JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Original Article

Epidemiology and costs of severe acute respiratory infection and influenza hospitalizations in adults with diabetes in India

Parvaiz A Koul[1], Amit Bhavsar[2], Hyder Mir[1], Mark Simmerman[3], Hemant Khanna[2]

[1] *Department of Internal and Pulmonary Medicine, Sher-I-Kashmir Institute of Medical Sciences, Soura, Srinagar, India*
[2] *Sanofi Pasteur, Powai, Mumbai, India*
[3] *Sanofi Pasteur, Bangkok, Thailand*

Abstract
Introduction: The incidence of diabetes mellitus is increasing rapidly in India. In addition to well-known complications, diabetes increases the risk for hospitalization and death from severe acute respiratory infection (SARI) and influenza. Here we examined the impact of SARI and influenza in Indian adults with diabetes.
Methodology: This was a single-center, active surveillance study conducted in Jammu and Kashmir State, India, during the 2015–2016 and 2016–2017 influenza seasons. Adults hospitalized for SARI and receiving at least one diabetes medication were included. Demographics, health care use, and direct costs were collected from medical records and interviews of patients or caregivers. Indirect costs were estimated based on lost earnings and WHO-CHOICE estimates for hospital costs.
Results: The study included 192 patients with type 2 diabetes. Median age was 66 years, median body mass index was 26.6 kg/m^2, and most patients had comorbidities, especially hypertension and cardiovascular disease (83.9%). Only 32.2% regularly monitored blood glucose or hemoglobin A1C, and median values at admission indicated poor glycemic control for most. Influenza was detected in 8.9% of cases. The median hospital stay for SARI was 8 days, and 22 patients (11.4%) died. Median total costs associated with hospitalization were US$710 (interquartile range, $539–$1067) for SARI patients and US$716 ($556–$1078) for influenza patients, mostly (~75%) from indirect costs.
Conclusions: Adults with diabetes in India hospitalized with SARI or influenza are generally older, in poor health, and suffer from poor glycemic control. The costs for their hospitalization and care are substantial.

Key words: diabetes mellitus; respiratory infections; hospitalization; India.

J Infect Dev Ctries 2019; 13(3):204-211. doi:10.3855/jidc.10903

(Received 28 September 2018 – Accepted 08 February 2019)

Introduction

The incidence of diabetes mellitus is increasing worldwide and especially in India [1]. The 2017 International Diabetes Federation reported an overall prevalence of 8.8% in India, and the number of adults with diabetes rose from 32.7 million in 2000 to 72.9 million in 2017 and is projected to increase to almost 150 million in 2045 [2]. This appears to be due to rapid socioeconomic development and demographic changes, coupled with increased susceptibility of the Indian population to diabetes [1]. Furthermore, compared to Population form Western countries, Asian Indian people have an earlier onset of type 2 diabetes mellitus, tend to have diabetes at lower body mass indexes, convert from pre-diabetes to diabetes more rapidly, and are more resistant to maintaining glycemic control with only lifestyle changes [1,3].

In addition to well-known complications, such as cardiovascular disease, renal disease, and peripheral neuropathy, diabetes increases the risk for hospitalization and death due to severe acute respiratory infection (SARI) [4-9]. This may be the result of decreased lung function caused by microangiopathy of pulmonary capillaries, autonomic neuropathy, myopathy of respiratory muscles, or changes in collagen in lung tissues [10]. These risks are further increased by cardiovascular, renal, and other comorbidities common in individuals with diabetes [11].

A substantial proportion of SARIs are caused by influenza viruses [12], which circulate across India in varied seasonal patterns governed by latitude and environmental factors [13]. The World Health Organization recommends that individuals with diabetes are vaccinated against influenza ahead of each season to prevent SARI and other complications [14].

To better understand the impact of SARI and influenza among individuals with diabetes in India, we analyzed active surveillance data collected over two influenza seasons (October to April) at Sher-i-Kashmir Institute of Medical Sciences (SKIMS), a 750-bed tertiary care institute in the State of Jammu and Kashmir [13,15]. Here, we describe the demographics, symptoms, healthcare use, and associated costs for these patients.

