IJBPAS, May, 2023, 12(5): 2295-2308

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

MAGNITUDE AND CLINICO-EPIDEMIOLOGICAL PATTERN OF INFLUENZA FROM 2014 TO 2019 IN CHENNAI, INDIA

RAMESH K[1, 2], KRISHNASAMY K[2], ANUPAMA CP[3], KANNAPIRAN E[4] AND RAJENDRAN K[5]

1: Research Scholar, Department of Animal Health and Management, Alagappa University, Karaikudi, Tamil Nadu, India

2: Deputy Director Department of Virology, King Institute of Preventive Medicine and Research, Guindy, Chennai, Tamil Nadu, India

3: Non-Medical Tutor, Department of Virology, King Institute of Preventive Medicine and Research, Guindy, Chennai, Tamil Nadu, India

4: Professor, Department of Fisheries Science, Alagappa University, Karaikudi, Tamil Nadu, India

5: Teaching Assistant, Department of Fisheries Science, Alagappa University, Karaikudi, Tamil Nadu, India

*Corresponding Author: Kiruba Ramesh: E Mail: kirubarv@gmail.com

Received 09th June 2022; Revised 16th July 2022; Accepted 29th Sept. 2022; Available online 1st May 2023

https://doi.org/10.31032/IJBPAS/2023/12.5.7155

ABSTRACT

Influenza is a highly contagious airborne disease that causes seasonal epidemics and pandemics. The present study is aimed to determine the epidemiological aspects of influenza virus in and around Chennai, Tamilnadu for a period of six years from 2014 to 2019.The study was attempted to identify and analyze the distribution of influenza viruses with respect to the age groups, seasonality and co-morbid conditions of patients during the study period besides studying the symptomatic profile of patients. Nasopharyngeal swabs were collected from ILI/OPD patients from Tertiary care centers. Real time PCR as per CDC guidelines was performed for detection of influenza viruses. A total of 3533 samples collected during the six years were subjected to Real Time PCR analysis, out of which 411 (11.63%) were found to be positive for influenza. The pdmA/H1N1 09 showed 59.12% positivity whereas 25.30% positivity

was observed for A/H3N2 strains. Influenza B was confirmed in 64 cases (15.57%). The seasonal pattern of influenza appeared to be diversified in the subtropical region. Moreover, this study highlighted the occurrence of epidemics or waves on a regular basis following a typical biennial pattern. This study on correlation of influenza occurrence and distribution with meteorological factors, symptomatic profile of patients and the influence of co-morbid conditions provide data with epidemiological significance useful for further investigation on burden due to respiratory viral infectious diseases.

Keywords: Influenza; Epidemiology; Real-time PCR; Seasonality; Co-morbid conditions

INTRODUCTION

Influenza viruses mainly A and B belong to Orthomyxoviridae family causing acute respiratory infection (ARI) and severe acute respiratory infection (SARI) through frequent outbreaks worldwide, affecting all age groups. A further threat is the non-seasonal emergence of new strains, which have the potential to cause major influenza pandemics. The virus play a vital role causing significant morbidity and mortality especially among high-risk category including pediatric group, antenatal, adults more than 65 years and patients with co-morbid conditions such as chronic heart or lung dysfunction, kidney, liver or metabolic disorders or weakened immune systems **[1, 2]**. Annual epidemics severely affecting approximately 5 million people with 5 to 10% mortality is documented. In India, about 2.5 million cases of acute respiratory tract infections are detected in children less than 5 years of age including 20% deaths and influenza virus is the predominant causative agent of ARI or SARI **[3-5]**.

Influenza A viruses undergo genetic re-assortment events resulting in antigenic shift and its associated pandemics. The progressive antigenic drift of hemagglutinin (HA) and neuraminidase (NA) viral proteins results in frequent epidemics also facilitates the viruses to circumvent immunity acquired in response to infection or vaccination. Frequent influenza outbreaks in India necessitate the strengthening and upgrading of surveillance capabilities to continuously monitor adversities at unpredictable moments. The chronicle of influenza epidemics is dynamic but puzzling and sustained studies related to influenza are uncommon **[6]**. This present study was attempted to analyze the magnitude and severity of A/H1N1 pdm09 and its association with co-morbid conditions. It also describes the pattern of circulation,

Seasonality and the susceptibility of various age groups in our domain. The study was performed at the Virology Department, King Institute of Preventive Medicine and Research, Chennai, Tamilnadu.

