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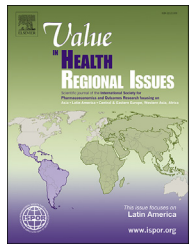

Economic Evaluation

Economic Cost of Severe Acute Respiratory Infection Associated to Influenza in Colombian Children: A Single Setting Analysis

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ABSTRACT

Background: Influenza is considered a leading public health problem because its large economic burden of disease worldwide, especially in low-and middle-income countries, such as Colombia. **Objective:** We aimed to estimate the economic costs of influenza-confirmed patients in a pediatric hospital in Cartagena, Colombia. **Methods:** We conducted a retrospective costing analysis. We estimated the direct (direct medical and out-of-pocket expenditures) and indirect costs for influenza-confirmed severe acute respiratory infection cases from a societal perspective. Total economic costs were calculated adding direct medical costs, out-of-pocket expenditures, and indirect costs owing to loss of productivity of caregivers. Mean, median, 95% confidence interval (95% CI) and interquartile range (IQR) of costs were measured. All costs are reported in USD ($1.00 = COP$2000.7) **Results:** Forty-four cases were included in the analysis: 30 had influenza B, 10 influenza A and B, and 4 influenza AH1N1. Thirty patients were hospitalized in the general ward, 14 went to the intensive care unit. The average duration of stay was ~9 days (95% CI, 6.3-11.5). The median direct medical cost for hospitalized case in general ward was $743.50 (IQR $590.20-$1404.60) and in intensive care unit $4669.80 (IQR $1614.60-$7801.50). The economic cost per hospitalized case was $1826.10 (IQR $1343.30-$2376.50); direct medical costs represented 93.8% of this cost. The median indirect cost was $82.10 (IQR $41.10-$133.40) and the median out-of-pocket expenditure per case was $45.70 (IQR $29.50-$64.90). **Conclusions:** Severe acute respiratory infection is an important source of economic burden for the health system, families, and society in Colombia. Seasonal influenza vaccination should be strengthened to prevent more cases and save economic resources.

Keywords: acute respiratory infection, cost analysis, direct cost, indirect cost, out-of-pocket.

Introduction

Influenza is considered a leading public health problem because of its large impact on morbidity and mortality around the world.[1-4] It is an acute respiratory vaccine-preventable disease that affects about 20% to 30% of children each year worldwide.[5] About 3 to 5 million severe cases and 250 000 to 500 000 deaths occur every year worldwide, with the highest impact in low- and middle-income countries.[6,7]

Influenza affects all ages and sex groups with the highest incidence rates among 5- to 9-year-old children, but the severest cases are observed among those <2 and >65 years old.[7-9] Influenza virus circulates mainly during the winter season in temperate climates, but they are less predictable in tropical regions and subtropical climates.[10-16] Developing countries contribute with almost 99% of all influenza related deaths among children <5 years of age.[11]

The epidemiologic burden of influenza in Colombia have been partially assessed. In 2007, a Colombian economic study estimated

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in 230 and 2500 the annual number of deaths among children <2 years and adults >65 years, respectively.[17] On average, >30 000 cases in both age groups would require in-hospital care every year. Another analysis found that general mortality increase between 2% and 11% when influenza virus circulated in Colombia.[18]

In 2017, the Colombian National Institute of Health, reported 6 955 075 outpatient and emergency consultations by acute respiratory infections (ARI), 264 771 hospitalizations in general ward for severe acute respiratory infection (SARI), and 20 268 hospitalizations in intensive care unit (ICU). For 2015, mortality from ARI in Colombian children <5 years old was 12.1 per 100 000.[19] At least 5% of severe ARI cases and deaths could be linked to influenza virus.[20]

Influenza significantly impairs people's quality of life and causes high economic burden to health systems, families, and society, but there is little evidence of that in Latin America.[21-23] In Colombia, no study has estimated the ARI costs using laboratory-confirmed influenza cases. This study aimed to help fill this gap by estimating the economic costs in a sample of confirmed influenza pediatric patients.