Methodology

Study design

This was a prospective, cross-sectional, hospital-based epidemiological study conducted at SKIMS. The study included adult patients (≥ 18 years of age) presenting with SARI during the 2015–2016 and 2016–2017 influenza seasons (October to April) at the Accident and Emergency Medicine, Internal Medicine, Clinical Endocrinology, and Pulmonary Medicine wards. To be included, patients had to be receiving at least one oral or injectable medication for diabetes. SARI was defined according to the World Health Organization as an acute respiratory infection with a fever or history of fever (≥ 38°C) and cough within the previous 7 days requiring hospitalization [16]. The primary objective was to describe the demographics and symptoms associated with SARI and influenza for adults with diabetes. The secondary objective was to estimate the costs associated with SARI and influenza hospitalizations in this population.

While hospitalized, patients were treated following the standard of care for SARI at SKIMS. Combined nasal and throat swabs were obtained from individuals with upper or lower respiratory tract symptoms and placed in 3 mL of HiViral Transport Medium (Hi Media, Mumbai, India). Samples were sent on ice or at 4°C to the laboratory within 2 hours. RNA was extracted using a QIAamp viral RNA Mini Kit (Qiagen, Hilden, Germany). Reverse transcription was performed using an AgPath-ID One-Step RT-PCR kit (Invitrogen, Carlsbad, CA, USA). Primers and probes (Invitrogen) for influenza viruses A and B were selected as recommended by the US Centers for Disease Control and Prevention and were based on genomic regions highly conserved in various subtypes and genotypes of influenza virus A (matrix protein gene) and influenza virus B (hemagglutinin gene segment). Amplification and detection were performed using a StepOnePlus Real-Time PCR System (Applied Biosystems, Foster City, CA, USA).

Data collection

Medical records were examined for patient demographics (age, gender); admission and discharge date; length of stay; type of accommodation; type of admission (general or intensive care unit [ICU] ward); entry type (outpatient, emergency room, referral); primary diagnosis; co-morbidities; details of medications given (type, duration, number of doses, cost); and blood glucose and hemoglobin A1C level at admission. Patients or caregivers were interviewed at admission of the patient to the hospital for demographics (age; gender; smoking status and duration; weight; height; symptoms and duration since onset; date of first consultation; duration since onset of antiviral medication; details and compliance with diabetes medications [yes/no]) and pre-hospitalization data (year diagnosed with diabetes; presence of underlying medical conditions; and details of consultation with other providers [types, medications given, and costs of medications, consultations, and other expenses]).

During a follow-up phone call 7 to 10 days after discharge, patients or caregivers were interviewed for hospitalization data (length of hospitalization; ICU admission (yes/no); cost of hospitalization to patient and insurance company; medications taken home after hospitalizations; and cost of laboratory work, imaging, and treatments) and post-hospitalization data (medications purchased after hospitalization and cost; other costs of admission; the number of working days lost by employed patients and caregivers due to hospitalizations and costs; how medical expenses were paid; cost of interest for any loans to pay for medical expenses; and receipt of influenza vaccination for the current season and costs).

Statistical analysis

Direct cost was calculated as the sum of medical costs and direct non-medical costs. Medical costs included hospital admission (including room rent, file charges, nursing charges, and attendant pass charges) medication, laboratory work, imaging, insulin therapy, and miscellaneous medical costs. Direct non-medical costs included transportation and lodging. Indirect cost was calculated as the sum of indirect hospital costs and the monetary value of lost earnings of adult patients and caregivers of all age groups due to inability to perform regular duties because of illness. Estimation of indirect cost was based on the assumption that labor was replaced at a cost to maintain societal productivity. Cost of missed work by the patient and caregiver was estimated as the product of missed work days and the median per capita income (US$ 1,861.5 per year for 2016 [17]). Missed work days were estimated by adding two days to the reported length of the hospital stay, as described by Molinari *et al*. [18]. Indirect hospital costs were calculated using WHO-CHOICE estimates [19] as a proxy for the cost to the government in public tertiary care facilities. WHO-CHOICE estimates are available for hospital bed-cost per day in public inpatient facilities. The 2008-based year estimates were adjusted to 2016 using the consumer price index (1.93) for India [20]. For inpatients, the cost to the government was the sum of the WHO-CHOICE estimates for the first day of hospitalization and the product of the WHO-CHOICE estimates for following days and (the median length in days of hospitalization − 1). Because data were not normally distributed, costs for subgroups are reported as medians and interquartile ranges. The exchange rate used was the average for 2016 (1 Indian Rupee = 0.014 US$) [21]. Statistical analysis was performed using SPSS version 23 (IBM Analytics, Armonk, NY, USA).

Ethics

The study was approved by the ethics committee of SKIMS. Informed consent was obtained from all participants or their caregivers at enrolment.

