Burden of Influenza in Patients visiting Emergency Department for Treatment of Influenza Like Illness at THQ Hospital Shujabad, Pakistan

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Significance:
Among Pakistani population, there is little information present about influenza. Normally in Pakistan, influenza activity starts to increase from September, and it peaks during months of winter. In different areas of Pakistan, currently circulating subtypes of seasonal influenza A are H1N1 also called swine flu and H3N2. Now, they are no more as dangerous as they were in 2008. So, it was necessary to conduct flu sentinel surveillance in the high-risk areas of Pakistan.

ABSTRACT

Background: Viral infection of the respiratory tract is a common illness syndrome in humans. Human respiratory tract is infected by large number of viruses. Self-constraining infections are caused by most of them e.g. normal chilly and intense bronchitis. Seriousness of illness relies upon specific infection and furthermore on host factors. Flu influences all age gatherings; an extensive number of bleakness and mortality happens in high hazard gathering e.g. elderly patients with chronic disease.

Methodology: The research was completed in Shujabad, Multan. A prospective study was conducted for a period of three months in order to define burden of flu among cases of influenza-like illness as they visited emergency department of the THQ Hospital Shujabad, Multan. Data was analyzed by using SPSS software with 95% confidence interval. Chi-square test was used to measure the association of risk factors. CI (cumulative incidence) of disease (influenza) was calculated by standard formula.

Results: There were 16332 patients visited emergency department of the hospital for the treatment different health issues. Total numbers of influenza like illness patients enrolled in current study were 244 and cumulative incidence was calculated to be 1.49%. Among these 244 ILI patients, 12 patients were hospitalized in the emergency department for advance respiratory care which was 4.9% of the ILI patients and 3 patients died among the 12 hospitalized patients due to the severe respiratory attack which was (1.2%) of ILI while rest of the patients were discharged as they were stable. All of the 244 ILI patient samples were sent to the laboratory for PCR and results was showing that 35 were influenza positive which was 14.3% of the ILI cases presented in emergency department of the hospital.

Conclusion: It was concluded that Influenza virus strains are circulating in general public of the Tehsil Shujabad, District Multan. This study therefore indorses the need for continuous surveillance of influenza as an important public-health issue. It also raises the question of rational vaccination policy for influenza. Finally, there is the question of clinical diagnosis where specific treatment/antiviral treatment is available.

Introduction
Viral infection of the respiratory tract is a common illness syndrome in humans. Human respiratory tract is infected by large number of viruses. Self-constraining infections are caused by most of them e.g. normal chilly and intense bronchitis. Seriousness of illness relies upon specific infection and furthermore on host factors. In patients with airway disease, for example, chronic obstructive disease (COPD), the morbidity due to respiratory virus infection is considerably high. Among all respiratory infections, flu infection has huge effect as far as sickness and mortality that it causes. Flu influences all age groups, an extensive number of bleakness and mortality happens among high risk groups e.g., elderly patients with chronic disease. (1) Among non-high risk group, seasonal flu is self-limiting illness. (2) Flu pandemic can possibly cause a large number of deaths and critical effect on the worldwide economy. (3) Flu is often described as cough, sore throat, headache, muscle pain and fever. Flu remains undefined from other respiratory viral illness without laboratory confirmation. (4) Flu viruses have negative-sense RNA genomes and are placed in the Orthomyxoviridae family. (5) Three known sorts of flu infection are commonly presenting among human population. Two (A & B) of the three sorts are related to essential respiratory illness. Subtypes of Flu infection are specified by characteristics of surface antigen (haemagglutinin & neuraminidase). In the last 20 years, H1N1 & H3N2 are the two subtypes of flu presenting among human population. Flu circulation starts in the beginning of winter and lasts for 8 to 12 weeks. (6)
The annual prevalence proportion of flu among preschool aged children is forty percent and among school aged children is thirty percent. (7) The illness differs in force and seriousness and can require therapeutic care. Medical complications, such as upper and lower respiratory tract problems and acute otitis media, often follow as part of the influenza illness itself. Apart from the burden of illness, children contribute a major part in the spread of influenza, as they contract the virus at school and then transmit it to household members. (8) However, vaccination status (full or partial) can reduce both in & out patient encounters. (9) According to Center for Disease Control and Prevention, influenza like illness is defined as a nonspecific respiratory illness with high grade fever, cough and sore throat. (10)

The influenza is a transmittable illness of the respiratory tract caused by virus that can infect the upper and lower respiratory tract even it reached to the lungs. Sometime illness results to death in the community. Flu vaccination each year is the best method for prevention from flu. Human influenza is generally related with seasonal (winter) pandemics in temperate areas of world but a year round pattern with a peak during rainy season is observed in tropical regions. (11) Globally annual attack rate of human influenza in elders is estimated as 5-10% and in children is 20-30% percent. Due to influenza epidemic, high level of absenteeism observed at workplaces and in schools. It also causes decrease in productivity and health facility centers are overcrowded during the winter season.

