

Original Article

**Incidence Rate of Device-Associated, Hospital Acquired Infections in ICUs:
A Systematic Review Developed Versus Developing Economies**

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Abstract

Background: Device-associated hospital-acquired infections (DA-HAIs) are a major threat to patient safety; as well as a contributing factor for increased morbidity, mortality, increased cost and length of ICU stay. Rates of occurrence of DA-HAIs can be associated with the economic status of the countries where they occur.

Aims: To assess all available DA-HAI incidence rates from studies published between 2007 and 2017, and compare them according to the economic status of the country of origin.

Methodology: Systematic review of the published literature between 2007 and 2017.

Results: 40 articles were included in this study. Central line-associated blood stream infection (CLABSI), ventilator-associated pneumonia (VAP) and catheter-associated urinary tract infection (CAUTI) incidence rates from various countries, together with data on the countries economic status (developed vs developing), were included and correlated accordingly. The highest reported CLABSI, VAP and CAUTI rate was 72.56, 73.4 and 34.2 respectively per 1000 device days, and these all originated from developing economies. The highest incidence rates for VAP and CLABSI in developed economies are demonstrably lower than those in developing economies, demonstrating a statistical significant correlation. Lower economic statuses tend to predominate higher rates of Ventilator-Associated Pneumonia and Central Line-associated Blood-stream Infections in a statistically significant correlation, whilst for CAUTI there was no statistical difference.

Conclusions: DA-HAI are affected directly in a positive or negative way according to the economic status of the originating country..

Keywords: Device Associated Infections, Central Line Associated Blood Stream Infection, Ventilator Associated Pneumonia, Catheter Associated Urinary Tract Infection, ICU.

Introduction

Infections acquired in the intensive care unit (ICU) are a major healthcare related problem as they contribute to length of stay (LOS) prolongation, elevated costs of care as well as increased morbidity and mortality (Apostolopoulou *et al.*, 2013; Tigen *et al.*, 2014). Furthermore, health-care associated infections (HAIs), with specific reference to invasive devices utilization in healthcare settings, when considered in the far more prevalent context of ICU patients are usually referenced as device-associated HAIs (DA-HAIs) and are a complicating factor with regard to positive patient's outcomes. Most of the infection surveillance reports comparing the outcomes of DA-HAIs with those of other countries do not consider that the economic status of the country in question can directly affect, positively or negatively. According to the WHO (World Health Organization, 2015), low economic country status (developing) may be an additional factor that influences the incidence of DA-HAIs with greater prevalence than is reported in developed areas.

Aim

The aim of the study was to investigate the DA-HAI rates published in public literature between the years 2007 and 2017 and compare rates between developed and developing countries.

Materials & Methods

This systematic review was guided by the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement. PRISMA is a 27-item checklist that is used to improve the reporting of systematic reviews and meta-analyses and has been endorsed by major biomedical journals for the publication of systematic reviews (Liberati *et al.*, 2009).

A comprehensive search of the available literature was conducted by the authors, using Medline, PubMed and Cumulative Index to Nursing and Allied Health Literature [CINAHL], for articles dated from 2007 until late 2017, using

these search terms: “ventilator associated pneumonia”, “VAP”, “central line associated blood stream infection”, “CLABSI”, “catheter associated urinary tract infection”, “CAUTI”, “device associated infection” and various combinations of these terms plus “Intensive Care Unit”.

Inclusion criteria

The inclusion criteria used during the search were:

Publication dates ranging from 01/01/2007 to 31/12/2017,

Data must have been obtained from adult ICU patients,

Publications written and published in the English language,

DA-HAIs rates to be reported as incidence per 1000 device days (DD).

Publications which studied only one of the DA-HAIs rates were not excluded if they met the remainder of the inclusion criteria. The primary outcome measures for this review were:

Infection rates per device per 1000 device days,

The number of patients,

The country and place of study,

Purpose and methodology of study.

Study Selection

A Medline search yielded 377 articles, PubMed yielded 1074 articles, and CINAHL yielded 289 articles. After duplicated results and articles with access to the abstract or the title only were removed, a total of 562 articles were left for screening. Of these, 367 were related to pediatric and neonatal ICUs, 106 were not related to ICU patients (hospital wards or home ventilated patients), 22 were not research studies, 17 had very small sample sizes and/or durations and 10 studies were dismissed for other reasons not meeting the study design, leaving a total of 40 articles. The flow chart below summarizes the article selection (Figure 1).

Table 1: Developing countries and DA-HAIs rates

Name, Country, Year	CLABSI	VAP	CAUTI
Talaat, Egypt, 2016 (after intervention)	2.6	4.3	1.9
Empaire, Venezuela, 2017	5.1	7.2	3.9
Mehta, India(INICC), 2016	5.1	9.4	2.1
Kanj, Lebanon(INICC), 2012	5.2	8.1	4.1
Mehta, India(INICC), 2007	7.92	10.46	1.41
Jahani-Sherafat, Iran, 2015	5.84	7.88	8.99
El-Kholy, Egypt, 2012	2.9	17	3.4
Peng, China(INICC), 2015	2.7	19.561	1.5
Tigen, Turkey, 2014	6.4	14.3	4.3
Kübler, Poland, 2012	4.01	18.2	4.8
Kumar, India, 2017	7.4	11.8	9.7
Datta, India, 2014	13.86	6.04	9.08
Tao, China, 2011	3.1	20.8	6.4
Ranjan, India, 2014		31.7	
Medeiros, Brasil, 2015	9.1	20.9	9.6
Leblebicioglou, Turkey, 2014	11.1	21.4	7.5
Patil, India, 2011	47.31		
Salgado Yopez, Ecuador, 2017	6.5	44.3	5.7
Singh, India, 2013	16	32	9
Ramirez, Mexico, 2007	23.1	21.8	13.4
Madani, Morocco, 2009	15.7	43.2	11.7
Ider, Mongolia, 2016	19.7	43.7	15.7
Bamigatti, India, 2017	72.56	3.98	12.4
Rasslan, Egypt, 2012	22.5	73.4	34.2