MATERIALS AND METHOD

Study Population

3533 Nasopharyngeal/ throat swabs were collected from patients of all age groups who met the clinical criteria from January 2014 to December 2019.

Inclusion criteria: A person presenting sudden onset of fever >38°C or history of sudden onset of fever in the recent past (less than three days) and cough or sore throat or rhinorrhea.

Exclusion criteria: Patients who do not provide consent, seriously ill patients and patients with terminal disease who were unable to give samples **[7]**.

Clinical specimens were collected from patients attending various Government Hospitals in and around Chennai. The study was approved by the Institutional Ethical Committee and informed consent was obtained from the patients or from guardians before collection of samples. The specimens were transported in virus transport medium in cold chain and were processed for molecular diagnosis.

Nucleic Acid Extraction

RNA was extracted from specimens using RNAeasy Mini kit (Qiagen GmbH, Hilden, Germany) following the manufacturer's instructions.

Real Time PCR

Real time PCR was performed according to the CDC Influenza Manual **[8]**. PCR was performed using ABI 7500 cycler (Applied Biosystems, USA).

Meteorological Data

Meteorological details; rainfall (in mm), humidity (%) and average temperature ($^{\circ}$C) were documented for the study period from Regional Meteorological Centre, Nungambakkam, Chennai.

Statistical Analysis

The data were analyzed using Graph pad prism version 5.0. ANOVA was used to analyze distribution of various influenza viruses during the study period. *p* value <0.05 was considered statistically significant.

RESULTS

Influenza activity during 2014 – 2019

A total of 3533 respiratory specimens were included in the study and among them, 411 (11.63%) were positive for influenza by Real time PCR analysis. In this study, maximum of 243 (59.12 %) samples were positive for A/H1N1 pdm09 followed by 104 (25.30%) for AH3N2 and 64 (15.57%) for Flu B. Though influenza activity was

detected throughout the surveillance period, seasonal H1N1 activity was not observed during the period and the activity was absent subsequent to A/H1N1 pdm09 outbreak, *i.e.* from 2009 to till date.

A characteristic pattern of influenza virus distribution was observed in this study, which was conducted after few years of pandemic period. Influenza virus typing study showed different circulation, co-circulation, and dominance patterns in the 6-year study period. It was observed that in 2014, H3N2 predominated with positive percentage of 61% whereas A/H1N1 pdm09 positivity was found to be a meager 23.7%. In the years 2015, 2017 and 2018, A/H1N1 pdm09 predominated with 74.65%, 70.23% and 68.85% respectively; but during the same period, positivity of H3N2 was 19.71%, 17.85% and 3.27%. In 2016, high proportion of H3N2 was observed with positivity of 50% while the proportion for A/H1N1 pdm09 was 25%. In 2019, minimal influenza activity was observed with respect all strains; however, occurrence of Influenza B activity was higher in this year than the previous years **(Table 1)**.

Virological Observation

Predominance of A/H1N1 pdm09 occurred in the years 2015, 2017 and 2018, cases of Type B Influenza for these years were found to be 5.6%, 11.9% and 27.86% respectively. Flu B positivity was observed throughout the study period. In the present study the detection of the virus showed huge variation on the prevalence among the cases in the entire study duration. In the year 2014, greater number of H3N2 cases was observed. The sudden spurt of Influenza A/H1N1 pdm09 had raised warning signs of unprecedented outbreaks affecting larger population. This alerted the public health authorities to take adequate action with respect to cleaning, distributing IEC materials, vaccinating the high-risk health care personnel and organizing programs to increase awareness among public.