As there is concern of the epidemiology of the flu, it varies from place to place where it happens. Mostly flu is seasonal in pattern; it starts in the beginning of the winter and reaches at its peak from December to March but sometimes it shows variation in its trend and occur early and reaches at its peak in October. Different types of flu are circulating between poultry and birds and are putting human beings at risk which emphasize to conduct sentinel researches to identify the flu virus who have ability to cause pandemics. These sentinel researches may be conducted to see the influenza like illness and trends of respiratory illness in the population. (12)

Sentinel studies are necessary to separate the different subtypes of circulating influenza stains through laboratory confirmation in the general population. Such studies also have the characteristics to identify other respiratory viruses having ability to cause pandemic. Sentinel flu studies are very important and efficient source of epidemiological variations with respect to the incidence, seasonal pattern and to identify the strains of virus. Through such studies policies can be formulated to control and prevent flu from pandemics. (13)

Among Pakistani population, there is little information present about influenza. Normally in Pakistan, influenza activity starts to increase from September, and it peaks during months of winter. In different areas of Pakistan, currently circulating subtypes of seasonal influenza A are H1N1 also called swine flu and H3N2. Now, they are no more as dangerous as they were in 2008. So, it is necessary to conduct flu sentinel surveillance in the high-risk areas of Pakistan. This surveillance will also help to define seasonal trends in influenza viruses circulation in the population, difference in seasonality with respect to region as well as to find optimal duration for implementation of influenza vaccination among different populations on priority. (14)

**Objectives**

To estimate the incidence of influenza infection among general population of Tehsil Shujabad, Multan visiting emergency department and to study the temporal pattern of influenza infection and to characterize trends in morbidity and mortality attributable to influenza.

**Materials and Methods**

The research was completed in Shujabad which is the first tehsil and old municipality of Multan and located 45 kilometers away from Multan district in south. This lies from 29.878673°N, north latitudes and 71.317224°E, east longitudes. Permission was taken from Independent Institutional Ethical Board of University of Veterinary and Animal Sciences, Lahore, Pakistan. A prospective study was conducted for a period of three month (2018) in order to define burden of flu among cases of influenza-like illness as they visited emergency department of the THQ Hospital Shujabad, Multan.

Study population was the patients having influenza like illness and visited emergency department of THQ hospital Shujabad for treatment. Influenza like illness is well-defined as temperature equal/more than 38°C with cough and sore throat.

Persons who were having influenza like illness, which is clarified by World Health Organization, persons who had permanent residence in study area and persons who were willing to participate in study were included in the study. People having disease other than influenza like illness, complicated cases having symptoms for more than 14 days of duration were excluded. Data was collected from the patients during
face-to-face interview. Data of influenza and influenza-like illness was collected on clinical proforma from people of all ages visiting emergency department Tehsil Hospital Shujabad after taking written permission. The oropharyngeal swabs were taken from patients who were coming in emergency department with influenza-like illness. For throat swab, a swab stick with rigid plastic shaft was inserted into the mouth to the lower part of pharynx and rubbed vigorously. These swabs were placed in virus transporting media vial and were labeled with unique ID. All the samples were transported at (-4°C) to the test center for further processing.

The swab sample collected during the study from respondents was processed for laboratory analysis. Reverse Transcriptase Polymerase Chain Reaction (PCR) was conducted to diagnose sample for influenza infection. Sub-typing of positive samples was done to identify the subtype circulatory among general population. Pattern of influenza infection in general population of Tehsil Shujabad was estimated with reference to descriptive epidemiology. Data was analyzed by using SPSS software with 95% confidence interval (CI). Chi-square test was used to measure the association of risk factors. CI (cumulative incidence) of disease (influenza) was calculated by standard formula.

