

Time trend and predictors of lab positivity among suspected cases in the post pandemic phase of H1N1: An observation from a tertiary care hospital, South India

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RESEARCH

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ABSTRACT

Background

WHO declared Influenza A H1N1 to have entered the post pandemic phase on August 10, 2010. Continued surveillance activities are recommended in the post pandemic phase to watch over the trend, severity and impact of Influenza like illnesses (ILI).

Aims

This study aimed to document the epidemiological profile of lab positive H1N1 cases in post pandemic period from August 2010-December 2014 in nodal H1N1 surveillance centre of Puducherry.

Methods

The study analysed secondary data collected during the period August 10, 2010 to Dec 2014 from ILI suspects attending a tertiary care hospital, for the Integrated Disease Surveillance Project (IDSP). Demographic details, lab positivity based on Real-time PCR technique for H1N1, clinical symptoms and outcomes were extracted. Data were analysed using STATA version 11.0. Independent predictors of lab positivity rate were identified using logistic regression analysis. Time trend of frequency of suspected cases and lab positivity rate were performed using time series plots.

Results

A total of 2065 suspected cases were reported, of whom 197 cases were positive for H1N1 (lab positivity rate 9.5 per cent). Being an adult (OR: 1.6; 95 per cent CI: 1.1-2.3; $p=0.02$), management in in-patient settings (OR: 2.5; 95 per cent CI: 1.3-4.7; $p=0.001$), history of contact (OR: 2.7; 95 per cent CI: 1.5-4.5; $p=0.0001$) and history of travel (OR: 2.3; 95 per cent CI: 1.2-4.3; $p=0.01$) were the independent predictors for lab positivity. Death rate among lab confirmed cases was found to be 9.6 per cent. After 2012, the trend of laboratory confirmed H1N1 cases became a plateau. One needs to screen 35 suspected cases to capture one lab confirmed case of H1N1 in 2014.

Conclusion

Lab positivity was seen among 9.5 per cent of cases and the independent predictors were severe cases, adult patients, positive history of contact and travel. The number needed to screen to get one lab positive H1N1 case is 35 suspected cases.

Key Words

Influenza H1N1, Influenza like illness, integrated disease surveillance, post pandemic, swine Influenza, epidemiology

What this study adds:

1. What is known about this subject?

The lab positivity rate and mortality rate for pandemic H1N1 in India during the pandemic and immediate post pandemic period is 18-23 per cent and 9 per cent respectively.

2. What new information is offered in this study?

Lab positivity rate for H1N1 among suspected cases of Influenza like illnesses (ILI) during the post pandemic period is 9.5 per cent. During the post pandemic period, there was a declining trend observed in proportion of cases needs to be managed in inpatient setting and case fatality.

3. What are the implications for research, policy, or practice?

Estimated numbers based on Number Needed to Screen had predicted routine screening for H1N1 among suspected cases of ILIs would cause a sevenfold increase in cost to the health care system in this recent post pandemic situation.

Background

The most recent pandemic type of Influenza virus, namely Influenza A (H1N1) had affected many people around the world within a short span of time.¹

As per the guidance from the International Health Regulations, India started screening and surveillance for Influenza A H1N1 at international airports from the month of May, 2009. The first lab confirmed case was of a passenger travelling from US to India reported on 16th May, 2009.² As of Sep 2010, India had reported 45,101 H1N1 cases and 2,679 deaths in total. Majority of the cases were from Delhi, Maharashtra followed by Rajasthan, Tamil Nadu, Kerala and Karnataka.³

On 10th August, 2010, the World Health Organization (WHO) had announced that Influenza AH1N1 had ceased to be a pandemic. However, the WHO requested all member countries to continue surveillance measures, since pandemics are unpredictable in nature and H1N1 virus may circulate along with other seasonal type of influenza virus.⁴ The objective of any surveillance program would be to detect change in age distribution of H1N1 illnesses and severity and its impact over hospitalization and mortality.

The recent pandemic H1N1 was different from other previous flu pandemics. The recent pandemic flu had lesser mortality compared to others. It did not mutate into more lethal forms during the pandemic period, there was no widespread resistance to the antiviral drug Oseltamivir and

the current strain of vaccine matches with circulating viruses with excellent safety profile.⁵ The WHO focussed main thrust over reporting of clustering of flu like illnesses.⁵ Surveillance activity targeting Influenza like illness from tertiary care hospitals provides opportunity to analyse the host factors and trend of infection. Most of the previous studies reported from India had focused mainly on the immediate post pandemic period not beyond 2011.⁶⁻⁹ This study focuses on the epidemiological profile of suspected cases attending the tertiary care referral hospital in post pandemic period till December, 2014 and demographic and medical factors associated with confirmed cases of Pandemic Influenza. Also this study aimed to present the changing trend in laboratory positivity rate, proportions of pandemic-H1N1 Influenza out of total Influenza like illnesses and severity of cases attending to the hospital. These kinds of information are necessary for the better clinical decision making in resource poor settings to optimize the screening and surveillance against H1N1.