Results

Patients

The study included 192 adults with diabetes mellitus hospitalized with SARI during the 2015–2016 and 2016–2017 influenza seasons (October to April) (Figure 1). Just over half of the patients were female (56.2%), and ages ranged from 35 to 93 years (median, 66 years) (Table 1). Most patients were not employed, and just over three-quarters were non-smokers. For those who smoked, they had been smoking for a median of 35 years and smoked a median of 365 packs of cigarettes per year.

All of the patients had type 2 diabetes mellitus, and the median time since diagnosis was 4 years. Mean blood glucose was 228 mg/dL (range, 34–515 mg/dL), and the mean hemoglobin A1C level was 8.4% (range, 5.1%–12.5%). Most (94.1%) reported complying with their anti-diabetes medications, mostly insulin, although only 32.2% reported regularly monitoring blood glucose or hemoglobin A1C level.

Most of the included patients had comorbidities, the most common of which were hypertension and cardiovascular disease (83.9%). Other comorbidities included chronic obstructive pulmonary disease (26.6%), hypothyroidism (13.5%), renal disease

Figure 1. Flow of patients included in the study.

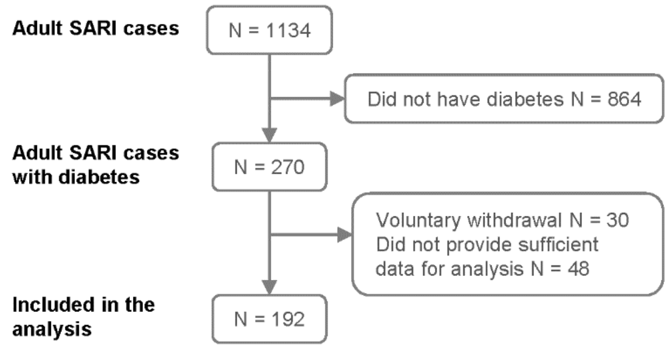

Table 1. Characteristics of patients included in the study.

Characteristic	Value
Age, median (range)	65 (35–93)
Gender, n (%)	
Male	84 (43.8)
Female	108 (56.2)
Employment status, n (%)	
Employed	36 (18.8)
Unemployed	104 (54.2)
Retired	52 (27.0)
Weight (kg), median (IQR)	70 (65–75)
Body mass index, median (IQR)	26.6 (24.3–29.3)
Smoking status, n (%)	
Non-smoker	147 (76.6)
Smoker	45 (23.4)
Duration of smoking (y), median (IQR)	35 (30–40)
Packs of cigarettes smoked per year, median (IQR)	365 (350–365)
Co-morbidities, n (%)	
Hypertension or cardiovascular disease	161 (83.9)
Chronic obstructive pulmonary disease	51 (26.6)
Hypothyroidism	26 (13.5)
Chronic kidney disease or end-stage renal disease	19 (9.9)
Rheumatic heart disease	3 (1.6)
Diabetes type, n (%)	
Type 2	192 (100.0)
Blood glucose at admission (mg/dl), mean (range)	228 (34–515)
Hemoglobin A1C at admission (%), mean (range)	8.4 (5.1–12.5)
Compliance with diabetes medications, n (%)	181 (94.2)
Duration of anti-diabetes (y), median (range)	4 (1–10)
Type of diabetes medication, n (%)	
Oral agents	51 (26.6)
Insulin	141 (73.4)
Regular monitoring of blood glucose and hemoglobin A1C concentration, n (%)	62 (32.2)
Vaccination received against influenza, n (%)	17 (8.9%)

IQR: interquartile range.

(9.9%), and rheumatic heart disease (1.6%). In addition, the median body mass index was 26.6 kg/m^2.

Only 17 (8.9%) of the 192 patients had received vaccination against influenza.

SARI characteristics

The most common symptoms of SARI at presentation were headache (98.8%), difficulty breathing (94.7%), malaise (88.8%), body aches (83.8%), and fever (74.0%) (Table S1 in additional files). All patients had a history of fever in the previous week. In most cases (85.9%), the primary diagnosis was community-acquired pneumonia, and in about one-quarter of cases, patients presented with congestive cardiac failure (28.9%) or acute exacerbation of chronic obstructive pulmonary disease (26.6%). Other diagnoses included encephalopathy (15.1%), sepsis (13.0%), stroke (4.7%), multi-organ dysfunction syndrome (4.7%), myocardial infarction (2.1%), and cancer (1.0%).