DA-HAIs rates per 1000 device days; *missing rates = not available

Table 2: Developed countries and DA-HAIs rates

Name, Country, Year	CLABSI	VAP	CAUTI
Worth, Australia, 2015	1.34		
Kaiser, Holland, 2014	1.7	3.3	
Watanabe, Japan, 2011	2.38	1.14	2.4
Chen, Taiwan, 2012	3.48	3.8	3.7
Velasquez, Italy, 2016		13.2	
Malacarne, Italy, 2010	1.9	8.9	4.8
Mertens, Belgium, 2013	2.3	12	5.5
Vanhems, France, 2011		20.6	
Dima, Greece, 2007	12.1	12.5	
Gikas, Cyprus, 2010	18.6	6.4	
Iordanou, Cyprus, 2017	15.9	10.1	2.7
Boncagni, Italy, 2015	6.6	23.1	5.45
Apostolopoulou, Greece, 2013	11.8	20	4.2

*DA-HAIs rates per 1000 device days; *missing rates
= not available*

Table 4: Summary of reviewed articles

1	Leblebicioglu et al., -Turkey	-Frequency Documentation	-Prospective	-94498	-CLABSI: 11.1
Ventilator Associated Pneumonia - VAP					
	Developed economies		Developing economies		
Cyprus	8.25†	Mongolia	43.7		
France	20.6	Venezuela	7.2		
Greece	16.3†	Brazil	20.9		
Italy	11†	China	20.18†		
Japan	1.14	Ecuador	44.3		
Holland	3.3	Egypt	31.56†		
Belgium	2.3	India	24.85†		
		Iran	7.88		
		Lebanon	8.1		
		Mexico	21.8		
		Morocco	43.2		
		Turkey	17.85†		
					P value
Mean (SD)	10.09(6.82)		24.29 (13.1)		0,016
Median (IQR)	9.62(2.76-17.37)		21.35 (10.5-40.29)		0,020
Central Line-Associated Bloodstream Infection - CLABSI					
	Developed economies		Developing economies		
Belgium	2.3	Mongolia	19.7		
Cyprus	17.25†	Venezuela	5.1		
Greece	11.95†	Brazil	9.1		
Italy	4.25†	China	2.9†		
Japan	2.38	Ecuador	6.5		
Holland	1.7	Egypt	9.33†		
Australia	1.34	India	14.15†		
		Iran	5.84		
		Lebanon	5.2		
		Mexico	23.1		
		Morocco	15.7		
		Turkey	8.75†		
					P value
Mean (SD)	5.88(5.75)		10.44 (6.07)		0,011
Median (IQR)	2.38(1.7-11.95)		8.92 (5.36-15.31)		0,025
Catheter-Associated Urinary Tract Infection - CAUTI					
	Developed economies		Developing economies		
Belgium	5.5	Mongolia	15.7		
Cyprus	2.75†	Venezuela	3.9		
Greece	4.5	Brazil	9.6		
Italy	5.45	China	6†		
Japan	2.4	Ecuador	5.7		
Poland	4.8	Egypt	34.1†		
		India	7.31†		
		Iran	8.99		
		Lebanon	4.1		
		Mexico	13.4		
		Morocco	11.7		
		Turkey	5.9†		
					P value
Mean (SD)	5.31 (3.18)		9.02 (3.66)		0,13
Median (IQR)	4.65 (2.6-7)		8.94 (5.75-12.75)		0,066

Abbreviation: † mean (more than one study)

Table 3: Developing vs developed economies DA-HAI incidence rates

	2014 (Turkey)	- 63 ICUs. from 29 hospitals in 19 cities	of Device Associated Hospital Acquired Infections	observational cohort study	ICU Patients	-VAP: 21.4 -CAUTI: 7.5
2	Kaiser et al., 2014 (The Netherlands)	-ICU Department of VU University Medical Centre -Amsterdam -Holland	-Evaluation of a Semi-Automated VAP and CLABSI detection protocol in the ICU	-Prospective surveillance study	-533 ICU Patients	-CLABSI: 1.7/1000 -VAP: 3.3/1000 -CAUTI: Not Measured
3	Datta et al., 2014 (India)	-Two ICUs at a 750-bed hospital in India	-Evaluation of infection frequency and risk factors from invasive devices in the ICU	-Prospective clinical observation study	-679 ICU Patients	-CLABSI: 13.86/1000 -VAP: 6.04/1000 -CAUTI: 9.08/1000
4	Kanj et al., 2012 (INICC Lebanon)	-University hospital ICU in Lebanon	-Evaluation of device related infection frequency in the ICU	-Prospective observational study	-666 ICU Patients	-CLABSI: 5.2/1000 -VAP: 8.1/1000 -CAUTI: 4.1/1000
5	Madani et al., 2009 (Morocco)	-12-bed ICU of the university hospital of Morocco	-Evaluation of device related infection frequency in the ICU. microbiological profile. resistance. length of stay and increase in mortality	-Prospective surveillance study	-1731 ICU Patients	-CLABSI: 15.7/1000 -VAP: 43.2/1000 -CAUTI: 11.7/1000
6	Chen et al., 2012 (Taiwan)	-42-bed ICU of a university hospital in Taiwan	-Evaluation of device related infection frequency in the ICU	-Retrospective and prospective observational study	-14734 ICU Patients	-CLABSI: 3.48/1000 -VAP: 3.8/1000 -CAUTI: 3.7/1000
7	Singh et al., 2013 (India)	-10-bed ICU in a tertiary care hospital in India	-Evaluation of the total frequency of DA-HAI incidence	-Prospective observational study	- 293 ICU Patients	-CLABSI: 16/1000 -VAP: 32/1000 -CAUTI: 9/1000
8	Watanabe et al., 2011 (Japan)	-20 ICUs from university hospitals in Japan	-Evaluation of the frequency of invasive device related infections using a data collection system to aggregate information in a national database and enhance quality improvement activities	-Prospective observational study	-1989 ICU Patients	-CLABSI: 2.38/1000 -VAP: 1.14/1000 -CAUTI: 2.4/1000
9	Ranjan et al., 2014 (India)	-12-bed ICU in a tertiary care hospital in India	-Evaluation of VAP incidence rate. risk factors and mortality	-Prospective observational study	-105 ICU Patients	-CLABSI: Not measured -VAP: 31.7/1000 -CAUTI: Not measured
10	Velasquez et al., 2016 (Italy)	-21 ICUs in Italy	- Evaluation of VAP incidence rate and risk factors	-Prospective observational study	-772 ICU Patients	-CLABSI: Not measured -VAP: 13.2/1000 -CAUTI: Not measured
11	Vanhems et al., 2011 (France)	-11 ICUs in France	-Evaluation of incidence rate of early onset VAP	-Prospective observational study	-3387 ICU Patients	-CLABSI: Not measured -VAP: 20.6/1000 -CAUTI: Not measured
12	Mehta et al., 2007 (INICC India)	-12 ICUs from 7 tertiary care hospitals in India	-Evaluation of DA-HAI s incidence rate. their microbiological profile. drug resistance. mortality and length of stay	-Prospective observational study	-10835 ICU Patients	-CLABSI: 7.92/1000 -VAP: 10.46/1000 -CAUTI: 1.41/1000
13	Patil et al., 2011 (India)	-1 ICU of a public University hospital in India	-Define incidence rate of BSIs related with CVCs	-Prospective observational study	-54 ICU Patients	-CLABSI: 47.31/1000 -VAP: Not measured -CAUTI: Not measured
14	Apostolopoulou et al., 2013 (Greece)	-3 ICUs from 3 hospitals in Greece	-Evaluation of DA-HAI incidence rate. microbiological profile. drug resistance and morbidity	-Prospective observational study	-294 ICU Patients	-CLABSI: 11.8/1000 -VAP: 20/1000 -CAUTI: 4.2/1000