Method

Study setting

The present study was conducted at the Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, a tertiary care referral teaching hospital in South India catering patient population for the union territory of Puducherry, Tamil Nadu and neighbouring southern states. With total bed strength of 2,059 including 195 for intensive care unit (ICU), the hospital caters to around 6,000-7,000 out-patients and 200-250 inpatient admissions every day. The Influenza lab of the hospital is the nodal centre identified by Ministry of Health and Family Welfare for testing of H1N1 in the area of Puducherry.^{10,11} Electronically maintained, line listing of all suspected Influenza cases encompassing the details of socio demography, address, clinical symptoms, type of influenza and severity, lab positivity status, treatment outcomes is being shared with district nodal officer every week under the Integrated disease surveillance project (IDSP).

Study design

A secondary, cross sectional data analysis was conducted from the records of the Integrated Disease Surveillance Project (IDSP) office operating at the Department of Preventive and Social Medicine, JIPMER. Details on demographics, clinical characteristics (presenting symptoms, severity, lab positivity) and outcomes including mortality in patients registered to have an Influenza like illness between August 10, 2010 to December 31, 2014 were retrieved.

In all the identified cases, a routine protocol was followed, with the clinicians filling a surveillance proforma. Suspected cases of Influenza like illnesses and Severe Acute Respiratory Syndrome were subsequently subjected to laboratory screening for confirmation of Influenza AH1N1 (2009). The suspects being referred to the Influenza laboratory for evaluation included referral from various out-patient settings including Internal Medicine, Paediatrics, Tuberculosis and Chest Unit, and Emergency Department. Throat swab or nasopharyngeal discharge were preserved at 2-8°C and subjected to RT-PCR screening for novel 2009-pandemic H1N1 influenza.

The operational definition for Influenza like illnesses (ILI) was presence of any of the following: sudden onset of fever >100°F, cough, sore throat. Similarly, Severe Acute Respiratory Syndrome (SARS) was defined as sudden onset of fever >100°F, cough, sore throat, or shortness of breath.¹² For clinical management purposes, patients were divided into three categories as per the National Centre for Disease Control (NCDC) guidelines: This comprised patients with mild illness (Category A): that were managed based upon with discharge disposition to home. Category B for patients requiring hospitalization to any medical admissions to any medical or infectious disease wards. Category C for critically ill patients warranting an ICU admission, with or without ventilator assistance.¹³ Age was classified based on WHO guidelines for reporting H1N1.¹⁴

Since data was collected within the routine hospital functioning and reporting systems consent from individual participants was not obtained and waiver for the consent is obtained.

Statistical Analysis

Data were entered in MS office Excel spreadsheet-07 as prescribed in IDSP portal. Dates entered in IDSP were transformed into time series dataset. All analysis was performed using STATA/SE 11.2 (StataCorp, College Station, Texas). Results are reported as proportions (per cent), median±SD or median with IQR. Univariate (unadjusted) analysis testing for association of individual exposure variables (demographic and clinical characteristics) with lab confirmed H1N1 positivity was performed using chi square test. Those with $p < 0.1$ were carried forward in a multivariate logistic regression analysis to identify potential predictors of lab confirmed H1N1 positivity. Adjusted odds ratio (OR) along with 95 per cent confidence intervals (CI) are reported. A type I error set at 5 per cent was deemed statistically significant. Number of suspected cases need to be screened was derived by total number of suspected

cases attended during the reference period divided by number of lab confirmed cases of H1N1 during the same period.¹⁵

Results

A total of 2,065 cases were reported to have Influenza like illness (ILI) during the reference period of 10th August 2010 to 31st December 2014 (229 weeks) (Figure 1).

Majority of the suspected cases were adults (median age 26 [IQR 13-40] years). More than half of the cases were from Puducherry district. Nearly one fourth (23.4 per cent) of suspected cases needed in-patient services. Less than 10 per cent suspects had a positive history of travel or contact (3.7 per cent & 4.6 per cent respectively). An overall mortality rate amongst suspected cases was observed at 0.9 per cent (Table 1).

