

## Annual Antibiotic Related Economic Burden of Healthcare Associated Infections; a Cross-Sectional Population Based Study

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### Abstract

So far, too little attention has been paid to total burden of healthcare associated infections (HAIs) in Iran. In the present study, we aimed to assess the rate of HAIs, as well as economic burden of hospitalization and antibiotic related cost associated with HAIs in ICU at training Taleghani hospital in Iran and to compare our results with national nosocomial infections surveillance (NNIS) system. This research to date for the first time has tended to focus on the economic burden of HAIs rather than epidemiology of HAIs evaluation. The total of 474 patients was followed up in this study. Overall, the rate of HAIs was 19.2 % in which ventilator associated pneumonia (VAP) was dominant HAIs and followed by urinary tract infection (UTI). Importantly, mortality rate increased significantly in infected patients. The highest total hospitalization economic burden and antibiotic related cost were observed for patients having blood stream infection (BSI). The results demonstrated significant differences between antibiotic related cost in patients and uninfected patients. Antibiotic related absolute extra cost for HAIs was 2.09 PPP\$ per day. Estimation of direct annually HAIs associated economic burden of antibiotic and Total hospitalization was 433,382.4 PPP\$ and 705,024 PPP\$ respectively in Iran at intensive care unit (ICU). The most obvious findings were a strong relationship between relatively heavy antibiotic related financial burden, higher mortality rate, longer hospitalization time, and HAIs emergence on the Iranian national health system. It also reflects, more fundamentally a shift toward the need for comprehensive thinking about HAIs at ICU ward from Iran's hospitals. On the question of the research found that: With the implementation of policies and strategies to reduce hospital infections, which will benefit; Patient, Society, and/or national health system?!

**Keywords:** Antibiotic related economic burden; Healthcare associated infection; Iranian national health system.

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## Introduction

Imposed economic burden of common disease was completely definite, but with wide range which differed based on the diseases and therapeutic methods (1, 2). Despite the hygiene improvement in the medical centers in the recent century, healthcare associated infections (HAIs) are considered as growing public health worldwide (3). The national nosocomial infection surveillance program was established in Iran since 2007 based on national nosocomial infection surveillance (NNIS) system definitions which classified for four major groups including pulmonary, urinary tract, blood stream, and surgical site infections (4). Annually six million patients admitted to hospitals in Iran. Of these patients, about six hundred thousand patients are infected with HAIs. The HAIs was announced 10 to 15 % by health system in Iran in recent years (5).

HAIs had the highest occurrence at ICU ward which was related to the most use of invasive therapeutic devices(6). HAIs may be assumed as leading causes of death especially at intensive care unit (ICU) ward in patients with terminal medical conditions, such as advanced malignancy or end stage kidney or liver disease (7, 8). HAIs create the socioeconomically impact on patients and nation's economy. HAIs caused the increased hospitalization stay, staff time, cost of laboratory tests on the pathogens and antimicrobial treatment (9, 10).

The antimicrobial treatment related financial cost is a main part of the health economic burden, but data about this subject are rarely found in Iran. Understanding differences in economic burden of HAIs and antimicrobial treatment compared to other patients in health system informs patients, physician and government in order to promote quality of patients' health besides reducing morbidity, mortality, and prevention of wasting time and money. This study focused on economic burden estimation and daily cost evaluation created by HAIs and limited for hospitalized patients at ICU of university hospital; because these patients are potentially susceptible to infections (11). This study highlighted the necessity for efficient policy making which aimed to increase

the survival rate of critical ICU's patients at university hospitals. Overall, the economic burden of 245 patients was estimated in this paper. One of the most significant current assay was attempting to summarize and highlight the major findings of the epidemiology of HAIs and evaluate economic burden of antimicrobial treatment and HAIs for ICU's patients.

## Methods

### *Study population*

This study conducted the cross-sectional prospective surveillance study for adult patients (15< years of age) admitted at medical-surgical ICU (MS-ICU) ward of Taleghani hospital between 2012 - 2013. Taleghani hospital is a public hospital with 620 beds located in Tehran, Iran. From 474 patients hospitalized at ICU, 245 patients were included in this study. ICU's Patients who previously acquired infections with non origin of hospital and non origin of ICU ward, neonatal patients (<15years), patients hospitalized for less than 2 days were excluded from this study. Also cases for superinfection were excluded. Inclusion criteria were age  $\geq 15$  and ICU hospitalization for more than 2 days. Common surveillance of HAIs was performed by infection control nurses and infectious diseases specialist physicians. HAIs were defined using the NNIS criteria (4). 198 studied hospitalized patients in ICU who do not infect with any HAIs were assumed as control group and also, patients with HAIs with origin of ICU ward were assumed as case group.