15	Bammigatti et al., 2017 (India)	-1 ICU in a university hospital in India	-Evaluation of risk factors and microbial resistance in DA-HAIs		-Prospective observational study	-341 ICU Patients	-CLABSI: 72.56/1000 -VAP: 3.98/1000 -CAUTI: 12.4/1000
16	Boncagni et al., 2015 (Italy)	-12 bed ICU of a tertiary care hospital in Italy	-Evaluation of incidence rate	DA-HAI	-Prospective observational study	-1382 ICU Patients	-CLABSI: 6.6/1000 -VAP: 23.1/1000 -CAUTI: 5.45/1000
17	Gikas et al., 2010 (Cyprus)	-4 ICUs in 4 major hospitals of Cyprus	-Evaluation of incidence rate and identification of areas of improvement	DA-HAI	-Prospective observational study	-2692 ICU Patients	-CLABSI: 18.6/1000 -VAP: 6.4/1000 -CAUTI: Not measured
18	Dima et al., 2007 (Greece)	-8 ICUs in Greece	-Evaluation of incidence rate	DA-HAI	-Prospective observational study	-1739 ICU Patients	-CLABSI: 12.1/1000 -VAP: 12.5/1000 -CAUTI: Not measured
19	Iordanou et al., 2017 (Cyprus)	-8 bed ICU in a major general hospital in Cyprus	-Evaluation of incidence rate for one year	DA-HAI	-Prospective cohort and active surveillance study	-198 ICU Patients	-CLABSI: 15.9/1000 -VAP: 10.1/1000 -CAUTI: 2.7/1000
20	Jahani-Sherafat et al., 2015 (Iran)	-6 ICUs of university hospitals in Tehran-Iran	-Evaluation of incidence rate	DA-HAI	-Prospective cohort and active surveillance study	-2584 ICU Patients	-CLABSI: 5.84/1000 -VAP: 7.88/1000 -CAUTI: 8.99/1000
21	Rasslan et al., 2012 (Egypt)	-3 ICUs of 3 hospitals in 2 towns in Egypt	-Evaluation of incidence rate	DA-HAI	-Prospective cohort and active surveillance study	-473 ICU Patients	-CLABSI: 22.5/1000 -VAP: 73.4/1000 -CAUTI: 34.2/1000
22	Salgado Yopez et al., 2017 (Ecuador)	-2 ICUs of 3 hospitals in Ecuador	-Evaluation of incidence rate	DA-HAI	-Prospective cohort and active surveillance study	-776 ICU Patients	-CLABSI: 6.5/1000 -VAP: 44.3/1000 -CAUTI: 5.7/1000
23	Tigen. et al., 2014 (Turkey)	-16 bed ICU of a university hospital in Turkey	-Evaluation of incidence rate	DA-HAI	-Prospective cohort and active surveillance study	-1798 ICU Patients	-CLABSI: 6.4/1000 -VAP: 14.3/1000 -CAUTI: 4.3/1000
24	Medeiros et al., 2015 (Brazil)	- 4 ICUs of 3 hospitals in 3 towns in Brazil	-Evaluation of incidence rate	DA-HAI	-Prospective cohort and active surveillance study	-1031 ICU Patients	-CLABSI: 9.1/1000 -VAP: 20.9/1000 -CAUTI: 9.6/1000
25	Ramirez et al., 2007 (Mexico)	-5 ICUs of 4 hospitals in Mexico	-Evaluation of incidence rate	DA-HAI	-Prospective cohort study	-1055 ICU Patients	-CLABSI: 23.1/1000 -VAP: 21.8/1000 -CAUTI: 13.4/1000
26	El-Kholy et al., 2012 (Egypt)	-3 ICUs of 3 hospitals in Egypt	-Evaluation of incidence rate	DA-HAI	-Prospective observational study	-1101 ICU Patients	-CLABSI 2.9/1.000 -VAP 17/1.000 -CAUTI 3.4/1.000
27	Tao et al., 2011 (China)	-398 ICUs of 70 hospitals in China	-Evaluation of incidence rate	DA-HAI	-Multicentered prospective cohort study	-391527 ICU Patients	-CLABSI 3.1/1.000 -VAP 20.8/1.000 -CAUTI 6.4/1000
28	Empaire et al., 2017 (Venezuela)	-2 ICUs of 2 hospitals in Venezuela	-Evaluation of incidence rate and microbiological resistance of microorganisms	DA-HAI	-Multicentered prospective observational study	-1014 ICU Patients	-CLABSI 5.1/1.000 -VAP 7.2/1.000 -CAUTI 3.9/1000
29	Kumar et al., 2017 (India)	-ICU of a tertiary care hospital in India	-Evaluation of incidence rate	DA-HAI	-Prospective observational study	-343 ICU Patients	-CLABSI 7.4/1.000 -VAP 11.8/1.000 -CAUTI 9.7/1000
30	Rosenthal et al., 2016	-703 ICUs of 50 countries from Latin America. Eastern Mediterranean. Southeast Asia and the West Pacific	-Evaluation of incidence rate	DA-HAI	-Prospective observational study	-861284 ICU Patients	-CLABSI 4.1/1.000 -VAP 13.1/1.000 -CAUTI 5.7/1000