Out of 2,065 cases that had ILI, 197 cases were positive for H1N1 (lab positivity rate 9.5 per cent). More than half of the H1N1 cases were women (56.8 per cent) Majority of laboratory confirmed H1N1 cases were seen among adults (73.7 per cent) Most of the cases were from the out-patient department (OPD); the ratio of cases from OPD, in-patient admissions and intensive care settings were found to be 5:3:2. Less than one fifth of confirmed cases (19.3 per cent) had at least one co-morbidity at the time of illness. Fever (84.8 per cent), cough (71.6 per cent) and throat pain (26.9 per cent) are the most commonly reported symptoms among lab confirmed cases. Breathlessness was reported among one fourth of cases (23.3 per cent) (Table 2).

Case fatality among lab confirmed cases was found to be 19 (9.6 per cent). Major proportions of deaths were reported among females, adults (15-59yrs) and those who were managed in intensive care settings ($p > 0.05$) (Table 3).

The suspected cases that belonged to adult age group of 15-59yrs (OR: 1.6; 95 per cent CI: 1.1-2.3, $p = 0.02$), who had been managed in in-patient settings (OR: 2.5; 95 per cent CI: 1.3-4.7, $p = 0.001$), and those who had a positive history of travel (OR: 2.3; 95 per cent CI: 1.2-4.3, $p = 0.01$) and contact with known case (OR: 2.7; 95 per cent CI: 1.5-4.5, $p = 0.0001$) were found to be independently associated with higher risk of having laboratory confirmed H1N1 compared to suspected cases belong to children <15yrs, managed as outpatient and No history of recent travel or contact with known case of H1N1 respectively. Gender did not have any influence over the laboratory positivity (Table 4).

The proportion of suspected flu cases who were treated as outpatients in 2010, 2011, 2012, 2013 and 2014 were 22.5 per cent, 47.1 per cent, 89.3 per cent, 92 per cent and 96 per cent respectively. Among the laboratory confirmed cases of H1N1, the proportion of patients who were treated as out-patients increased in subsequent years from 11 per cent in 2010 to 92 per cent in 2014 (Figure 2).

The month-wise plotting of laboratory confirmed cases showed that peak laboratory positivity was found during the month of Aug-Nov in all the four years. After the year 2012, the trend of laboratory confirmed H1N1 cases became a plateau, except for the occurrence of few cases during seasonal peak (Figure 3).

During the immediate post pandemic period every sixth patient (with ILI features) screened was found to be positive for H1N1 pandemic strain. After 2012, the lab positivity rate reduced to a larger extent, and it was found that one needed to screen 35 suspected cases to capture one lab confirmed case of H1N1 (Table 5).

Discussion

The present study was carried out in one of the tertiary care hospitals in South India during the post pandemic period (Aug 2010-Dec 2014) and reports a total of 197 (9.5 per cent) laboratory confirmed cases of H1N1 Pandemic Influenza strain from 2065 suspected cases of flu. This lab positivity rate is much lesser than the positivity rate reported during pandemic phase in India (23 per cent).¹⁶ Studies conducted from various parts of India like Cochin, Pune, Tamil Nadu and Calcutta had reported a laboratory positivity rate that ranged from 18-23 per cent.^{6,8,17} However, all these studies had either included observations a few months prior to the post pandemic period or both pandemic period and post pandemic period of H1N1 Influenza. Dangi et al. included observations restricted to two years post pandemic period alone, and reported a lab positivity rate of 15.8 per cent closely resembling to the positivity rate reflected in our study (9.5 per cent).¹⁸ Most national reports including the present study demonstrated an increase in the number of laboratory confirmed H1N1 cases during the period of Aug-Sep. Incidence of febrile acute respiratory illnesses were also found to be more during Aug-Nov.⁹ Most studies depicted lab positivity rate being more among persons aged 15-45yrs.^{6,8,17,18} Yet, these results do not corroborate the shift in lab confirmed cases towards older age group during post pandemic period as observed in other South Asian countries.^{19,20} Case fatality rate obtained in this current study (9.6 per cent) is higher than the figures reported in national updates published

during pandemic period and few study reports of tertiary care hospitals.^{7,8,16} This difference might be due to the smaller number of cases that were studied in those regions. Since the tertiary care centre where the present study was conducted is a major referral hospital for 3-4 states in South India majority of the lab confirmed cases were captured among inpatients as evident from Table 2. This study reported higher likelihood of lab positivity for H1N1 among adults, cases who reported history of contact with H1N1 cases, history of travel and Influenza like illnesses treated as in-patients especially in intensive care settings. These findings were similar to findings from other studies.²¹⁻²⁵