Results
This prospective study was conducted at Tehsil Headquarter Hospital Shujabad, Multan to see the incidence of influenza among ILI patients presenting to the emergency department of the hospital. Patients were assessed on clinical signs and symptoms and throat swabs were taken along with detailed questionnaire filled to see the related risk factors.

During this study period of three month from December (2017) to February (2018), a total of 16332 patients visited emergency department of the hospital which was 14.3% of the ILI cases presented in emergency department of the hospital. This study was showing that ILI was one of the major causes of emergency visits among respiratory diseases. The people of mid ages (15-44 years) were at higher risk i.e. 59.8% of the ILI patients. Out of total 244 ILI cases, 53.3% were the female and 46.7% were the male which showed that females are more prone to the ILI. Based on education status, 28.7% were with secondary level education while at the same time 26.6% had no formal education. Most patients (78.3%) had very poor knowledge about the vaccination of influenza disease while only 16% of the patients were vaccinated with influenza vaccine during last year. This study showed that 86.9% of the participants and their families visited hospitals for medical care. Among all 244 ILI cases, 54.1% of the participants had extended families; their family members were using the public transport and educational institutes. This study also showed that 43.9% participants and their family members visited the epidemic area in last 7 days prior to the onset of illness. Among the ILI cases, 37.3% participant’s family members and neighbors were suffering from ILI and 35.2% were exposed to confirmed and probable cases of influenza. Current study showed that 29.9% participants and their family members visited hospitals in last 7 days. 23% of the participants and their family members are working in hospital and possibly contacted with the infected patients of ILI. Among ILI cases, 85.7% did not have any past medical history while 2% were having malnutrition, 2% chronic liver illness, 1.6% chronic heart illness, 1.6% kidney problem and 1.6% were having hypertension.

As there is concern of association among influenza and different risk factors, chi-square test was applied, and p-value calculated. Some of the factors e.g. use of the transport on daily basis and visits to the epidemic areas, area of their residence locality, attending educational institute by the participant or family member and pneumococcal vaccination status showed significant association with ILI (p<0.05). Some of the participants were hospitalized due to complications and mostly recovered after treatment.

During 3 months of study, influenza illness trend was calculated which showed that flu activity started early in the winter with low rate of 5.7% in December and it reached at high rate 54.28% in January and then a gradual decrease at 40% was seen in February. Same type of trend was calculated relative for ILI cases which showed 22.13% in December, 54.50% in January and 23.36% in February.
Table 1 Association of Influenza cases with education, residence, hand washing before eating/drinking, pneumococcal vaccination and epidemic area visit

| Association of Influenza cases and educational institute attendance | Parameters | PCR Negative | PCR Positive | Total | p-value  |
|---------------------------------------------------------------------|------------|--------------|--------------|-------|----------|
| Education                                                           |            |              |              |       |          |
| No                                                                  | Count      | 59           | 4            | 63    | 0.036    |
|                                                                     | % within the group | 28.2%     | 11.4%        | 25.8% |          |
| Yes                                                                 | Count      | 150          | 31           | 181   |          |
|                                                                     | % within the group | 71.8%     | 88.6%        | 74.2% |          |

| Association between Influenza cases and locality of residence       | Parameters | PCR Negative | PCR Positive | Total | p-value  |
|---------------------------------------------------------------------|------------|--------------|--------------|-------|----------|
| Residence                                                           |            |              |              |       |          |
| Rural                                                               | Count      | 108          | 9            | 117   | 0.014    |
|                                                                     | % within the group | 51.7%     | 25.7%        | 48.0% |          |
| Urban                                                               | Count      | 45           | 10           | 55    |          |
|                                                                     | % within the group | 21.5%     | 28.6%        | 22.5% |          |
| Major Urban                                                         | Count      | 56           | 16           | 72    |          |
|                                                                     | % within the group | 26.8%     | 45.7%        | 29.5% |          |

| Association between Influenza cases and hand washing before eating/drinking | Parameters | PCR Negative | PCR Positive | Total | p-value  |
|----------------------------------------------------------------------------|------------|--------------|--------------|-------|----------|
| Hand Washing                                                           |            |              |              |       |          |
| No                                                                     | Count      | 67           | 1            | 68    |          |
|                                                                     | % within the group | 32.1%     | 2.9%         | 27.9% |          |
| Yes                                                                   | Count      | 142          | 34           | 176   | 0.000    |
|                                                                     | % within the group | 67.9%     | 97.1%        | 72.1% |          |