Methods

Study Design

A retrospective costing analysis was conducted in a pediatric hospital that participated in a national network of influenza virus surveillance. Direct and indirect costs were estimated from a societal perspective on a sample of laboratory confirmed influenza SARI cases looking for healthcare at a university hospital (Fundación Hospital Infantil Napoleón Franco Pareja) in the city of Cartagena.

Population and Data

Pediatric patients (<18 years old) fulfilling the World Health Organization definition for SARI,[24] and with a positive confirmatory test for influenza (polymerase chain reaction or viral culture), were retrospectively selected between January and August 2014. At that time, SARI hospitalization cases were peaking in the study site and in the country from 7th to 18th epidemiologic week.[25] Patients with diagnosis of nosocomial influenza virus infection were excluded as were those who declined to provide information on indirect and out-of-pocket costs.

Estimation of Direct Costs

A standardized questionnaire was used to capture information from the clinical records. It extracted data on health resource use; number of medical consultations; type and quantity of drugs, supplies, laboratory and image tests, bed costs (length of stay [LOS]), and procedures performed in each selected patient. Direct medical costs were analyzed from the third-party payer perspective and were estimated using electronic billing records (bottom-up costing).[26-28]

Direct medical costs per patient were estimated as follows:

$$\forall i \in K : \textit{Total item cost per patient} = h_i * p_i$$

$$K = \{drugs, lab.\Lambda images, hospital\ stay, consults, procedures\}$$

K: health services set; h: use frequencies of health services, P: price per item

$$\textit{Direct costs per patients} = \sum_{j=i}^{k} Costs_j$$

Estimation of Out-of-Pocket and Indirect Costs

Out-of-pocket expenditures and indirect costs related to loss of productivity were estimated in 17 patients (38.6%, 17 out of 44) through a structured and standardized questionnaire applied by telephone during the first 7 days after hospital discharge. Caregivers of pediatric patients were asked about personal or familiar expenditures on drugs, transportation, food, or other items before, during, and after the hospitalization. For car owners the cost of transportation was estimated multiplying the vehicles' average fuel consumption per kilometer multiplied by the distance (kms) from patient's residence to the hospital multiplied by the fuel gallon cost by August 2014.

To estimate indirect costs, caregivers were asked to calculate the reduced work time due to hospitalization. Loss of productivity was calculated as a measure of income forgone using the number of days of work lost and the salary of the caregiver. Value loss owing to absences from work was made equal to: number of days absent from work × average of daily wage. Indirect costs in students, housewives, and caregivers with no job or formal employment were estimated using the 2014 Colombian legal daily minimum wage.[29]

Total economic costs were calculated by the addition of direct costs (direct medical costs and out-of-pocket health expenditures) and indirect costs owing to loss of productivity. All costing of resource utilization was reported in USD ($1.00 = COP$2000.70 according to 2014 exchange rate).[30]

Costs were described using means, medians, 95% confidence intervals (95% CI) and inter quartile ranges (IQR). Standard nonparametric analysis of variance (Mann-Whitney-Wilcoxon)[31] was used to compare cost differences between complicated and noncomplicated patients. Cost differences by type of virus were assessed using Kruskal-Wallis test. All data were organized and analyzed using Microsoft Excel (Microsoft Corporation, Redmond, WA) and STATA 13 (Stata Corporation, College Station, TX).

This study carried no risks to patients (Resolution 8430 of 1993 of the Ministry of Health).[32] Nonetheless, patients' caregivers were asked to grant permission to access clinical records, answer our questionnaires, and sign an informed consent. All identification data was removed from the dataset to protect the anonymity and private rights of participants.

Results

Forty-four cases of influenza confirmed SARI cases with an average age of 8 months were included in the study. Most (75.6%) were male, 34.1% had a previous history of an underlying disease, 30 had influenza B infection, 10 influenza A and B, and 4 influenza AH1N1. Thirty patients were hospitalized in general ward and 14 in the ICU. The average LOS was 8.9 days (95% CI, 6.3-11.5). Twenty-six patients developed clinical complications, including respiratory failure ($n = 10$). No deaths were reported in the sample (Table 1).