31	Talaat et al., 2016 (Egypt)	-91 ICUs of 28 hospitals in Egypt	-Evaluation of incidence rate and the effectiveness of a reduction program	DA-HAI	-Prospective observational study before and after intervention	-59318 ICU Patients	Results following intervention -CLABSI 2.6/1.000 -VAP 4.3/1.000 -CAUTI 1.9/1000
32	Ider et al., 2016 (Mongolia)	-3 ICUs of 3 hospitals in Mongolia	-Evaluation of incidence rate	DA-HAI	-Prospective observational/surveillance study	-467 ICU Patients	-CLABSI 19.7/1.000 -VAP 43.7/1.000 -CAUTI 15.7/1000
33	Mehta et al., 2016 (INICC India)	-Hospitals from 20 cities in India	-Evaluation of incidence rate	DA-HAI	-Prospective observational study	-236.700 ICU Patients	-CLABSI 5.1/1.000 -VAP 9.4/1.000 -CAUTI 2.1/1000
34	Hui-Peng et al., 2015 (INICC China)	-26 bed ICU of a tertiary care hospital in China	-Evaluation of incidence rate	DA-HAI	-Prospective observational study	-4013 ICU Patients	-CLABSI 2.7/1.000 -VAP 19.56/1.000 -CAUTI 1.5/1000
35	Worth et al., 2015 (Australia)	-ICUs of 29 hospitals in Australia	-Describe time-trends in CLABSI rates. Infections by ICU peer-groups. Etiology. and antimicrobial susceptibility of pathogens		-Prospective observational study	-No Data	-CLABSI 1.34/1.000 -VAP Not measured -CAUTI Not measured
36	Rosenthal et al., 2014 (International Nosocomial Infection Control Consortium (INICC) report. data summary of 43 countries for 2007-2012. Device-associated module.)	-503 ICUs from 43 countries in Latin America. Asia. Europe and Africa	-Evaluation of incidence rate	DA-HAI	-Prospective observational study	-605310 ICU Patients	-CLABSI 4.9/1.000 -VAP 16.8/1.000 -CAUTI 5.5/1000
37	Mertens et al., 2013 (Belgium)	-ICUs of 18 hospitals in Belgium	-Evaluation of incidence rate (VAP & CLABSI) and the surveillance procedure	DA-HAI	-Prospective observational study	-6478 ICU Patients	-CLABSI 2.3/1.000 -VAP 12/1.000 -CAUTI 5.5/1000
38	Rosenthal et al., 2012 (International Nosocomial Infection Control Consortium (INICC) report. data summary of 36 countries. for 2004-2009)	-422 ICUs from 36 countries in Latin America. Asia and Europe	-Evaluation of incidence rate	DA-HAI	-Prospective cohort study	-313008 ICU Patients	-CLABSI 6.8/1.000 -VAP 15.8/1.000 -CAUTI 6.3/1000
39	Kübler et al., 2012 (Poland)	-15 bed ICU of a university hospital in Poland	- Evaluation of incidence rate	DA-HAI	-Prospective surveillance study	-847 ICU Patients	-CLABSI 4.01/1.000 -VAP 18.2/1.000 -CAUTI 4.8/1000
40	Malacarne et al., 2010 (Italy)	-125 ICUs in Italy	- Evaluation of incidence rate	DA-HAI	-Prospective epidemiological study	-34472 ICU Patients	-CLABSI 1.9/1.000 -VAP 8.9/1.000 -CAUTI 4.8/1000

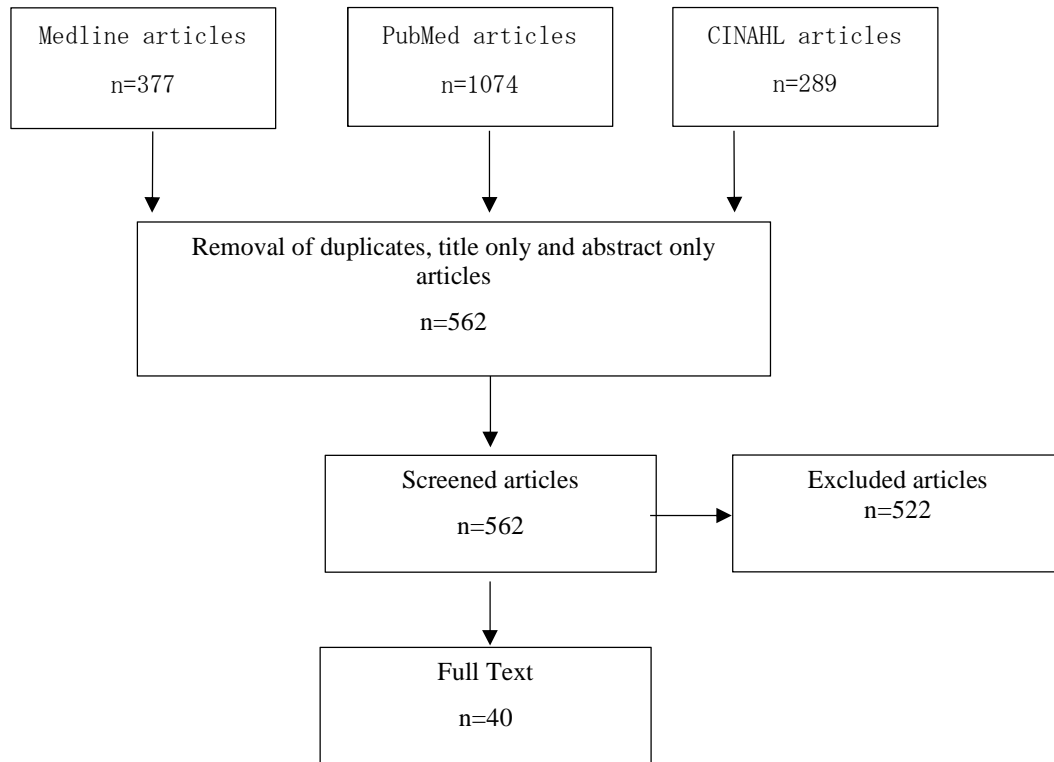


Figure 1: Flow diagram for article selection, as per Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and CINAHL recommendations