Age wise distribution of influenza positives

The median age of ILI patients enrolled in the study was 31.45 years (range: 1 month to 81 years). The highest number of ILI samples positive cases among ILI samples was in the adolescent age group 13 to 18 (n=724; 20.49% of total ILI cases), of which 16.3% were found to be flu positives, followed by pediatric age group of 6-12 years (13.18%), young adult group of 19-30 years (12.1%), pediatric age group of below 5 years (10.72%), 31-to-55-year group (8.62%) and elder age group (≥ 56 y; 5.64%). The elderly population was least affected (5.64%) when compared to other age groups. Analysis

between influenza suspected and positives across the population revealed that all age groups were affected significantly. Likewise, analysis between flu positives and flu types A/H1N1pdm09 (p = 0.109), H3N2 (p = 0.0074) and B (p=0.0018) showed slight difference and the distribution pattern of influenza viruses across the age groups was significant (p = 0.0055) **(Table 2)**. Among the positive cases, 245 (59.61%) and 166 (40.38%) cases were males and females respectively

Seasonal Correlation with Influenza Positivity

Data on assessing the seasonality pattern of influenza revealed that there was varying seasonality observed during the study period. The flu activity was high during May of 2014 (Summer) and from January to March of 2015. Flu activity was observed during October, November and December in 2016 and 2018 (Monsoon) and from January to April of 2017 (Winter and early Summer) indicating the need for continuous surveillance activity throughout the year (2019). Strain wise analysis during variable seasons of the study showed that this seasonality trend was comparable for both A/H1N1 pdm09 and A/H3N2. Occasional activity of Flu B was noticed during post monsoon and winter months. A relatively strong correlation was observed between the temperature and influenza positivity, whereas the correlation between rainfall, humidity and flu positivity was weak **(Figure 1 & 2)**.

Symptoms and Clinical Co-morbidities

Influenza positive individuals were found to exhibit the following symptoms such as fever (97.81%), cough (85.16%), sore throat (54.01%), chills & rigor (26.76%), nasal discharge (78.1%), breathlessness (13.38%) and head ache (57.18%), Malaise (41.61%), myalgia (48.18%) and vomiting (13.87%). Few individuals exhibited symptoms like diarrhoea (6.57%), expectoration (6.81%), crepitation (5.11%), wheezing (3.41%), seizures (2.19%) and ear discharge (1.70%).

Besides, co-morbid conditions including diabetes mellitus (32.18%), hypertension (27.4%) and bronchial asthma (17.98%) were observed in influenza positive cases. Patients with predisposing factors like Chronic Obstructive Pulmonary Disease (COPD) were at high risk of developing influenza infection (8.52%). Patients with hematological malignancies were susceptible to infection with influenza positivity (4%) and 2.21% of pregnant women had infection with influenza virus **(Figure 3)**.