### *Measurement of HAIs associated economic burden*

Prescription of Antimicrobial agents was recommended by an infectious disease consultant. All of charts, prescriptions and therapeutic indications were registered in medical record of patients. Therapeutic methods and agents cost were calculated and examined in US dollars based on 2012 prices of antimicrobial agents and were mentioned in text and tables. According to the reports released by Iranian Central Bank and World Bank Organization from 2012 to 2013; for example, one PPP\$ (purchasing power parity \$) was estimated around 24, 850 Rials in 2013. Therefore, 24,8850 Rials were used as the

**Table 1.** Comparison of frequency of criteria in infected and uninfected patients.

Characteristics	Patients with HAIs	Patients without HAIs	P-value
Male-female (Percent)	56.04-39.6	55.8-44.2	0.62
Age (Mean $\pm$ SD), year	63.60 $\pm$ 3.24	52.74 $\pm$ 1.32	0.003
Age Range	17-89	15-89	-
Mortality (Percent)	47.90	27.40	0.009
Unit of Blood (Mean $\pm$ SD), unit	10.83 $\pm$ 2.25	5.36 $\pm$ 0.64	0.023
Hospitalization (Mean $\pm$ SD), day	13.50 $\pm$ 2.85	5.78 $\pm$ 0.30	0.01
Glossary Common scale (GCS) (Mean $\pm$ SD), scale	10.88 $\pm$ 0.37	12.36 $\pm$ 0.17	0.63
Total cost of antibiotic/Day (Mean $\pm$ SD), PPP\$	3.32 $\pm$ 0.43	1.23 $\pm$ 0.12	0.000
Total cost of HAIs/Day (Mean $\pm$ SD), PPP\$	86.08 $\pm$ 2.76	82.68 $\pm$ 1.08	0.19

reference value to convert costs from Iranian Rials to PPP\$ (12, 13).

#### Data analysis

The patients with HAIs were assumed as the case group and patients without any HAIs as the control group. The total economic burden was evaluated for the case. The descriptive statistics and frequency distribution such as mean, standard deviation and percentage were used.

The Differences were analyzed by T tests and one way ANOVA for continuous data. Odds ratios (OR) and the confidence intervals (95 % CI) of the ORs were calculated by logistic regression analysis. All of statistical analysis were two sided, and  $p < 0.05$  was considered significant. Also, SPSS, version 16 (SPSS Inc., Chicago. IL. USA) was used for data analysis.

### Results and Discussion

Of 474 patients, 245 patients entered in this study. 19.2 % of included patients were infected with HAIs. The patients contained 139 male and 106 females. The mean age of infected patients was  $63.6 \pm 3.24$  and  $52.74 \pm 1.32$  at uninfected patients ( $P = 0.047$ , Table 1). The results showed that mortality for infected patients was more than un-infected (ADJ. OR: 2.5; 95 %CI: 1.3-4.90,  $P$ -value=0.005). In addition, the unit of blood for infected patients was  $10.38 \pm 2.5$  and for un-infected was  $5.36 \pm 0.64$  ( $P = 0.023$ ). Also,

there is an association between Hospitalization days and risk of infection (ADJ. OR: 1.14; 95 %CI: 1.07-1.21,  $P$ -value<0.001).

The excess day of hospitalization for infected patients was 7.7 days. The most common type of HAIs was ventilator associated with pneumonia (VAP) (9.39 %) followed by the urinary tract infection (UTI) (5.71 %) and blood stream infection (BSI) (3.26 %). However, the cost of antibiotic per day increased in the infected patients but the total economic burden of hospitalization for two groups was approximately equal. Albeit, the highest antibiotic associated economic burden was observed for patients with BSI; the highest total economic burden of hospitalization was allocated for patients BSI which was followed by UTI and VAP (Table 2).

Although, there are abundant epidemiological researches about HAIs around the world (8, 14-18), so far, there have been little researches about HAIs in Iran especially for ICU hospitalized patients, related economic burden and antibiotic associated cost. In this study, we aimed at obtaining an estimate of the cost of antibiotic and HAIs for the first time in Iran. 19.2 % HAIs rate that we found was somewhat higher than rate report by Iranian national health system (5).

It can potentially cause higher rate of HAIs in ICU ward rather than other wards of hospitals consistent with other studies (19). The predominant site of infection differs by the studied population, ward of hospitalization,

**Table 2.** The incidence of HAIs by site of infection and its impact on the length and cost of hospital stay/Day.

Site of HAI	Incidence		Antibiotic Related Cost (PPP\$)			Length of Stay (days)		
	N	Incidence Rate% (95% CI)	Mean costs	Ratio of costs (model estimate: 95% CI)	Additional cost	Means LoS	Ratio of days (model estimate: 95% CI)	Additional days
No HAI	198	80.8	1.23±0.12	(0.98-1.4)	Reference	5.77±0.29	(5.18-6.36)	Reference
BSI	8	3.3	5.63±1.64	(1.75-9.52)	4.40	9.25±1.55	(5.57-12.93)	3.48
UTI	14	5.7	2.61±0.33	(1.89-3.34)	1.38	9.36±3.10	(2.26-16.05)	3.59
SSI	2	0.8	2.26±0.71	(-6.81-11.34)	1.03	13±5.00	(-50.53-76.5)	7.23
VAP	23	9.4	3.04±0.58	(1.82-4.26)	1.81	17.29±5.52	(6.51-29.4)	11.52

type of performed surveillance, sampling and season in which the search is concluded (1, 20). This study was done in winter and spring. It may be the reason of high prevalence of VAP. However, the longest hospitalization, mechanical ventilation and the oldest age were observed for VAP (Table 3). Instrumentation of the catheter is an established external risk factor of infection. In addition, the presence of invasive devices, type of prescribed antibiotics, length of hospitalization and severity of underlying disease can be assumed as the main risk factors of HAIs at ICU's patients. Similar to Rosenthal meta analysis study, *Klebsiella pneumoniae*, *Escherichia coli* and *Staphylococcus* were mostly found in the common site of infections in this study (19).