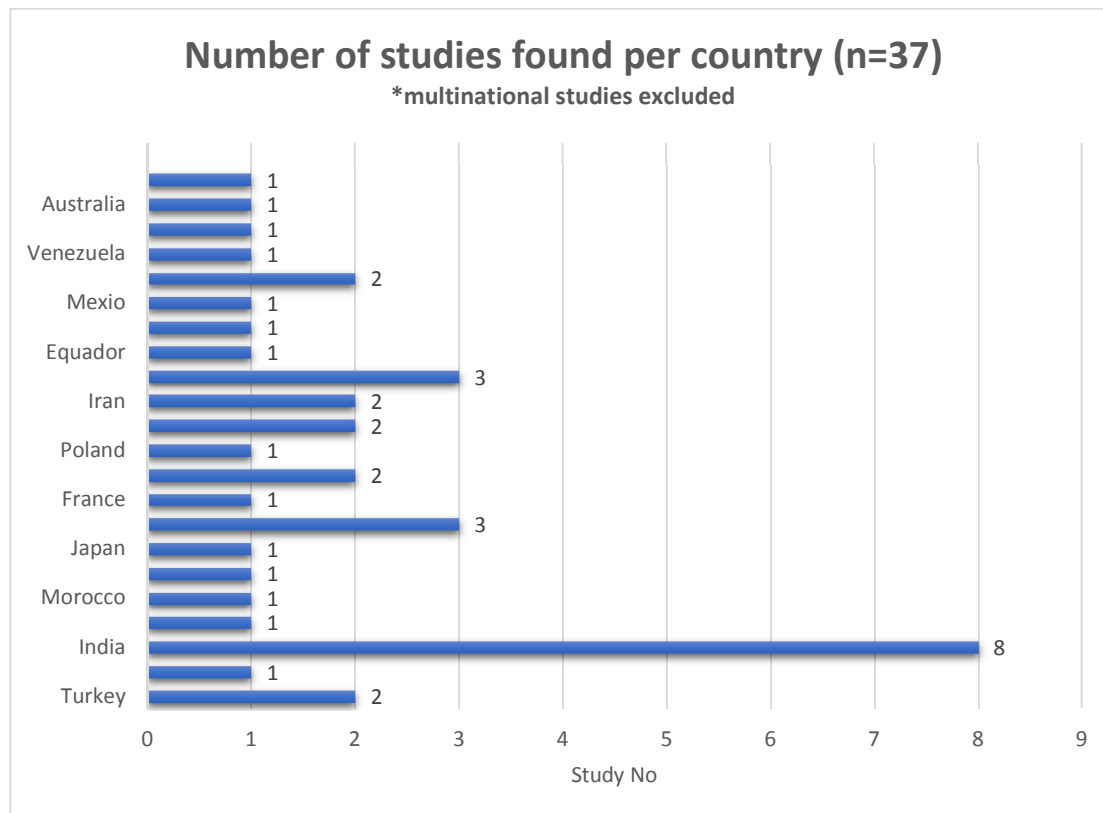


Figure 2: Number of studies per country

Characteristics of Studies

Table 4 summarizes the characteristics of the 40 studies used in this review. Although highly developed countries are pioneers in infection surveillance, in this review no studies were included from the USA, UK, Canada or Scandinavia. A search for older articles yielded numerous texts from these countries but they were not relevant to this study nor did they meet the study inclusion criteria (specifically age < 10 years), so their results were not included but their content supported the conclusion that DAI rates were a popular research topic for advanced health provision countries in the past decades, but are no longer as relevant. Despite the absence of appropriate articles from the aforementioned countries, many other countries have studies that were conducted during the last decade and were relevant to the subject. Most of the articles (92.68%) came from 22 countries (Figure 2), whilst the remaining 7.32% articles came from multinational studies conducted on behalf of the International Nosocomial Infection Control Consortium (INICC) and were included in this

review as their multinational nature was not a restriction in article selection.

Developed & developing countries

The International Monetary Fund (IMF) (IMF, 2017) classifies national economies by their degree of development and publishes this list yearly. Of the participating countries in this review, the economies of Brazil, China, Ecuador, Egypt, India, Iran, Lebanon, Mexico, Mongolia, Morocco, Poland, Turkey and Venezuela are listed as developing (table 1) while the economies of Australia, Belgium, Cyprus, France, Greece, Holland, Italy, Japan and Taiwan are listed as advanced (table 2). Poland however, is listed by the United Nations (UN) (United Nations Development Programme, 2016) among the list of countries with a high human development index (HDI), along with all of the countries on the advanced economies list and is the only country in this review that does not appear in the developed economy list.

Overall, the most represented country in terms of reviewed articles was India with eight

articles (Mehta *et al.*, 2007, 2016; H. Patil *et al.*, 2011; Singh *et al.*, 2013; Datta *et al.*, 2014; Ranjan *et al.*, 2014; Bammigatti *et al.*, 2017; Kumar *et al.*, 2017) (20%), followed by Egypt (El-Kholy *et al.*, 2012; Rasslan *et al.*, 2012; Talaat *et al.*, 2016) and Italy (Malacarne *et al.*, 2010a; Boncagni *et al.*, 2015; Velasquez *et al.*, 2016) with 3 studies each (7.5% each or 15% of the total), whilst China (Tao *et al.*, 2011; Peng *et al.*, 2015), Greece (Dima *et al.*, 2007; Apostolopoulou *et al.*, 2013), Cyprus (Gikas, M. Roumelaki, *et al.*, 2010; Iordanou *et al.*, 2017) and Turkey (Leblebicioglu *et al.*, 2014; Tigen *et al.*, 2014) are represented with 2 studies each (5% each or 20% of the total). Australia (Worth *et al.*, 2015), Belgium (Mertens, Morales and Catry, 2013), Brazil (Medeiros *et al.*, 2015), Ecuador (Salgado Yopez *et al.*, 2017), France (Vanhems *et al.*, 2011), Holland (Kaiser *et al.*, 2014), Iran (Jahani-Sherafat *et al.*, 2015), Japan (Watanabe *et al.*, 2011), Lebanon (Ss Kanj *et al.*, 2012), Mexico (Ramirez Barba *et al.*, 2007), Mongolia (Ider *et al.*, 2016), Morocco (Madani *et al.*, 2009), Poland (Kübler *et al.*, 2012), Taiwan (Chen *et al.*, 2012) and Venezuela (Empaire *et al.*, 2017) were represented by one study each (2.5% each or 37.5% combined). 80% of studies (32/40) studied all three DAIs (CLABSI, VAP and CAUTI) while a smaller number (3/40 or 7.5%) studied two out of the three DA-HAIs, specifically CLABSI and VAP. The remaining five articles looked at only one of the three DA-HAIs (5/40, 12.5%). Interestingly, no researchers chose to study CAUTI with either CLABSI or VAP and none of the researchers that chose to study a single type of DA-HAI in the ICU chose to focus on CAUTI, unlike VAP with 3/40 (7.5%) articles or CLABSI with 2/40 (5%) articles. On the other hand, CAUTI is highly researched with regard to non-ICU patients and many of the rejected articles focussed on CAUTI outside the ICU. Urinary catheter care in the ICU differs very little from urinary catheter care elsewhere in healthcare setting and since subject is heavily studied outside the ICU, this may explain the apparent lack of interest among ICU researchers.