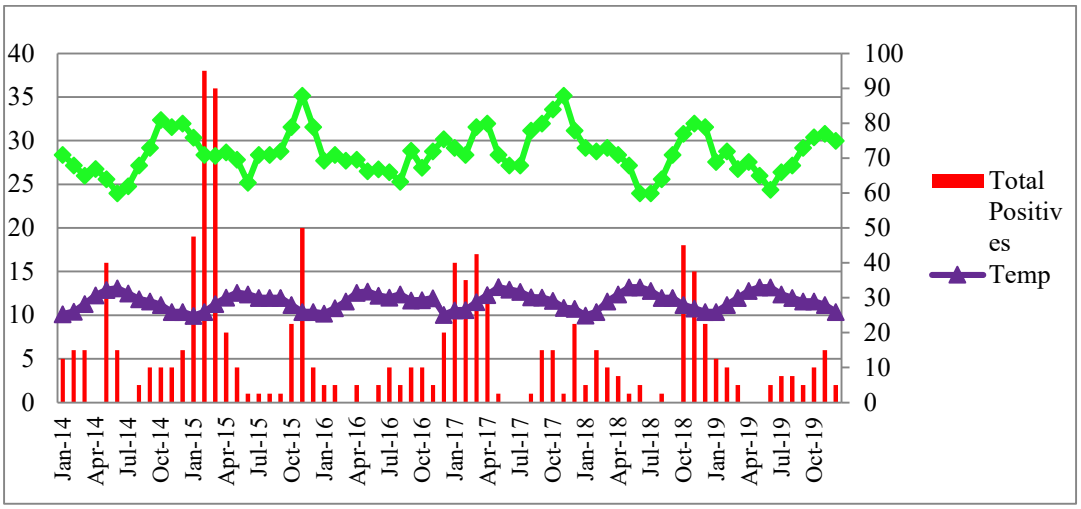

Figure 1: Correlation of Month wise positivity with Temperature & Humidity

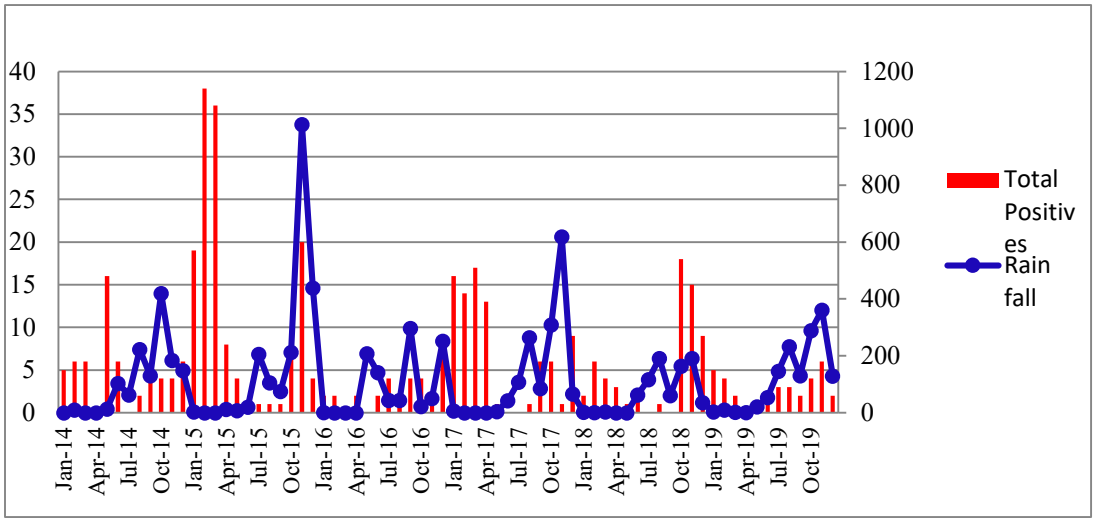

Figure 2: Correlation of Month wise positivity with Rainfall

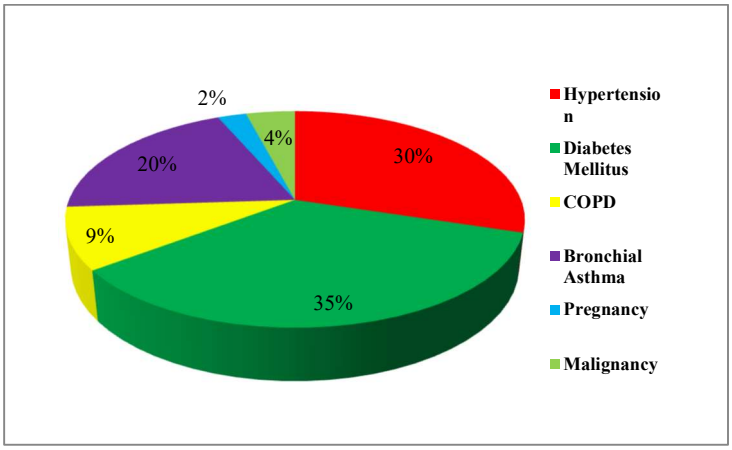

Figure 3: Cases with co-morbidities among Influenza positives (n=411)