Changing epidemiological trends in H1N1

The suspected cases of Influenza A H1N1 showed a decreasing trend after 2012, and reached nearly one third of the levels that were seen in the immediate post pandemic phase. Lab positivity rate for H1N1 influenza had also reduced from 17.6 per cent in immediate post pandemic period to 4.2 per cent after 2012. Dangi et al. had reported lab positivity rate as 15.8 per cent two years later to the post pandemic period.¹⁸ Case fatality ratio had become negligible after 2012. During the year 2013, none of the fatal cases of ILI were found to be positive for H1N1 Influenza. The proportion of influenza suspects who required only OPD care increased from 22.5 per cent in 2010 to 96 per cent in 2014. After 2012, almost all positive cases were found among outpatient cases alone.

Yield of routine screening for H1N1 cases

The number of suspected Influenza like illness cases that needed to be screened in order to capture one laboratory confirmed case of H1N1 had increased from 5.5 in 2010 to 37 in the year 2014. Screening during the seasonal period resulted in higher yields compared to non-seasonal period. The epidemiological changes like low positivity rate for H1N1 among ILI cases, decrease in severity among cases and reduction in mortality rate necessitates re-examination whether routine screening for H1N1 among suspected ILI cases is useful. Routine screening for H1N1 among suspected cases of ILIs would cause a sevenfold increase in cost to the health care system (comparison of Number Needed to Screen). The decision to follow whether the cluster based approach as suggested by the World Health Organization or routine screening especially during the seasonal period needs further exploration. Despite the fact of India has faced resurgence of H1N1 in 2015, these results will help to focus on target based screening among high risk individuals in resource poor settings.

Strengths & Limitations: Our study captures observations for a considerably prolonged duration for post pandemic period of H1N1 illness as compared to other studies. Our findings reflect the changing epidemiological trend in lab positivity, severity of illness and mortality in suspected patients with ILI. Though we could demonstrate that the peak increase in H1N1 cases occurred during Aug-Nov, we could not demonstrate the association with meteorological factors. The limitations governing the present analysis are inherent to retrospective studies. Our study is limited in identifying associations and no causal inferences of H1N1 positivity could be explored. The present analysis was performed on a single-institute data belong to the major tertiary care institute in southern India. This could have catered lot of referred cases which necessitated them to be managed in inpatient settings. Hence, presence of selection bias cannot be ruled out there by the generalizability of these results in other contexts.

Conclusion

The present study reflects post-pandemic H1N1 data based on an analysis of suspected cases of ILI at a tertiary care, academic centre located in South India. We observed 9.5 per cent lab positivity among suspected cases tested for Influenza pandemic H1N1 strain tested using RT-PCR technique in the post pandemic period. Factors like adult age group, H/o travel, H/o contact and cases requiring management in in-patient care were independently associated with lab positivity. Over the time period the proportion of cases which needed inpatient treatment followed a decreasing trend. Number of cases needed to be screened to yield one lab positive case increased to 35 suspected cases.

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PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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Table 1: Characteristics of suspected cases of ILI attended to JIPMER facility during the post pandemic period (August 2010 –December 2014)

Characteristics	Number N=2065 (%)
Age (n=2038)	
Children (<15yrs)	708 (34.8)
Adult (15-59yrs)	1211 (59.4)
Elderly (≥60yrs)	119 (5.8)
Sex (n=2065)	
Male	891 (43.1)
Female	1174 (56.9)
Residence (n=1946)	
Pondicherry	1241 (63.8)
Tamil Nadu	699 (35.9)
Other states	6 (0.3)
Category (n=1976)	
A	1514 (76.6)
B	286 (14.5)
C	176 (8.9)
H/o Contact (n=2029)	
No	1936 (95.4)
Yes	93 (4.6)
H/o travel (n=1965)	
No	1905 (96.9)
Yes	60 (3.7)
Outcome (n=2065)	
Needed ventilator support	37 (1.8)
Deaths	19 (0.9)

Table 2: Characteristics of laboratory confirmed H1N1 cases that attended JIPMER clinic during the post pandemic period (August 2010 –December 2014)