Less than a third of the articles (12/40, 30%) were conducted in a single ICU, while the remaining 70% (28/40) of articles study data gathered from more than one ICU. Furthermore, three articles, published by the INICC combine data from ICUs in different countries and even different continents;

more specifically 422 ICUs from 36 countries in Latin America, Asia and Europe (Rosenthal *et al.*, 2012), 503 ICUs from 43 countries in Latin America, Asia, Europe and Africa (Rosenthal *et al.*, 2014) and 703 ICUs from 50 countries from Latin America, Eastern Mediterranean, Southeast Asia and the West Pacific (Rosenthal *et al.*, 2016).

The sample sizes among studies vary greatly. The largest sample of ICU patients is seen in the INICC studies, and more specifically in Rosenthal's *et al* report from 703 ICUs in 50 countries (Rosenthal *et al.*, 2016), with 861,284 ICU patents, followed by another INICC report, in 503 ICUs from 43 countries with a sample of 605,310 ICU patients (Rosenthal *et al.*, 2014) and the third largest study is the Chinese (Tao *et al.*, 2011) one with a sample size of 391,527 patients, from 398 ICUs of 70 hospitals. On the other hand, the smallest sample is found in one of the studies from India (H. Patil *et al.*, 2011) with 54 ICU patients, followed by another study from the same country (Ranjan *et al.*, 2014) with 105 patients, whilst the third smallest sample is found in one of the studies from the republic of Cyprus (Iordanou *et al.*, 2017) with 198 ICU patients.

Statistical analysis

For statistical analysis, median and interquartile range (IQR) values, the mean and standard deviation (SD) values of the DA-HAIs were used to describe the constant variables. T-test was used to examine the means between developed and developing countries and the Wilcoxon rank-sum test was used for comparing the medians.

Methodological Quality

Of the 40 reviewed articles, 32.5% (13/40) were conducted in single ICUs. The remaining 27 articles are multicentered, while the three of the 27 INICC articles were not only multicentered but conducted in multiple countries on multiple continents. Also, a great variation in sample size is noted. The results cannot be used to extract conclusions about all the ICUs of a country and, even though there may be many studies in a country, the results are not necessarily indicative of all the ICUs in that country as these individual units may vary greatly from the infection standpoint norm. India is the most represented among the 40 studies. While results may not

considered necessarily representative for an entire country, this does not mean they are not useful. Potentially, comparison among ICUs can help researchers and infection control staff to develop better infection prevention practices.

DA-HAI Incidence rates

Both the first and second highest identified CLABSIs rates were found in India (H. Patil *et al.*, 2011; Bammigatti *et al.*, 2017) with a frequency of 72.56 and 47.31 incidents per 1000 device days respectively. The third highest infection rate was found in the Mexican study (23.1) (Ramirez Barba *et al.*, 2007). The lowest rates were found in the Australian study (Worth *et al.*, 2015) with a reported incidence rate of 1.34 infections per 1000 device days. The Australian study reports only CLABSI rates, so there is no data available for VAP and CAUTI. The study with the second lowest CLABSI rate was from the Netherlands (Kaiser *et al.*, 2014) with 1.7 cases per 1000 device days and the third best result was from Italy (Malacarne *et al.*, 2010).

The highest VAP rates are reported in an Egyptian study (73.4/1000DD) (Rasslan *et al.*, 2012), second highest in an Ecuadorian study (44.3/1000DD) (Salgado Yopez *et al.*, 2017) and the third in a Mongolian study (43.7/1000DD) (Ider *et al.*, 2016). The lowest reported VAP rates come from a Japanese study (1.14/1000DD) (Watanabe *et al.*, 2011), with the second lowest being reported in the Netherlands (3.3/1000DD) (Kaiser *et al.*, 2014) and the third in Taiwan (3.8/1000DD) (Chen *et al.*, 2012). Ventilator associated pneumonia was researched in 38 of the 40 reviewed studies and the total sum of the 38 studies is 672161 instances of VAP.

CAUTIs appear to be the third and least encountered type of all DA-HAI, where rates of infection are much lower than VAP and CLABSIs in most studies. Higher CAUTI rates were found in an Egyptian study (34.2/1000DD) (Rasslan *et al.*, 2012), second highest in a Mongolian study (15.7/1000DD) (Ider *et al.*, 2016) and third in a Mexican and Mongolian study (13.4/1000DD) (Ramirez Barba *et al.*, 2007; Ider *et al.*, 2016) with exactly the same incidence rate per 1000 DD. The lowest CAUTI incidence rates comes from India (1.41/1000DD) (Mehta *et al.*, 2007), the second lowest from China

(1.5/1000DD) (Peng *et al.*, 2015) and third from Egypt (1.9/1000DD) (Talaat *et al.*, 2016).

The results of this particular Egyptian study (Talaat *et al.*, 2016) are reportedly after intervention, noting that the results prior the intervention are not disclosed.