Table 1: Distribution of Influenza virus during the years 2014 to 2019

Year	# No of tested	Influenza Positive		Influenza A(H1N1)pdm09		Seasonal Influenza A H3N2		Influenza B	
		n	%	n	%	n	%	n	%
2014	720	59	8.19	14	23.7	36	61.01	9	15.3
2015	704	142	20.17	106	74.65	28	19.71	8	5.63
2016	508	32	6.3	8	25	16	50	8	25
2017	529	84	15.87	59	70.23	15	17.85	10	11.9
2018	607	61	10.04	42	68.85	2	3.27	17	27.86
2019	465	33	7.10	14	42.42	7	21.21	12	36.36
Total	3533	411	11.63	243	59.1241	104	25.30	64	15.57

***p* value is 0.024; ANOVA at 0.05 significance level between the influenza virus groups for all the years.**

Table 2: Age-wise distribution of influenza positive cases

Age-wise distribution							
	0-5 (n=681)	6-12 (n=713)	13-18 (n=724)	19-30 (n=513)	31-55 (n=441)	≥56 (n=461)	p value*
Flu Positives	73	94	118	62	38	26	2.81E-06
Strains and positivity							
	0-5	6-12	13-18	19-30	31-55	≥56	p value**
pH1	47	55	68	35	21	10	0.109
H3	19	25	34	18	14	11	0.0074
Flu B	7	14	16	9	3	5	0.0018

n: suspected samples; *p* value based on ANOVA.

***p* value*: Analysis between influenza suspected samples and flu positives across different age groups; *p* value**: Analysis between flu positive samples and flu types A/H1N1pdm09, H3N2 and B.**

ANOVA of distribution of Flu strains among the flu positives across age groups (*p* value: 0.0055).

DISCUSSION

Among communicable diseases, respiratory infections caused by influenza viruses are the predominant cause of mortality globally. Globalization and its associated geographical changes accelerate the dimension of spread of influenza diseases among global human community. Further, dense population and intense mobility across nation and globe potentially drive the spread of flu viruses. Hence, continuous monitoring of flu activity through diagnosis and surveillance and sharing of such region-specific information are essential to evaluate the disease burden and to implement the anti-viral drugs and vaccination strategy as disease mitigation measures. Symptomatic profile and co-morbid complications in influenza suspected and diagnosed patients across different age groups were reported in the present study and focused on the pattern of distribution of influenza viruses in Chennai during the years 2014 to 2019. A study from Bethesda, Maryland also reported similar activity and demonstrated a regular biennial pattern every alternate year **[9]**. A previous study on the distribution of Influenza viruses in Tamilnadu during 2009 to 2015 observed that though the activity of A/H1N1 pdm09 was dominant for years such as 2009, 2010, 2012 and 2015, the remaining years displayed a moderate trend of A/H3N2

activity **[10]**. However, a striking observation of the present as well as the previous studies spanning almost a decade from 2009 to 2019 is that the number of samples subjected to influenza diagnosis almost steadily declined. This could be due to two plausible reasons: absence of active surveillance of influenza among the patients exhibiting influenza symptoms, or those developing ARI, SARI and COPD conditions; reduction in case detection might also be due to reduced influenza activity. The epidemic pattern of influenza was found to be difficult to understand in major parts of the world due to lack of sufficient data on flu type distribution.

A/H3N2 activity was moderate to minimal and there was complete absence of seasonal A/H1N1 in the study period. It was demonstrated previously that the seasonal A/H1N1 activity was marked only in the year 2009 with meagre presence followed by complete absence till 2019 in Tamilnadu. The displacement and replacement of seasonal A/H1N1 virus was the most notable outcome of the introduction of the pandemic strain, and the virus co-circulated preferentially with influenza A/H3N2 and B viruses. This event was substantiated by earlier reports on influenza surveillance studies focusing on distribution of influenza viruses across the Northern and Southern Hemispheres **[11-13]**.