Influenza was detected in 17 (8.9%) cases (Table 2). In most of these cases (16 of 17), the patient had not been vaccinated for influenza.

Healthcare use

Patients were admitted a median of 1 day after the onset of symptoms (Table 3). Following diagnosis of SARI, six patients (3.1%) were admitted to an ICU and the rest (96.9%) to a general ward. The median length of hospitalization was 8 days for SARI patients and 9 days for patients with laboratory-confirmed influenza.

Almost half of the patients (48.4%) had a prior visit to a hospital for the current respiratory infection, and 3.1% had a prior visit to a clinic. Approximately one-third (34.4%) had visited a non-medical practitioner (e.g. pharmacist or non-traditional healer) for the current respiratory infection. Of the 66 patients who had visited a non-medical practitioner, 64 had purchased medications following the recommendation of the practitioner.

Table 2. Influenza and vaccination for influenza.

Measure	n (%)
Laboratory-confirmed influenza	
Any	17 (8.9)
A/H1N1	4 (2.1)
A/H3N2	8 (4.2)
B	5 (2.6)
Laboratory-confirmed influenza by vaccination status	
Not vaccinated	16 (8.3)
Vaccinated	1 (0.5)

All patients received the standard of care at SKIMS, including antibiotics, an antiviral (oseltamivir), and supportive care. Approximately three-quarters of patients (73.4%) were administered insulin, and 18.8% received hypoglycemic agents. Antibiotics were administered for a median of 7 days. Other medications include insulin, nebulized salbutamol, budesonide, heparin, diuretics, proton pump inhibitors, thiamine, and steroids. Invasive ventilation in an ICU was administered in six cases.

Outcome

Twenty-two patients (11.4%) died during hospitalization (Table 3), of which one was positive for influenza. All others recovered. All patients were prescribed medication after they went home from the hospital.

Working days lost by patients and caregivers

Employed patients lost a median of 25 days of work due to hospitalization for SARI, and a median of 30 days of work if they had laboratory-confirmed influenza. Employed caregivers lost a median of 9 days of work from caring for SARI or influenza-positive patients.

Costs

The median total cost associated with hospitalization due to SARI in diabetic patients was US $710 (IQR, $539–$1067) (Table 3). About three quarters of this was due to indirect costs to the hospital (median = $258.4 [IQR, $192–$324.8]) and from missed work days by the patients (median = $137 [IQR, $86.6–$163]) and their caregivers (median = $134 [IQR, $74.5–$290]). Of the direct medical cost, the largest contributor was medications (median = $74.5 [IQR, $50–$149]). Costs were not overly different for patients with laboratory-confirmed influenza. The cost of caregiver lodging was not included because it was needed for only one patient.

Discussion

This study, performed over two influenza seasons at a single site in Srinagar, India, showed that medical needs and costs are substantial for diabetes patients hospitalized with SARI. Medication was used in all cases, but accounted for relatively little of the overall cost. Most of the cost was instead due to indirect costs incurred by the hospital and missed work days by patients and their caregivers.

Table 3. Hospitalization, outcomes, and costs.