| Association between Influenza cases and Pneumococcal vaccination        | Parameters | PCR Negative | PCR Positive | Total | p-value  |
|------------------------------------------------------------------------|------------|--------------|--------------|-------|----------|
| Pneumococcal vaccination                                               |            |              |              |       |          |
| No                                                                     | Count      | 178          | 25           | 203   | 0.044    |
|                                                                     | % within the group | 85.2%     | 71.4%        | 83.2% |          |
| Yes                                                                   | Count      | 31           | 10           | 41    |          |
|                                                                     | % within the group | 14.8%     | 28.6%        | 16.8% |          |

| Association between Influenza cases and epidemic area visit            | Parameters | PCR Negative | PCR Positive | Total | p-value  |
|------------------------------------------------------------------------|------------|--------------|--------------|-------|----------|
| Epidemic area visit                                                   |            |              |              |       |          |
| No                                                                     | Count      | 124          | 13           | 137   | 0.014    |
|                                                                     | % within the group | 59.3%     | 37.1%        | 56.1% |          |
| Yes                                                                   | Count      | 85           | 22           | 107   |          |
|                                                                     | % within the group | 40.7%     | 69.9%        | 43.9% |          |
| Total                                                                 | Count      | 209          | 35           | 244   |          |
|                                                                     | % within the group | 85.6%     | 14.4%        | 100.0%|          |

**Weekly temporal trend of Influenza positive cases among ILI patients:** Results showed that number of positive cases were low in the 4 week of December then sudden increase in number during next 4 week of January and then slight decrease in the influenza cases during 4 week of February which showed that flu activity started early in the winter with low rate and it reached at its peak in mid of winter than gradual decrease in rate at end of the winter season. (Figure 1)

**Cumulative Incidence (Burden) of disease:** Influenza among ILI cases was 1.49%. Cumulative Incidence of Influenza among ILI Cases was 14.34%. Morbidity of ILI among general population was 4.1%. Morbidity of Influenza among general population was 0.6%. Morbidity of Influenza among emergency cases...
Influenza in ILI Patients

was 21.4%. Mortality of Influenza among emergency cases was 1.22%. Mortality of Influenza among general population was 0.03%. Mortality of ILI among general population was 0.5%. Mortality of ILI among emergency cases was 18.36%. Hospitalization rate of ILI was 4.9%. Hospitalization rate of Influenza was 34.28%.

**Fig. 1:** Weekly trend of Influenza positive cases during three months of winter season

**Fig. 2:** Weekly trend of ILI cases during three months of winter season

**Discussion**

A prospective study was conducted to check the burden of influenza in patients visiting emergency department for the treatment of influenza like illness in Tehsil Headquarter Hospital Shujabad, Multan. In Pakistan, influenza season starts during winter from November to January and reaches at its maximum point at the end of winter season. Same results are reported from the previous study that flu was present throughout whole year in countries of temperate region but it shows high increase in cases during the winter season. (15)

Data was collected from the 244 ILI cases, out of 16332 patients who visited the emergency department for the treatment of different health problems during 3 months of study. Some of the participants presented in critical conditions with low saturation of oxygen and were hospitalized for advance medical care. In present study, adults were the high risk group (15 to 44 years) which are similar to results reported earlier. (6) There were many factors which made them more prone to the disease like making use of the transport on daily basis and visits to the epidemic areas, area of their residence locality, attending educational institute by the participant or family member and pneumococcal vaccination status.

Participants suffering from ILI showed symptoms of nausea, vomiting, headache and muscle pain. Vaccination rate of the participants was very low and most of the patients were unaware of the vaccination process of the influenza, same results reported from past study conducted among French population which showed that people were not interested in vaccination due to low education status. About 14.3% of the participants were having past medical history of malnutrition, heart diseases, kidney illness, liver and lung diseases which made them more prone to the ILI and influenza. However, another study reported 18% had one past medical condition which is higher than
the current study. (16) Travelling before 7 days of illness was a major cause of getting ILI. Patients were having low compliance for ILI and influenza treatment due to poor knowledge about this viral infection. Best method for the influenza prevention and prophylaxis is flu vaccine while there are some cases when vaccination is not sufficient and antiviral therapy is necessary. (17) In Pakistan, variety of vaccines are available for flu but most active against flu illness is Sometimes vaccines are not 100% effective due to the mismatch between the circulating strain and vaccine strain. (2)

Conclusion
It was concluded that influenza virus strains are circulating in general public of the Tehsil Shujabad, District Multan. This study, therefore, indorses the need for continuous surveillance of influenza as an important public health issue. It also raises the question of rational vaccination policy for influenza. Finally, there is the question of clinical diagnosis where specific treatment/antiviral treatment is available. Study had provided valuable information about the risk factors related to influenza along with disease temporal trend and morbidity and mortality rates which will be very useful for the policy makers for the prevention and control of the illness.