Overall, the highest reported DA-HAI rate was reported by Rasslan (Rasslan *et al.*, 2012) whose VAP infection rate was at 73.4 per 1000 ventilator days, followed closely behind by Bammigatti *et al.*'s (Bammigatti *et al.*, 2017) who reported 72.56 CLABSI incidents per 1000 central line days (Bammigatti *et al.*, 2017). The lowest reported DAI rate was 1.14 (Watanabe *et al.*, 2011) pneumonias associated with mechanical ventilation per 1000 device days.

Developing economies DA-HAI Incidence rates

In developing economies, VAP incidence rates per 1000 device days are reported by several studies included in the present review. These reports originate from twelve geographical locations, specifically Mongolia (43.7/1000), Venezuela (7.2/1000), Brazil (20.9/1000), China (20.18 [mean]), Ecuador (44.3/1000), Egypt (31.56/1000 [mean]), India (24.85/1000 [mean]), Iran (7.88/1000), Lebanon (8.1/1000), Mexico (21.8/1000), Morocco (43.2/1000) and Turkey (17.85/1000 [mean]). Mean and median values computed using data from all developing economies gives VAP rates of 24.29 (SD, 13.1) and 21.35 (IQR, 10.5-40.29) respectively. Also, CLABSI rates were found for 12 developing economies, specifically Mongolia (19.7/1000), Venezuela (5.1/1000), Brazil (9.1/1000), China (2.9/1000 [mean]), Ecuador (6.5/1000), Egypt (9.33/1000 [mean]), India (14.15/1000 [mean]), Iran (5.84), Lebanon (5.2/1000), Mexico (23.1/1000), Morocco (15.7/1000) and Turkey (8.75/1000). Mean developing economies CLABSI rate is 10.44/1000 (SD, 6.07) and median 8.92 (IQR, 5.36-15.31).

CAUTI rates are reported in public literature for 12 developing economies, Mongolia (15.7/1000), Venezuela (3.9/1000), Brazil (9.6/1000), China (6/1000 [mean]), Ecuador (5.7/1000), Egypt (34.1/1000 [mean]), India (7.31/1000 [mean]), Iran (8.99/1000), Lebanon (4.1/1000), Mexico (13.4/1000), Morocco (11.7/1000) and Turkey

(5.9/1000). Developing economies mean and median value is 9.2 (SD: 3.66) and 8.94 (IQR; 5.75-12.75) (Table 3).

Developed Economies DA-HAI Incidence

Examining DA-HAIs found in publicly available literature over the last ten years (2007-2017). VAP incidence rates for developed economies include data from for Cyprus (8.25/1000[mean]), France (20.6/1000), Greece (16.3/1000[mean]), Italy (11/1000[mean]), Japan (1.14/1000), Holland (13.3/1000) and Belgium (2.3/1000). Mean and median values for VAP rates in developed economies were found to be 10.09 (SD, 6.82) and 9.62 (IQR, 2.76-17.37) respectively.

CLABSI rates are mentioned in several reports from eight countries, Belgium (2.3/1000), Cyprus (17.25/1000[mean]), Greece (11.95/1000[mean]), Italy (4.25/1000[mean]), Japan (2.38/1000), Holland (1.7/1000) and Australia (1.34/1000). Mean and median values for CLABSI rates in developed economies were found to be 5.88 (SD, 5.75) and 2.38 (IQR, 1.7 – 11.95) respectively.

CAUTI is mentioned in seven studies reporting incidence rates from six countries. Belgium reports 12 instances of CAUTI per 1000 device days (5.5/1000), Cyprus 2.75/1000 (mean), Greece 4.5/1000, Italy 5.45/1000, Japan 2.4/1000 and Poland 4.8/1000. Developed countries' mean and median values per 1000 device days is 5.31 (SD, 3.18) and 4.65 (IQR, 2.6-7.08) (Table 3).

Overall, the highest reported infection rate was described by Rasslan (Rasslan *et al.*, 2012) whose VAP infection rate was 73.4 per 1000 ventilator days, followed closely behind by Bammigatti's 72.56 CLABSI incidents per 1000 central line days (Bammigatti *et al.*, 2017).

Aggregated Results

In total, 40 articles were found and reviewed in this project, coming from 22 countries over the last 10 years and published in international literature. The majority of these articles came from developing economies (24/41) while the sample from economies classified as developed, according to the IMF (IMF, 2017) classification, was limited to 14 articles (14/41). The remaining three articles (3/41) came from the INICC and were based on research conducted in multiple ICUs from

36 (Rosenthal *et al.*, 2012), 43 (Rosenthal *et al.*, 2014) and 50 (Rosenthal *et al.*, 2016) countries respectively, so these studies cannot be classified based on the economic status of a specific originating country.

The highest DAI rates come from Egypt (Rasslan *et al.*, 2012), India (Bammigatti *et al.*, 2017) and Mongolia (Ider *et al.*, 2016) while the lowest come from Japan (Watanabe *et al.*, 2011) and the Netherlands (Kaiser *et al.*, 2014). The most frequently reported DAI among the reviewed articles was VAP with 73.4 lung infections per 1000 ventilator days (Rasslan *et al.*, 2012), the second highest reported DAI was CLABSI with 72.56 BSIs per 1000 central line days (Bammigatti *et al.*, 2017) and the least frequently encountered DAI was CAUTI with a highest reported rate of 34.2 UTIs per 1000 urinary catheter days (Rasslan *et al.*, 2012). The overall mean and median values for all articles were 10.83 and 6.45 respectively for BSIs, 17.28 and 13.2 for pneumonia and for UTIs 6.89 and 5.5.

In general, the incidence rate of infections related to invasive device use is higher in developing economies than in those considered developed. The mean and median values of all DAI rates in developing economies are from 40% to 60% higher than those of developed economies, confirming the World Health Organization's findings (World Health Organization, 2015).

DA-HAI rate comparison between developed and developing countries

Mean and median VAP value for developed economies are 10.09 (SD. 6.82) and 9.62 (IQR. 2.76-17.37) respectively, while in developing countries, mean was 24.29 (SD.13.1) and median 21.35 (IQR.10.5-40.29). P Values between means and medians for developed vs developing economies were found in both correlations to have statistical significance (mean correlation [p=0.016], median correlation [p=0.02]) (table 3).