Measure or characteristic	All (N = 192)	Influenza-positive (N = 17)
Time between onset of symptoms and first consultation, median (IQR)	1 (1–2)	1 (1–2)
Length of hospitalization (days), median (IQR)	8 (5–11)	9 (5–11)
Type of admission, n (%)		
General ward plus ICU	6 (3.1)	1 (5.9)
General ward only	186 (96.9)	16 (94.1)
Length of ICU stay (days), median (IQR)	3.0 (2.0–4.8)	4.2 [a]
Entry type, n (%)		
Outpatient	3 (1.6)	–
Emergency room	188 (97.9)	17 (100.0)
Referral	1 (0.5)	–
Visited a hospital or clinic for the current respiratory infection prior to admission, n (%)		
Clinic	6 (3.1)	2 (11.8)
Hospital	93 (48.4)	7 (41.2)
Visited a non-medical practitioner for the current respiratory infection prior to admission, n (%)	66 (34.4)	–
Resulted in the purchase of medication, n (%)	64 (32.8)	3 (17.6)
Medications given, n (%)		
Antibiotics	192 (100.0)	17 (100.0)
Antiviral (oseltamivir)	192 (100.0)	17 (100.0)
Insulin	141 (73.4)	12 (70.6)
Proton pump inhibitors	116 (60.4)	13 (76.5)
Salbutamol nebulizer	111 (57.8)	9 (52.9)
Budesonide nebulizer	89 (46.4)	5 (29.4)
Diuretics	83 (43.2)	7 (41.2)
Heparin	72 (37.5)	4 (23.5)
Thiamine	67 (34.9)	3 (17.6)
Oral hypoglycemic agents	36 (18.8)	0 (0.0)
Steroids	23 (12.0)	0 (0.0)
Statins (atorvastatin or torsemide)	21 (10.9)	2 (11.8)
Aspirin	21 (10.9)	2 (11.8)
Anti-hypertensive agents	16 (8.3)	1 (5.9)
Other	149 (77.6)	6 (35.3)
Duration of antibiotic therapy (days), median (IQR)	7 (2–15)	7 (5–10)
Insulin therapy		
Duration (days), median (IQR)	9 (5–11)	9 (5–11)
Doses, median (IQR)	18 (10–22)	18 (10–22)
Outcome, n (%)		
Discharged	170 (88.6)	16 (94.1)
Death	22 (11.4)	1 (5.9) [b]
Median work days missed by the patient (IQR)	25 (15–30)	30 (24–30)
Median work days missed by the caregiver (IQR)	9 (5–15)	9 (5–15)
Direct medical cost (US$), median (IQR)		
Admission [c]	15 (10.4–22.3)	14.9 (7.4–17.8)
Medication	74.5 (50–149)	64.8 (50–132)
Laboratory work	18.6 (11.1–18.6)	18.6 (11.1–18.6)
Imaging	7.4 (5.5–15)	7.4 (2.9–7.4)
Insulin therapy	4.4 (2.2–7.4)	4.4 (3.8–4.4)
Materials	7.4 (4.4–12)	4.4 (4.4–10.0)
Direct non-medical cost (US$)[d], median (IQR)		
Transportation	10.4 (7.4–15)	14.9 (7.4–29.8)
Indirect cost (US$), median (IQR)		
Lost work days by the patient	137.7 (86.6–163)	163.2 (134–163)
Lost work days by the caregiver	134 (74.5–290)	56.0 (35.7–86.7)
Hospital cost [e]	258.4 (192–324.8)	280.4 (192–347)
Total (US$), median (IQR)	**710 (539–1067)**	**716 (556–1078)**

IQR: interquartile range; [a] N = 1; [b]: Patient was positive for A/H1N1/pdm09 influenza; [c]:Room rent, file charges, nursing charges, attendant pass charges; [d]:The cost of lodging was not included because only one caregiver required lodging; [e]:WHO choice estimate + cost of reverse transcription-polymerase chain reaction for detection of influenza.

The study also showed that many of the patients visited a non-medical practitioner or had a previous hospital visit, indicating that their respiratory illness had not been adequately controlled.

Hospitalization due to SARI in diabetic patients amounted to a median total cost of US $710 (IQR, $539–$1067). This represents more than one-third of the median annual per capita income in India (US$ 1,861.5 per year for 2016 [17]), and suggests a substantial economic impact for these patients and their families. By comparison, for non-diabetic patients admitted for acute respiratory infections in the same Indian region, the median total cost for tertiary care hospitalization is considerably lower (US $145 [IQR: $84-279] in public settings, and US $414 [IQR: $254-771] in private settings) [22].

All patients in this study had type 2 diabetes, and most were diagnosed with community-acquired pneumonia. They were mostly old, overweight, and in poor medical condition with frequent hypertension or cardiovascular disease, all of which commonly associated with diabetes [4] and are risk factors for community-acquired pneumonia and SARI [4-9,11,23]. Just over 11% of the patients died during hospitalization. This fatality rate is higher than that found in other studies of hospitalized SARI patients without diabetes (~3−4%) [24-26], although care should be taken with such comparisons because non-diabetic SARI admissions may be younger than our study population, and may suffer from fewer co-morbidities.

Although most patients reported complying with their anti-diabetes medications, based on their blood glucose and hemoglobin A1C levels, many had poor glycemic control according to American Diabetes Association guidelines [27]. This is not surprising because relatively few patients regularly monitored their blood glucose or hemoglobin A1C.