We found rare economic evidences on HAIs in Iran. The economic burden of HAIs seems to be moderately high in Iran and it imposes a relatively heavy financial burden on the Iranian national health system because of its high prevalence at ICU and its impact on survival rate, waste of time, and money.

However, this high economic burden may have been due to HAIs, they may have also been related to our research strategy focused

on HAIs. Therefore, caution is needed in interpreting these results. The financial burden of HAIs related to total antibiotic was doubled for the other patients (ADJ. OR: 1.5; 95%CI: 1.25-1.80, P-value<0.001). HAIs imposed the excess economic burden related to antibiotic which is on average 2.09 PPP\$ per day for each infected patients in this study. Although, there isn't significant relation between total economic burdens of hospitalization/day between infected and un-infected patients; maybe, the time of study and number of samples were the reasons of that. If the results of the study are emerged with other hospitals, the different results will be likely obtained. The financial burden of HAIs related to excess total hospitalization per day increased to 3.4 PPP\$ than the un-infected patients. This study showed that BSI and VAP caused the highest antibiotic economic burden. It may be due to prescription of infrequent and normally more expensive antibiotics which imposed high financial burden. Although it was observed that BSI and UTI had the most total economic burden of hospitalization. The highest rate of morbidity and mortality was demonstrated in the BSI patients. Table 4 illustrated the related financial burden and associated criteria. In

**Table 3.** The Mean age, mean transfused blood and incidence of mortality by site of infection.

Hospital Acquired Infection	Mean Age ± SD	Mean Transfused Blood ± SD	Mortality Rate %
BSI	55.50±8.24	12.25±5.51	62.5
UTI	57.14 ±6.44	8.43±2.96	50
SSI	53.00 ±33.00	7.00±7.00	50
VAP	70.30 ±3.82	12.35±3.92	43.47
No HAIs	52.91±1.32	5.36±0.63	55.1

**Table 4.** The criteria for HAIs financial burden.

<b>Economic Burden of HAIs associated antibiotics/per person/day</b>	<b>2.09 PPP\$ (51,936.5 Rails)</b>
Mean of hospitalization at ICU ward	7.29 days
ICU beds in Iran	3000 beds
HAIs rate at ICU	19.20 percent
Infected patients at ICU/week in Iran	576 patients
Infected patients at ICU/year in Iran	29622 patients
Economic burden of antibiotics/week in Iran	8,426.88 PPP\$ (209,407,968 Rails)
Annually economic burden of HAIs associated antibiotics in Iran (range)	433,382.40 - 457,083.00 PPP\$ (10,769,552,640 - 11,358,512,550 Rails)
Annually economic burden of HAIs associated hospitalization in Iran (range)	705,024 - 734,210.89 PPP\$ (17,519,846,400-18,245,140,616.50 Rails)

accordance with Iranian national health system report, in which 3000 beds are belonging to ICU (21) and 19.2 % HAI rate and 7.29 days as the mean of hospitalization days in this study, it was estimated that 576 patients involved in HAIs at ICU ward in Iran per week. It was approximated weekly and annually that HAIs associated economic burden of antibiotic was 8,426.882 PPP\$ and 433,382.40 PPP\$ respectively in Iran.

### Conclusion

In this study, we examined the HAIs antibiotic financial and economic burden. HAIs is more prevalent in ICU's patients and remains as an important patient safety problem and the financial and social costs are staggering. The economic burden of HAIs and antibiotic seems to be moderately high in Iran and it imposes a relatively heavy economic burden on the Iranian national health system because of its high prevalence at ICU and its impact on survival rate, hospitalization length, implementation of more expensive therapies, more prescription and infrequent antibiotics with heavier costs. However, possible mistreatment of patients certainly effects on the financial burden, but one of the limitations of the study is the disability to examine possible mistreatment. The NNIS has established in recent decade in Iran which has weak point as a neoteric program (5). This research highlights the importance of HAIs in our country and establishes scientific policies to prevent the loss of patients, waste of time, and money.

In conclusion, length of stay and antibiotic prescription were the main cost of ICU's patients that could be minimized by enhancement of the quality of insurance industry in our country and deletion of possible mistreatments.

### Acknowledgments

The authors thank Ms. Rahmati, an infection control nurse, Dr. Homiera Yazdinejad and Dr. Alizadeh as the head of infection control team. This study was supported by Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center of Shahid Beheshti University of Medical Sciences.

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