Total number of suspected cases reported during the reference period	2065
Total number of cases positive for H1N1	197 (9.5%)
Gender (n=197)	
Male	85 (43.2)
Female	112 (56.8)
Age	
Children (<15yrs)	41 (21.1)
Adult (15-59yrs)	143 (73.7)
Elderly (≥60yrs)	10 (5.2)
Residence	
Pondicherry	126 (65.3)
Tamil Nadu	65 (33.7)
Other states	2 (1.0)
Disease category	
A	107 (57.2)
B	45 (24.1)
C	35 (18.7)
List of co-morbidities found among H1N1 cases	
No co-morbidities	159 (80.7)
At least one co-morbidity	38 (19.3)
Clinical symptoms	
Fever	167 (84.8)
Cough	141 (71.6)
Throat pain	53 (26.9)
Breathlessness	46 (23.3)
Cold	54 (27.4)
Myalgia	13 (6.6)
Head ache	11 (5.6)
Others*	21 (10.6)

*Other symptoms: Vomiting, diarrhoea, skin rashes and abdominal pain

Table 3: Characteristics of the H1N1 cases that suffered mortality during the post pandemic period (2010-2014)

Total number of cases positive for H1N1	197
Number of deaths	19 (9.6)
Gender	
Male	6 (31.6)
Female	13 (68.4)
Age	
Children (<15yrs)	2 (10.5)
Adult (15-59yrs)	14 (73.7)
Elderly (≥60yrs)	3 (15.8)
Disease category	
A	4 (21.0)
B	3 (15.8)
C	11 (63.2)
List of co-morbidities found among H1N1 cases	
No co-morbidities	11 (57.9)
At least one co-morbidity	8 (42.1)

Table 4: Factors associated with lab positivity among Flu suspects attending the JIPMER clinic during post pandemic period

Characteristics	Lab results	Unadjusted OR (95% CI)	p value*	Adjusted OR (95% CI)	p value**
	+ve for H1N1				
Age					
Children (<15yrs) N=708	41 (5.8)	Ref		Ref	
Adult (15-59yrs) N=1211	143 (11.8)	2.2 (1.5 to 3.2)	0.00001	1.6 (1.1 to 2.3)	0.021
Elderly (≥60yrs) N=119	10 (8.4)	1.5 (0.6 to 3.1)	0.27	1.0 (0.5 to 2.2)	0.91
Sex					
Male N=891	85 (9.5)	1.0 (0.7 to 1.4)	0.99	-	
Female N=1174	112 (9.5)	Ref		-	
Residence					
Puducherry N=1241	126 (10.2)	Ref		-	
Tamil Nadu N=699	65 (9.3)	0.9 (0.7 to 1.3)	0.54	-	
Others N=6	2 (33.3)	4.4 (0.4 to 31.2)	0.06	-	
Category					
A N=1514	107 (7.1)	Ref		Ref	
B N=286	45 (15.7)	2.5 (1.6 to 3.6)	0.00001	2.0 (1.3 to 3.0)	0.001
C N=176	35 (19.9)	3.3 (2.1 to 5.0)		3.0 (1.9 to 4.7)	0.0001
H/o Contact					
No N=1936	167 (8.6)	Ref		Ref	
Yes N=93	25 (26.9)	3.9 (2.3 to 6.4)	0.00001	2.7 (1.5 to 4.5)	0.0001
H/o Travel					
No N=1905	176 (9.2)	Ref		Ref	
Yes N=60	16 (26.7)	3.6 (1.8 to 6.6)	0.00001	2.3 (1.2 to 4.3)	0.01

*p value by chi square test determined in univariate analysis

**p value obtained in multi variate logistic regression analysis

Table 5: Epidemiological trend in yield of screening for lab confirmed H1N1 among Influenza like illnesses treated at JIPMER hospital (Aug 2010–Dec 2014)

Year	Number needed to be screened for one lab confirmed case (throughout the year)	Number needed to be screened for one lab confirmed case (during the seasonal period Aug-Dec)
2010	5.5	5.5
2011	4.8	3.9
2012	6.8	5.0
2013	35.7	21.2
2014	28.4	37.3

Figure 1: Time trend of suspected cases, lab confirmed cases and deaths during post pandemic period