Influenza was detected in 9% of SARI cases, which is consistent with the 4−12% rates reported by other studies conducted in India and elsewhere in Asia [28-30]. Since 2015, the Ministry of Family and Health Welfare in India has recommended influenza vaccination for individuals with diabetes [31]. In support of this and recommendations in other countries, a recent systematic review concluded that influenza vaccination reduces the risk of hospitalization and mortality in individuals with diabetes, particularly those aged ≥ 65 years [32]. In the current study, however, only 9% of participants were vaccinated for influenza. Similarly, in a previous study conducted between 2010 and 2012, we found that only about 9% of adults with diabetes had received influenza vaccines during the previous 1 to 5 years [33].

This study had some limitations. Importantly, the results were from a single public hospital in India, so care should be taken when generalizing them to private hospitals, where costs are expected to be higher [22], or to other regions of India or other countries. Also, our study lacked a comparator group of individuals admitted for SARI without diabetes. However, non-diabetic SARI admissions may have different characteristics (e.g., fewer co-morbidities, younger in age) that could lead to bias and limit comparisons. Another limitation is that the WHO-CHOICE estimates may underestimate indirect hospital costs [34]. A further limitation is that some of the results relied on patient or caregiver recollection, so they may not have accurately remembered or accounted for costs. To help avoid this, whenever possible, we verified each expense claim using prescriptions and hospital records. However, inaccurate recollection would have had little impact on total costs. Finally, the study did not allow incidence rates to be calculated or comparisons to be made, and although data on influenza infection were collected with the goal of comparing influenza-positive and -negative cases, too few patients were positive for influenza to make meaningful comparisons.

Conclusion

This study showed that medical needs and costs are substantial for diabetes patients in India hospitalized with SARI or influenza. These findings support recommendations that individuals in India with diabetes, especially those with additional risk factors, be better monitored for diabetes control and that they and healthcare workers be made aware of the risk of respiratory infections and the need for vaccinations to prevent them.

Acknowledgements

Medical writing was provided by Drs. Phillip Leventhal and Jonathan Pitt (4Clinics, France) and paid for by Sanofi Pasteur.

Authors' contributions

P.A.K., A.B., H.K., and M.S. conceived and designed the study. P.A.K. and H.M. acquired data. All authors helped analyze or interpret the data; draft or critically revise the manuscript; approved the final version; and agreed to be accountable for it.

References

1. Unnikrishnan R, Anjana RM, Mohan V (2016) Diabetes mellitus and its complications in India. Nat Rev Endocrinol 12: 357-370.

