, Nishikawa M, Shobugawa Y, Nguyen DC, et al. (2007). Epidemiology of influenza in Hanoi, Vietnam, from 2001 to 2003. J Infect. (55): 58-63.
[15]. Elliot AJ, Powers C, Thornton A, Obi C, Hill C, Simms I, et al. (2009). Monitoring the emergence of community transmission of influenza A/H1N1 2009 in England: A cross sectional opportunistic survey of self-sampled telephone callers to NHS direct. BMJ. (339): e3403.
[16]. Lin J, Kang M, Zhong H, Zhang X, Yang F, Ni H, et al.(2004-2012). Influenza seasonality and predominant subtypes of influenza virus in Guangdong, China, J Thorac Dis 2013; (5)2: s109-17.
[17]. IDSP (2020, May 22). Integrated Disease Surveillance Programme. Seasonal Influenza (H1N1) - State/ UT- wise, Year- Wise Number of Cases and Death from 2010 to 2017. Available from: www.idsp.nic.in/showfile.php?lid=3908.
[18]. Dhanya, V. C. et al. (2014). Demographic and Clinical Characteristics of Pandemic Influenza A (H1N1) Outbreak in Kerala, Southern India. British Microbiology Research Journal. (4), 1142–1153.