Several studies reported that there was a definite seasonality of influenza especially in tropical areas including India. The current data revealed that the activity of A/H1N1 pdm09 was frequently observed during monsoon and post monsoon months. There was also an overall change in the trend of influenza activity after the appearance of the pH1N1 virus with seasonality becoming less marked. The increased incidence of A/H3N2 was observed during post monsoon period of 2014 and 2016. The dominance of A/H1N1 pdm09 in 2015, 2017 and 2018 was displaced by H3N2 and Influenza B during 2014 and 2016 **[14]**. It was interesting to observe that one of the flu types dominated in each study year and the pattern of flu type infection varied widely throughout the study period. This suggested the dynamicity of flu infection involving all flu types except the seasonal A(H1N1) which was completely absent in the study years but substituted by A/H1N1 pdm09.

In temperate regions, incidence of ARI including influenza peaks in winter, but seasonality is not well documented in the tropics. The data from this subtropical region show discrete peak of influenza from December to March similar to what has been

observed in temperate regions of the northern hemisphere **[15, 16]**.

Though relative humidity and temperature are correlated with increased virus activity during the winter months in temperate zones, transmission by the contact route is insensitive to these geographical factors, which supports the occurrence of influenza in the tropical and subtropical region throughout the year or in sporadic outbreaks with no clearly defined seasonality **[17, 18]**.

Further, dense population of susceptible individuals influences the transmission of the virus laden aerosols, thereby enhancing the potential for the spread.This data suggest that uniform vaccination timing throughout India may have difficulty as this region experiences flu infection in various seasons **[19]**.

Reports show that children and elderly were more susceptible due to reduced immune potential. Though the study did not show huge variation among the number of cases in different age groups, the infection rate was slightly higher in adolescent (13-18 years) than other age groups and the observation is similar to the study conducted at Delhi during the same period. In contrast, studies from Rajasthan showed higher infection rate among adults than other age group. There are also reports showing that influenza viruses most often affect younger adults and teenagers **[20-22]**. These observations suggest that population belonging to all age group may be vulnerable and factors associated with immune status, geography, demography and virulence play a role in spread of influenza.

Co-morbid conditions such as diabetes, hypertension, bronchial asthma, COPD and leukemia are known to increase the burden of respiratory infections including influenza **[23-25]**. The study also shows that these co-morbid conditions along with hematological malignancies were observed in flu confirmed cases **[26, 27]**. In addition, pregnant women were also found to be at high risk of acquiring influenza infection, similar to earlier studies **[28, 29]**.

According to the reports of A/H1N1 pdm09 from National Centre for Disease Control Delhi, the number of cases in Tamilnadu was high during the year 2015 and 2017 with mortality of 3.22% and 0.51% respectively. However, at the national level, mortality due to A/H1N1 pdm09 was found to be 7.02% in 2015 and 5.84% in 2017 **[30]**. We were not able to follow up all the cases with co-morbid conditions in this study; hence, mortality as well as disease burden among the subjects tested in our center could

not be assessed, which is a limitation of the present study. Reduction in influenza surveillance activities will underestimate the real disease burden and this could impede the decision on vaccination by policy makers and health authorities. Studies on possibilities on the emergence of virulent strains due to mutations and their associated impact on vaccine and antiviral development are necessary. The emergence of COVID-19 pandemic also severely impacted the influenza surveillance activities regionally and globally, and hence, limited information or reports are available on influenza since the emergence of SARS-CoV-2 pandemic in the year 2020.This surveillance study would facilitate the public health officials in India to evolve staggered and sustained approaches to rejuvenate tasks on regular and multisite monitoring of influenza viruses as well as planning and implementation of vaccination strategy considering the regional differences in influenza seasonality.

CONCLUSION

Continuous surveillance of influenza viruses will throw insights on their distribution patterns, various subtypes, seasonality and their impact on clinical course and outcome. This can aid the research personnel for identification of the period on scheduling vaccination based upon the circulating strains.

ACKNOWLEDGEMENTS

Our sincere gratitude and thanks to the ICMR Director General for providing the funds to carry out this study. Authors thanks to Director and Influenza Head (Influenza Group), National Institute of Virology, Pune for providing training and appropriate guidance. Our sincere thanks to the authorities of Alagappa University, Karaikudi and the Head, Department of Animal Health and Management for their support.