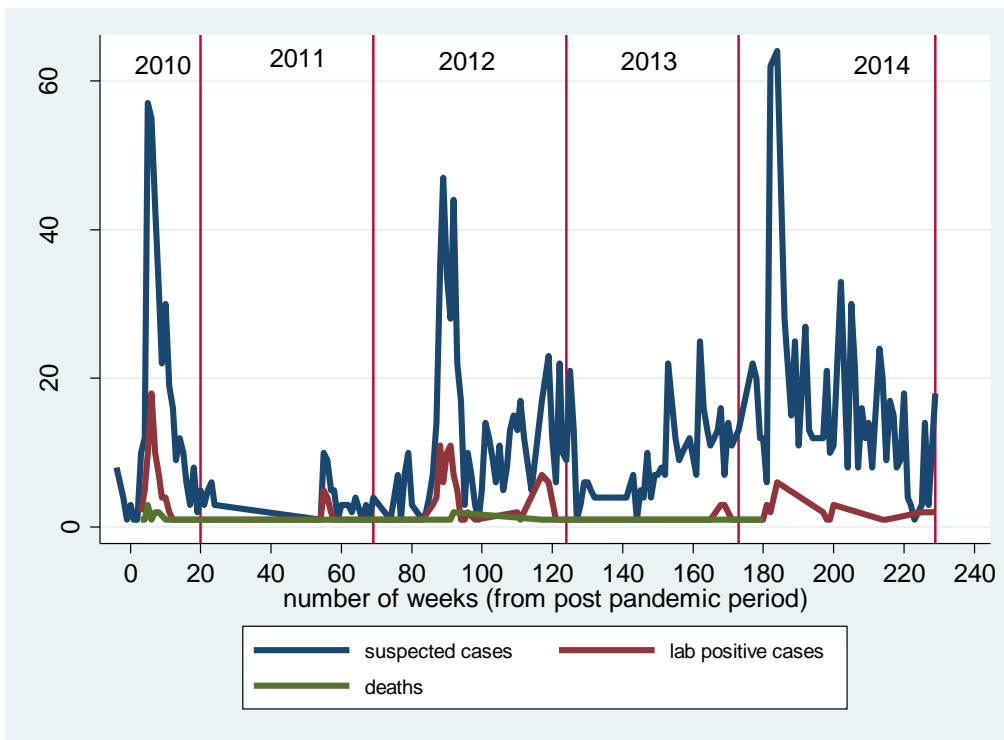


Figure 2: Trend of disease severity of suspected cases of Flu during post pandemic period

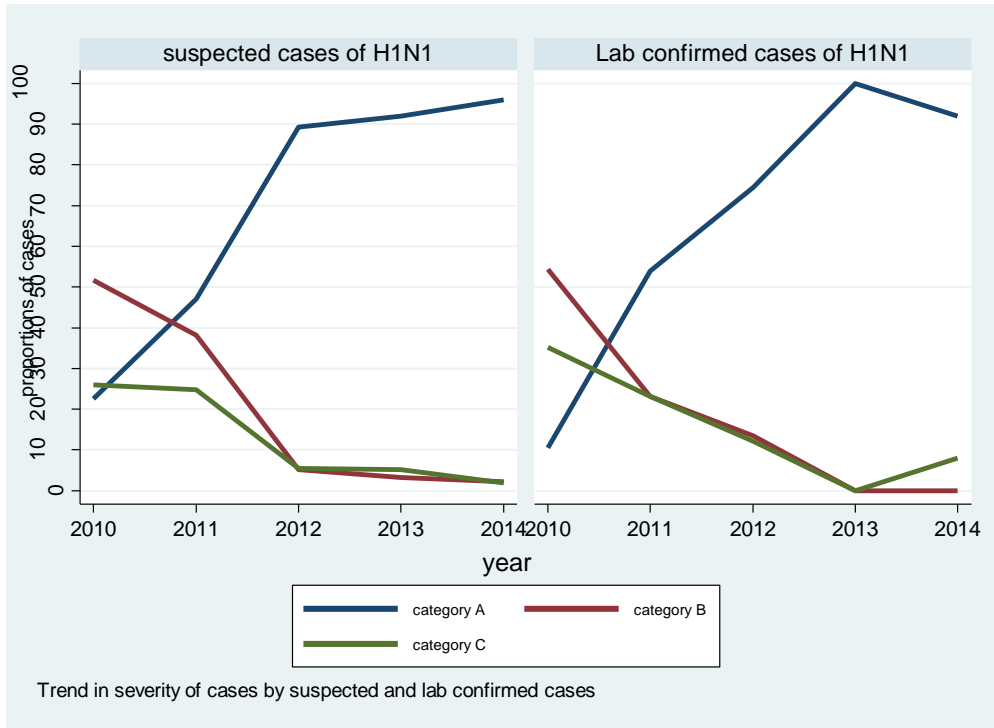


Figure 3: Distribution of seasonal trend on total number of suspected cases and laboratory confirmed cases by year