Overall, the median total direct medical cost for hospitalization related to influenza was $1361 (IQR $662.5-$2595; Table 2). Total median direct medical cost was higher for children hospitalized in ICU than for those in general ward ($4669.80 [IQR $1614.60-$7801.50] vs $743.50 [IQR $590.20-$1404.60]). The largest share of direct medical cost was associated to bed cost (36.4%), followed by drugs (32.9%) and diagnostic tests (laboratory and images) with 11.2% (Fig. 1).

Costs by type of virus are shown in Fig. 2. The median total direct medical cost to treat a pediatric patient with confirmed influenza AHIN1, is twice the cost incurred by a patient with influenza B ($P = .444$).

Out-of-pocket and indirect costs are also described in Table 2. Incomplete secondary education was the most frequent level of schooling (35.3%). No caregiver reported out-of-pocket expenditures on procedures, consultation, laboratory and images tests or

Table 1 – General characteristics of study group ($n = 44$).

Variable	Value
Males, *n* (%)	33 (75.6%)
Patients attended in clinical ward (%)	30 (68.2%)
Patients attended in ICU (%)	14 (31.8%)
Mean of age in months (±SD)	8.34 (±10.8)
Duration of stay (days)	
Mean length of stay (±SD)	8.9 (±8.7)
Mean length of hospital stay (±SD)	5.1 (±3.5)
Mean length of ICU stay (±SD)	12.1 (±10.5)
Laboratory results (% of patients)	
Infuenza AH1N1	9.1
Infuenza A and B	22.7
Infuenza B	68.2
Initial symptoms (% of patients)	
Cough	81.8
Breathing difficulty	63.6
Fever	47.7
Intercostal retractions	36.4
Complications (% of patients)	
With complications	59.1
Respiratory failure	22.7
Persistence of the initial symptoms	27.3
Deaths	0
History of any disease (% of patients)	
Bronchiolitis	11.4
Community acquired pneumonia	9.1
Previous ICU event	4.5
Preterm birth	4.5
Other	4.6

ICU indicates intensive care unit; SD, standard deviation.

other expenses associated to hospitalization. Out-of-pocket expenditures were incurred on food, transportation, and drugs. The sources to finance out-of-pocket expenditures included personal or familiar savings (41.2%), money save from cutting other needs (23.5%), borrowing money (17.7%), and selling consumables or assets (5.9%).

Indirect costs were reported by all 17 interviewed caregivers. Most were mothers (70.6%) and housewives (83.3%), and paid work was reported by 17%. All fathers (23.5%) were engaged in paid work. The average number of days caring for hospitalized children was 10.2 days (95% CI, 5.4-14.9) in mothers and 1.5 days (95% CI, 0.6-2.4) in fathers. The average indirect cost was $118, and the median total indirect cost was $82.10 (IQR $41.10-$133.40; Table 2).

Clinical complications increased costs by 6.7 when compared with noncomplicated patients ($6137.20 for complicated vs $1183.90 for noncomplicated; $P < .01$). The difference was largely explained by the LOS (12.1 days for complicated vs 5.1 for noncomplicated; $P < .001$).

Discussion

This is the first economic cost estimation of pediatric SARI among influenza-confirmed patients in Colombia. Costs of ARI had been calculated previously in Colombia but none of the study used confirmed cases of influenza.[33] We found that the median total economic cost of a pediatric SARI hospitalized case was $1826.10 (IQR $1343.30-$2376.50), suggesting that SARI is an important source of economic burden for the health system, families, and society. Our estimations showed that the direct medical costs represented 93.8% of the economic cost of a SARI hospitalized case. In addition, the median direct medical cost of pediatric patients hospitalized in ICU was 6.3 times greater than the estimated in those hospitalized in general ward. These costs are paid by the Colombian health system.