REFERENCES:

[1] Blut A. Influenza virus. Transfusion Medicine and Hemotherapy. 2009 Feb;36(1):32.

[2] Moghadami M. A narrative review of influenza: a seasonal and pandemic disease. Iranian journal of medical sciences. 2017 Jan;42(1):2.

[3] Reddaiah VP, Kapoor SK. Acute respiratory infections in rural underfives. The Indian Journal of Pediatrics. 1988 May;55(3):424-6.

[4] Rao BL. Epidemiology and control of influenza. National medical journal of india. 2003 May 1;16(3):143-9.

[5] World Health Organization. Children: reducing mortality. Weekly

Epidemiological Record= Relevé épidémiologique hebdomadaire. 2014;89(38):418-20.

[6] Treanor J. Influenza vaccine—outmaneuvering antigenic shift and drift. New England Journal of Medicine. 2004 Jan 15;350(3):218-20.

[7] World Health Organization. WHO manual on animal influenza diagnosis and surveillance. 2002. Department of Communicable Diseases Surveillance and Control, WHO, Geneva. 2002.

[8] World Health Organization (WHO. CDC protocol of realtime RTPCR for swine influenza A (H1N1). InCDC protocol of realtime RTPCR for swine influenza A (H1N1) 2009 Apr 28. World Health Organization (WHO).

[9] Bjørnstad ON, Viboud C. Timing and periodicity of influenza epidemics. Proceedings of the National Academy of Sciences. 2016 Nov 15;113(46):12899-901.

[10] Kiruba R, Babu BS, Sheriff AK, Gunasekaran P, Anupama CP, Saran N, Kumar VS, Padmapriya P, Chakravarthy NN, Kaveri K. Dynamics of the occurrence of influenza in relation to seasonal variation in Chennai, Tamil Nadu: a 7-year cumulative study. Indian journal of medical microbiology. 2019 Jul 1;37(3):401-5.

[11] Blyth CC, Kelso A, McPhie KA, Ratnamohan VM, Catton M, Druce JD, Smith DW, Williams SH, Huang QS, Lopez L, Schoub BD. The impact of the pandemic influenza A (H1N1) 2009 virus on seasonal influenza A viruses in the southern hemisphere, 2009. Eurosurveillance. 2010 Aug 5;15(31):19631.

[12] Laguna-Torres VA, Gómez J, Aguilar PV, Ampuero JS, Munayco C, Ocaña V, Pérez J, Gamero ME, Arrasco JC, Paz I, Chávez E. Changes in the viral distribution pattern after the appearance of the novel influenza A H1N1 (pH1N1) virus in influenza-like illness patients in Peru. PLoS One. 2010 Jul 27;5(7):e11719.

[13] Majanja J, Njoroge RN, Achilla R, Wurapa EK, Wadegu M, Mukunzi S, Mwangi J, Njiri J, Gachara G, Bulimo W. Impact of influenza A (H1N1) pdm09 virus on circulation dynamics of seasonal influenza

strains in Kenya. The American Journal of Tropical Medicine and Hygiene. 2013 May 5;88(5):940.

[14] Dangi T, Jain B, Singh AK, Mohan M, Dwivedi M, Singh JV, Kumar R, Singh KP, Chaddha MS, Mishra AC, Jain A. Influenza virus genotypes circulating in and around Lucknow, Uttar Pradesh, India, during post pandemic period, August 2010-September 2012. The Indian journal of medical research. 2014 Mar;139(3):418.

[15] Agrawal AS, Sarkar M, Chakrabarti S, Rajendran K, Kaur H, Mishra AC, Chatterjee MK, Naik TN, Chadha MS, Chawla-Sarkar M. Comparative evaluation of real-time PCR and conventional RT-PCR during a 2 year surveillance for influenza and respiratory syncytial virus among children with acute respiratory infections in Kolkata, India, reveals a distinct seasonality of infection. Journal of medical microbiology. 2009 Dec 1;58(12):1616-22.

[16] Moura FE. Influenza in the tropics. Current opinion in infectious diseases. 2010 Oct 1;23(5):415-20.