2. International Diabetes Federation (2017) IDF Diabetes Atlas, 8th edition. Available: www.diabetesatlas.org. Accessed 18 February 2019.
3. Shrivastava U, Misra A, Mohan V, Unnikrishnan R, Bachani D (2017) Obesity, diabetes and cardiovascular diseases in India: Public health challenges. Curr Diabetes Rev 13: 65-80.
4. Goeijenbier M, van Sloten TT, Slobbe L, Mathieu C, van Genderen P, Beyer WEP, Osterhaus A (2017) Benefits of flu vaccination for persons with diabetes mellitus: A review. Vaccine 35(38):5095-101.
5. Cook CB, Tsui C, Ziemer DC, Naylor DB, Miller WJ (2006) Common reasons for hospitalization among adult patients with diabetes. Endocr Pract 12: 363-370.
6. Klekotka RB, Mizgala E, Krol W (2015) The etiology of lower respiratory tract infections in people with diabetes. Pneumonol Alergol Pol 83: 401-408.
7. Yende S, van der Poll T, Lee M, Huang DT, Newman AB, Kong L, Kellum JA, Harris TB, Bauer D, Satterfield S, Angus DC (2010) The influence of pre-existing diabetes mellitus on the host immune response and outcome of pneumonia: analysis of two multicentre cohort studies. Thorax 65: 870-877.
8. Kornum JB, Thomsen RW, Riis A, Lervang HH, Schonheyder HC, Sorensen HT (2008) Diabetes, glycemic control, and risk of hospitalization with pneumonia: a population-based case-control study. Diabetes Care 31: 1541-1545.
9. Benfield T, Jensen JS, Nordestgaard BG (2007) Influence of diabetes and hyperglycaemia on infectious disease hospitalisation and outcome. Diabetologia 50: 549-554.
10. Vojtkova J, Ciljakova M, Michnova Z, Turcan T (2012) Chronic complications of diabetes mellitus related to the respiratory system. Pediatr Endocrinol Diabetes Metab 18: 112-115.
11. Falcone M, Tiseo G, Russo A, Giordo L, Manzini E, Bertazzoni G, Palange P, Taliani G, Cangemi R, Farcomeni A, Vullo V, Violi F, Venditti M (2016) Hospitalization for pneumonia is associated with decreased 1-year survival in patients with type 2 diabetes: Results from a prospective cohort study. Medicine 95: e2531.
12. Simonsen L, Clarke MJ, Schonberger LB, Arden NH, Cox NJ, Fukuda K (1998) Pandemic versus epidemic influenza mortality: a pattern of changing age distribution. J Infect Dis 178: 53-60.
13. Chadha MS, Potdar VA, Saha S, Koul PA, Broor S, Dar L, Chawla-Sarkar M, Biswas D, Gunasekaran P, Abraham AM, Shrikhande S, Jain A, Anukumar B, Lal RB, Mishra AC (2015) Dynamics of influenza seasonality at sub-regional levels in India and implications for vaccination timing. PLoS One 10: e0124122.
14. World Health Organization (2012) Vaccines against influenza WHO position paper - November 2012. Wkly Epidemiol Rec 87: 461-476.
15. Koul PA, Mir MA, Bali NK, Chawla-Sarkar M, Sarkar M, Kaushik S, Khan UH, Ahmad F, Garten R, Lal RB, Broor S (2011) Pandemic and seasonal influenza viruses among patients with acute respiratory illness in Kashmir (India). Influenza Other Respir Viruses 5: e521-527.
16. World Health Organization (2014) WHO surveillance case definitions for ILI and SARI. Available: http://www.who.int/influenza/surveillance_monitoring/ili_sari_surveillance_case_definition/en/. Accessed 05 March 2018.
17. Trading Economics (2018) India GDP per capita 1960-2017. Available: https://tradingeconomics.com/india/gdp-per-capita. Accessed 05 March 2018.
18. Molinari NA, Ortega-Sanchez IR, Messonnier ML, Thompson WW, Wortley PM, Weintraub E, Bridges CB (2007) The annual impact of seasonal influenza in the US: measuring disease burden and costs. Vaccine 25: 5086-5096.
19. World Health Organization (2018) CHOosing Interventions that are Cost Effective (WHO-CHOICE). Country-specific unit costs. Available: http://www.who.int/choice/country/country_specific/en/. Accessed: 05 March 2018.
20. Triami Media BV (2018) inflation.eu. Worldwide Inflation Data: Inflation India 2016. Available: http://www.inflation.eu/inflation-rates/india/historic-inflation/cpi-inflation-india-2016.aspx. Accessed: 05 March 2018.
21. XE Corporation (2018) X-RATES: Monthly average 2016. Available: https://www.x-rates.com/average/?from=USD&to=EUR&amount=1&year=2018. Accessed: 11 April 2018.
22. Peasah SK, Purakayastha DR, Koul PA, Dawood FS, Saha S, Amarchand R, Broor S, Rastogi V, Assad R, Kaul KA, Widdowson MA, Lal RB, Krishnan A (2015) The cost of acute respiratory infections in Northern India: a multi-site study. BMC Public Health 15: 330.
23. Almirall J, Bolibar I, Balanzo X, Gonzalez CA (1999) Risk factors for community-acquired pneumonia in adults: a population-based case-control study. Eur Respir J 13: 349-355.
24. Koul P, Potdar V, Mir H, Chadha M (2018) The 2015 Outbreak of severe influenza in Kashmir, North India: Emergence of a new clade of A/H1n1 influenza virus. PLoS Curr 10: pii: ecurrents.outbreaks.519e170f2740fabd4ccd1642ff533364.
25. Abdel-Hady DM, Al Balushi RM, Al Abri BA, Al Abri SS, Al Kindi HS, Al-Jardani AK, Al Yaqubi FM, Al Abaidani IS (2018) Estimating the burden of influenza-associated hospitalization and deaths in Oman (2012-2015). Influenza Other Respir Viruses 12: 146-152.
26. Cohen C, Moyes J, Tempia S, Groome M, Walaza S, Pretorius M, Dawood H, Chhagan M, Haffejee S, Variava E, Kahn K, von Gottberg A, Wolter N, Cohen AL, Malope-Kgokong B, Venter M, Madhi SA (2015) Mortality amongst patients with influenza-associated severe acute respiratory illness, South Africa, 2009-2013. PLoS One 10: e0118884.
27. American Diabetes Association (2018) Standards of medical care in diabetes-2018 abridged for primary care providers. Clin Diabetes 36: 14-37.
28. Cheng W, Yu Z, Liu S, Zhang X, Wang X, Cai J, Ling F, Chen E (2017) Comparison of influenza epidemiological and virological characteristics between outpatients and inpatients in Zhejiang Province, China, March 2011-June 2015. Int J Environ Res Public Health 14: E217.
29. Huai Y, Guan X, Liu S, Uyeki TM, Jiang H, Klena J, Huang J, Chen M, Peng Y, Yang H, Luo J, Zheng J, Peng Z, Huo X, Xiao L, Chen H, Zhang Y, Xing X, Feng L, Hu DJ, Yu H, Zhan F, Varma JK (2017) Clinical characteristics and factors associated with severe acute respiratory infection and influenza among children in Jingzhou, China. Influenza Other Respir Viruses 11: 148-156.
30. Chadha MS, Broor S, Gunasekaran P, Potdar VA, Krishnan A, Chawla-Sarkar M, Biswas D, Abraham AM, Jalgaonkar SV, Kaur H, Klimov A, Lal RB, Moen A, Kant L, Mishra AC (2012) Multisite virological influenza surveillance in India: 2004-2008. Influenza Other Respir Viruses 6: 196-203.
31. Ministry of Health and Family Welfare (2017) Seasonal influenza: Guidelines for vaccination with influenza vaccine.