If we extrapolate these findings to Colombia, using the number of SARI hospitalization cases reported by the National Institute of Health,[19] and assuming that 5% to 10% of them are due to influenza,[20] then influenza SARI cases may cost between $4 732 375 ($1 636 236-$7 906 040) and $9 464 751 ($3 272 471-$15 812 080) per year, only for ICU hospitalizations. Hospitalizations in general ward may cost between $24 174 916 ($ 17 783 344-$31 454 795) and $48 349 832 ($35 566 688-$62 909 590) per year. This extrapolation must be interpreted with caution and it was done only for illustrative purposes. According to the structure of the Colombian health system, it was very likely that the estimated costs in the setting we chose were potentially representative to other similar cities in the country. This is explained by the fact that the Colombian health system structure does not differentiate between private and public hospitals.[34] In Colombia, there is nearly universal coverage in the health system.[34,35] Because of these reasons, our

Table 2 – Economic costs of hospitalized patients.

	Cost in general ward ($n = 30$)		Cost in ICU ($n = 14$)		Total cost ($n = 44$)	
	Mean	Median (IQR)	Mean	Median (IQR)	Mean	Median (IQR)
Direct costs	—	—	—	—	3688.30	1647.50 (1220.10-2304.70)
Out-of-pocket	—	—	—	—	50	45.70 (29.50-64.90)
Direct medical cost	982	743.50 (590.20-1404.60)	7441.50	4669.80 (1614.60-7801.50)	3570.40	1361.70 (662.50-2595)
Consultation	140.8	122.40 (71.80-178.60)	252.10	80.00 (51.30-143.40)	201.80	126.70 (89.50-193.50)
Bed cost	327.5	283.90 (180.70-448.00)	3115.10	2086.20 (863.30-4707.60)	1299.60	421.60 (220.00-877.50)
Laboratory and images	155.9	142.50 (96.00-185.50)	812.90	547.30 (218.90-1058.70)	399.20	175.90 (105.70-407.60)
Materials and medical supplies	45.3	36.60 (19.90-54.80)	610.50	463.80 (86.50-908.30)	283.10	54.30 (31.40-200.80)
Drugs	182.9	70.60 (29.80-160.00)	2610.60	931.00 (312.10-3329.50)	1172.90	136.40 (40.20-1020.90)
Procedures	140.5	121.20 (59.40-179.80)	420.90	231.10 (71.40-955.90)	213.70	149.40 (68.20-263.60)
Indirect costs	—	—	—	—	118	82.10 (41.10-133.40)
Economic cost	—	—	—	—	3806.30	1826.10 (1343.30-2376.50)

ICU indicates intensive care unit; IQR, interquartile range.
Costs given in USD 2014.

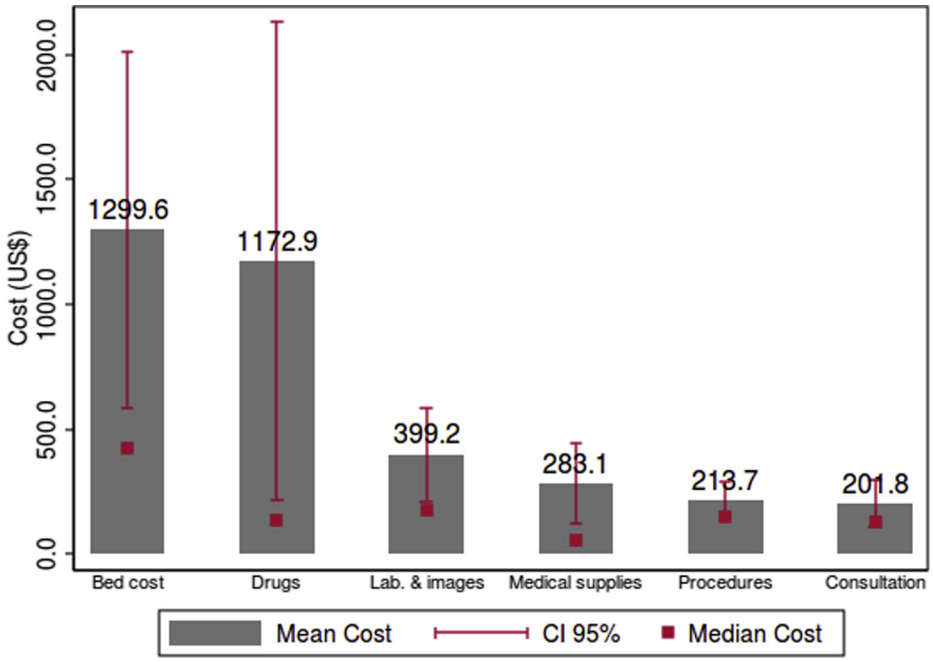

Fig. 1 – Direct medical cost distribution per items.

results could be extrapolated to the Colombian setting. However, it is more difficult to assume that similarity in rural areas.