[17] Tamerius J, Nelson MI, Zhou SZ, Viboud C, Miller MA, Alonso WJ. Global influenza seasonality: reconciling patterns across temperate and tropical regions. Environmental health perspectives. 2011 Apr;119(4):439-45.

[18] Koul P, Khan U, Bhat K, Saha S, Broor S, Lal R, Chadha M. Recrudescent wave of A/H1N1pdm09 influenza viruses in Winter 2012-2013 in Kashmir, India. PLoS Currents. 2013 Sep 26;5.

[19] Lowen AC, Steel J, Mubareka S. High temperature (30 C) blocks aerosol but not contact transmission of influenza virus. Journal of virology. 2008 Jun 1;82(11):5650-2.

[20] Malhotra B, Singh R, Sharma P, Meena D, Gupta J, Atreya A, Meena BR. Epidemiological & clinical profile of influenza A (H1N1) 2009 virus infections during 2015 epidemic in Rajasthan. The Indian journal of medical research. 2016 Dec;144(6):918.

[21] Broor S, Krishnan A, Roy DS, Dhakad S, Kaushik S, Mir MA, Singh Y, Moen A, Chadha M, Mishra AC, Lal RB. Dynamic

patterns of circulating seasonal and pandemic A (H1N1) pdm09 influenza viruses from 2007–2010 in and around Delhi, India. PloS one. 2012 Jan 3;7(1):e29129.

[22] Das RR, Sami A, Lodha R, Jain R, Broor S, Kaushik S, Singh BB, Ahmed M, Seth R, Kabra SK. Clinical profile and outcome of swine flu in Indian children. Indian pediatrics. 2011 May;48(5):373-8.

[23] Kalyani D, Srikanth Bhatt S, Chitralekha T, Rajarao M, Shankar K. Comorbidities In H1N1 Positive Patients–Hospital Based Study. IOSR Journal of Dental and Medical Sciences. 2016;15:52-5.

[24] Konomi L, Simaku A, Çomo N, Kolovani E, Ramosaço E, Roshi E. Influenza associated comorbidities. International Journal of Science and Research. 2017;6(4):1739-40.

[25] Gubio AB, Muhammad SJ, Mamman A, Zakari A, Biya O. Co-morbidity Factors Associated with Influenza in Nigeria. Online Journal of Public Health Informatics. 2013 Mar 23;5(1).

[26] Hermann B, Lehners N, Brodhun M, Boden K, Hochhaus A, Kochanek M, Meckel K, Mayer K, Rachow T, Rieger C, Schalk E. Influenza virus infections in patients with malignancies—characteristics and outcome of the season 2014/15. A survey conducted by the Infectious Diseases Working Party (AGIHO) of the German Society of Haematology and Medical Oncology (DGHO). European Journal of Clinical Microbiology & Infectious Diseases. 2017 Mar;36(3):565-73.

[27] Tantawy AA, Barakat MM, Adly AA, Ebeid FS, Shamaa MF, Yassin M. One-year prospective study of community acquired influenza and parainfluenza viral infections in hospitalized egyptian children with malignancy: single center experience. Pediatric Hematology and Oncology. 2015 Jul 4;32(5):304-14.

[28] Palani G, Krishnasamy K, Arunagiri K, Sambasivam M, Ramesh K, Bommala SB, Natarajan S, Ramalingam SR. Influenza A/H1N1 2009 in pregnancy-experience in Tamilnadu, India. Indian Journal of Scientific Research. 2012 Jan 1;3(1):31.

[29] Hewagama S, Walker SP, Stuart RL, Gordon C, Johnson PD, Friedman ND, O'Reilly M, Cheng AC, Giles ML. 2009 H1N1 influenza A and pregnancy outcomes in Victoria, Australia. Clinical Infectious Diseases. 2010 Mar 1;50(5):686-90.

[30] National Centers for Disease Control. Seasonal Influenza (H1N1)–State/UT-wise, Year-wise number of cases and death from 2011 to 2018 (till 02 nd December, 2018).