Conflict of interest: Authors do not have any conflict of interest.

Disclosure: None

Human/Animal Rights: No human or animal rights are violated during this study.

References
1. Akgün KM, Crothers K, Pisani M. Epidemiology and management of common pulmonary diseases in older persons. Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences. 2012;67(3):276-91.
2. Michiels B, Van Puyenbroeck K, Verhoeven V, Vermeire E, Coenen S. The value of neuraminidase inhibitors for the prevention and treatment of seasonal influenza: a systematic review of systematic reviews. PLoS ONE. 2013;8(4):e60348.
3. Barbazan P, Thitithanyanont A, Misse D, Dubot A, Bosc P, Luangseri N, et al. Detection of H5N1 avian influenza virus from mosquitoes collected in an infected poultry farm in Thailand. Vector-borne and zoonotic diseases. 2008;8(1):105-10.
4. Molinari N-AM, Ortego-Sanchez IR, Messonnier ML, Thompson WW, Wortley PM, Weintraub E, et al. The annual impact of seasonal influenza in the US: measuring disease burden and costs. Vaccine. 2007;25(27):5086-96.
5. Alexander DJ. A review of avian influenza in different bird species. Veterinary microbiology. 2009;121(3):9-13.
6. Zambon M, Stockton J, Clewley J, Fleming D. Contribution of influenza and respiratory syncytial virus to community cases of influenza-like illness: an observational study. The Lancet. 2001;358(9291):1410-6.
7. Monto AS. Epidemiology of influenza. Vaccine. 2008;26:D45-D8.
8. Hayward AC, Fragaesy EB, Bermingham A, Wang L, Copas A, Edmonds WJ, et al. Comparative community burden and severity of seasonal and pandemic influenza: results of the Flu Watch cohort study. The Lancet Respiratory Medicine. 2014;2(6):445-54.
9. Rahmqvist M, Gjessing K, Faresjo T. Influenza-related healthcare visits, hospital admissions, and direct medical costs for all children aged 2 to 17 years in a defined Swedish region, monitored for 7 years. Medicine. 2016;95(33).
10. Lamson D, Renwick N, Kapoor V, Liu Z, Palacios G, Ju J, et al. MassTag polymerase-chain-reaction detection of respiratory pathogens, including a new rhinovirus genotype, that caused influenza-like illness in New York State during 2004–2005. The Journal of infectious diseases. 2006;194(10):1398-402.
11. Russell CA, Jones TC, Barr IG, Cox NJ, Garten RJ, Gregory V, et al. The global circulation of seasonal influenza A (H3N2) viruses. Science. 2008;320(5874):340-6.
12. Ghendon Y. Introduction to pandemic influenza through history. European Journal of Epidemiology. 1994;10(4):451-3.
13. Mainassara HB, Lagare A, Tempia S, Siddiki A, Issaka B, Siikonsu BA, et al. Influenza Sentinel Surveillance among Patients with Influenza-Like-Illness and Severe Acute Respiratory Illness within the Framework of the National Reference Laboratory, Niger, 2009-2013. PLoS ONE. 2015;10(7):e0133178.
14. Badar N, Aamir UB, Mehmood MR, Nisar N, Alam MM, Kazi BM, et al. Influenza virus surveillance in Pakistan during 2008-2011. PLoS ONE. 2013;8(11):e79959.
15. Lofgren E, Fefferman NH, Naumov YN, Gorski J, Naumova EN. Influenza seasonality: underlying causes and modeling theories. Journal of virology. 2007;81(11):5429-36.
16. Neuzil K, Reed GW, Mitchel, Jr EF, Griffin MR. Influenza-associated morbidity and mortality in young and middle-aged women. JAMA. 1999;281(10):901-7.
17. Moscona A. Neuraminidase Inhibitors for Influenza. New England Journal of Medicine. 2005;353(13):1363-73.