On the other hand, indirect and out-of-pocket expenditures (the remaining 6.2% of the total economic cost) represented 41.5% of the 2014 Colombian legal minimum wage ($307.90). This is a huge economic burden to be carried by families, especially among poor households.

Compared to other countries, our hospital LOS (mean 8.9 SE ± 8.7) was slightly greater to that found in other countries like China.[36,37]

The overall direct medical costs estimated in this study ($1361.70) were 17.2% of the Colombian annual gross domestic product (GDP) per capita ($7939) in 2014.[38] A similar estimation was done in Nicaragua in 2011, where the direct medical cost was ($314.90) 18.7% of the Nicaraguan gross domestic product per capita.[22,39] Comparison with studies from other settings shows

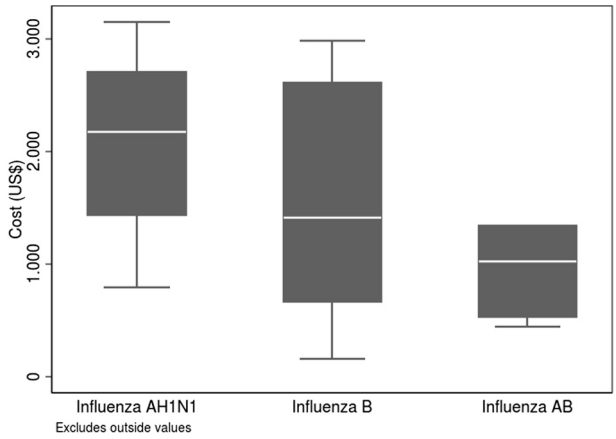

Fig. 2 – Direct medical costs according to influenza viruses. Median and interquartile range.

that an hospitalized SARI case estimated in this study in international dollars for 2014 (I$2,282) was greater than the estimated in Honduras (I$1,494), Guatemala (I$1,175) and Nicaragua (I$830), and lower than the reported in Brazil (I$2,432).[23,40] Hospitalization owing to influenza-related illness incurred a high cost to the health systems in Latin-American countries.

Our study is a step forward in the cost estimation of SARI in a tropical country. An important strength of this study was related to its designs. The bottom-up costing technique is the gold standard method to estimate the cost of hospital services.[28] Cost description analysis play an important role in the economic evaluation in health and in decision making regarding the allocation of scarce resources in the health sector.[33,41] Collecting data de novo is often expensive and highly laborious, especially when a bottom-up approach is conducted in an upper middle-income setting.[42] Our cost estimations are a useful and essential input to carry out future complete health economic evaluations.

This study has several limitations. First, it was impossible to interview all parents or caregivers of SARI hospitalized cases, because most refused to participate in the study. Reasons for refusal to participate in our study were not collected. However, we gathered out-of-pocket and indirect costs of 38.6% of all hospitalized patients. Our results should be carefully interpreted considering the included population. Our sample was gathered in people with low socio-economic status. The percentage of poor population in Colombia ranges from 24.6 for urban to 41.4% for rural population, according to most surveys,[43] and the economic costs are probably underestimated. Despite limitations, it clearly shows a disaggregated costing of a high prevalent disease in Colombia.

This work focused on the estimation of economic cost of influenza-related hospitalizations among pediatric SARI cases. Usually, the estimations are only about direct medical costs, or out-of-pocket costs or indirect costs, separately. The main strength of this study was the estimation of the cost from a societal perspective, including all the cost components. Future work should include other hospitals, in order to conduct a multicenter

study for cost comparisons between territories and to consolidate a national SARI hospitalized cost. Also, it could be interesting to approximate to the estimations of economic costs in ambulatory laboratory confirmed cases.

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Supplemental Material

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.vhri.2019.07.010.

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