Available: https://mohfw.gov.in/sites/default/files/30580390001493710612.pdf. Accessed 18 February 2019.
32. Dos Santos G, Tahrat H, Bekkat-Berkani R (2018) Immunogenicity, safety, and effectiveness of seasonal influenza vaccination in patients with diabetes mellitus: A systematic review. Hum Vaccin Immunother 14:1-14.
33. Koul PA, Bhat MA, Ali S, Rahim S, Ahmad SJ, Ahmad S, Yusuf R, Masoodi SR (2014) Influenza and pneumococcal vaccination in patients with diabetes. J Diabetol 5: 6.
34. Stenberg K, Lauer JA, Gkountouras G, Fitzpatrick C, Stanciole A (2018) Econometric estimation of WHO-CHOICE country-specific costs for inpatient and outpatient health service delivery. Cost Eff Resour Alloc 16:11.

Corresponding author
Parvaiz A. Koul
Department of Internal & Pulmonary Medicine
Sher-I-Kashmir Institute of Medical Sciences
Soura, Srinagar
190011 India
Tel: +91 194 2401353
Fax: +91 194 2403470
Email: parvaizk@outlook.com

Conflict of interests: No conflict of interests is declared.

Annex – Supplementary Items

Supplementary Table 1. SARI characteristics at presentation.

Measure or characteristic	All (N = 192)	Influenza-positive (N = 17)
Symptoms		
Fever	142 (74.0)	15 (88.2)
Rigors	81 (42.1)	4 (23.5)
Sputum production	92 (48.0)	7 (41.2)
Sore throat	63 (32.8)	8 (47.0)
Ear discharge	1 (0.2)	0 (0.0)
Body aches	161 (83.8)	15 (88.2)
Chest pain	80 (41.6)	5 (29.1)
Vomiting	49 (25.5)	4 (23.5)
Difficulty breathing	182 (94.7)	17 (100.0)
Chills	105 (54.6)	6 (35.3)
Hemoptysis	3 (1.6)	0 (0.0)
Nasal discharge	66 (34.3)	5 (29.4)
Headache	123 (98.4)	9 (52.9)
Malaise	170 (88.5)	15 (88.2)
Abdominal pain	24 (12.5)	2 (11.8)
Diarrhea	19 (9.8)	3 (17.6)
Seizures	3 (1.6)	0 (0.0)
Primary diagnosis		
Community-acquired pneumonia	165 (85.9)	7 (41.2)
Congestive cardiac failure	55 (28.9)	6 (35.3)
Acute exacerbation of chronic obstructive pulmonary disease	51 (26.6)	6 (35.3)
Encephalopathy	29 (15.1)	2 (11.8)
Sepsis	25 (13.0)	2 (11.8)
Stroke	9 (4.7)	0 (0.0)
Respiratory failure	9 (4.7)	1 (5.9)
Multi-organ dysfunction syndrome	9 (4.7)	0 (0.0)
Myocardial infarction	4 (2.1)	0 (0.0)
Lung cancer	3 (1.6)	0 (0.0)
Esophageal cancer	1 (0.5)	0 (0.0)
Asthma	1 (0.5)	0 (0.0)