Furthermore, CLABSI mean and median comparisons between developed and developing economies resulted in a significant statistical correlation (mean correlation [p=0.011], median correlation [p=0.025]). Mean and median for developed and developing economies was 5.88 (SD. 5.75) vs 10.44 (SD. 6.07) and 2.38 (IQR.

1.7-11.95) vs 21.35 (IQR. 10.5-40.29) respectively (table 3).

Comparing CAUTI mean and median figures, no statistical correlation was found since the p value was, in both cases, more than 0.05 ($p > 0.05$). Mean and median for developed and developing economies was found to be 5.31 (SD. 3.18) vs 9.02 (SD. 3.66) and 4.65 (IQR. 2.6-7) vs 8.94 (IQR.5.75-12.75) (table 3).

Discussion

Systematic surveillance, recording and analysis of local DA-HAI events in comparison to published DA-HAI literature is highly significant in the ICU setting. A single ICU's results may be lost in a countrywide multicentered study, but comparison of local results with better results from a wider source(es) and identification of possible areas for improvement can directly affect ICU patient's hospitalization and outcomes by reducing the risk of DA-HAIs and so impacting the negative consequences of ICU hospitalization.

The aim of the current review was to gather articles published since the 01/01/2007 to determine DAI infection rates per 1000 device days per article and per country and then use this data to extract conclusions. Following an extensive search in the scientific databases PubMed, Medline and CINAHL and subsequent evaluation; 40 articles were found (table 4) from 22 countries and reviewed.

In an attempt to improve analysis of the articles and extract more conclusive results, the articles were grouped for analysis in various ways. By examining the articles based on their total number of infections, the worst results come from Egypt(Rasslan *et al.*, 2012), India(Bammigatti *et al.*, 2017) and Mongolia(Ider *et al.*, 2016). The best results come from Japan(Watanabe *et al.*, 2011) and Egypt(Talaat *et al.*, 2016). It was noted that Australia(Worth *et al.*, 2015) and the Netherlands(Kaiser *et al.*, 2014) have very low results for CLABSI and CLABSI and VAP respectively but do not have collective results for all DAIs. First and third results were obtained following intervention, making them of greater interest as they demonstrate the effectiveness of studying research backed literature and applying

the conclusions reached to daily practice in order to identify and eliminate unsafe practices.

According to the WHO(World health Organization, 2015), developing economies have more DA-HAIs per 1000 device days than developed ones. In order to avoid bias, the reviewed articles were grouped based on their geographical location and their economic status (developed or developing). According to the IMF(IMF, 2017), of the countries participating in this review, the economies of Australia, Belgium, Cyprus, France, Greece, Holland, Italy, Japan and Taiwan are listed as developed, while the economies of Brazil, China, Ecuador, Egypt, India, Iran, Lebanon, Mexico, Mongolia, Morocco, Poland, Turkey and Venezuela are listed as developing. Three of the reviewed articles, published on behalf of the INICC were conducted in multiple countries and cannot be used in a comparison by means of economic status of their source country(Rosenthal *et al.*, 2012, 2014, 2016). Of the remaining 37 articles, 13 referred to ICUs in developed economies (Dima *et al.*, 2007; Gikas, Á. M. Roubelaki, *et al.*, 2010; Malacarne *et al.*, 2010b; Watanabe *et al.*, 2011; Vanhems *et al.*, 2011; Chen *et al.*, 2012; Apostolopoulou *et al.*, 2013; Mertens, Morales and Catry, 2013; Kaiser *et al.*, 2014; Boncagni *et al.*, 2015; Worth *et al.*, 2015; Velasquez *et al.*, 2016; Iordanou *et al.*, 2017), while 24 of the reviewed articles were in developing economies (Boyce *et al.*, 2002; Mehta *et al.*, 2007; Ramirez Barba *et al.*, 2007; Madani *et al.*, 2009; Tao *et al.*, 2011; H. V Patil *et al.*, 2011; Rasslan *et al.*, 2012; SS Kanj *et al.*, 2012; El-Kholy *et al.*, 2012; Kübler *et al.*, 2012; Singh *et al.*, 2013; Leblebicioglu *et al.*, 2014; Ranjan *et al.*, 2014; Datta *et al.*, 2014; Tigen *et al.*, 2014; Medeiros *et al.*, 2015; Peng *et al.*, 2015; Jahani-Sherafat *et al.*, 2015; Rosenthal *et al.*, 2016; Talaat *et al.*, 2016; Ider *et al.*, 2016; Bammigatti *et al.*, 2017; Salgado Yopez *et al.*, 2017; Empaire *et al.*, 2017; Kumar *et al.*, 2017).

Among developed economies, the highest reported DAI rate was 23.1/1000 DD, specifically VAP in Italy(Boncagni *et al.*, 2015), and the second highest was again VAP with an incidence rate of 20.6/1000 DD in France(Vanhems *et al.*, 2011). Of the 13 articles, 12 reviewed the incidence of VAP with the highest reported incidence being 23.1 infections to the lowest 1.14(Watanabe *et al.*,

2011) per 1000 DD. In comparison, the highest VAP incidence rate for developing economies was in Egypt with 73.4(Rasslan *et al.*, 2012) per 1000 ventilator days and the best result came from India(Bammigatti *et al.*, 2017) with 3.98 VAP incidents per 1000 ventilator days. For developing economies, 23 researchers studied VAP rates as opposed to 12 researchers for developed economies. The mean value of the samples was 24.29 vs 10.09 ($p=0.016$) for developed economies. The median value is 21.35 against 9.62 ($p=0.02$) for developed economies.

The same statistically significant correlation was found in the comparison of mean and median values for CLABSI. The mean value for CLABSI rates among developing economies is 10.44 versus 5.88 ($p=0.011$) for advanced economies and median value is 8.92 against 2.38 ($p=0.025$), where the highest advanced economies rate was found in Cyprus(Gikas, M. Roubelaki, *et al.*, 2010) (18.6/1000DD) and the lowest in Australia(Worth *et al.*, 2015) (1.34/1000DD). The highest rate for developing economies comes from India(Bammigatti *et al.*, 2017) (72.56/1000DD) and the lowest from Egypt(Talaat *et al.*, 2016) (2.6/1000DD).

Despite the fact that mean and median values for developed economies are higher than is described in the NHSN ICUs report(Dudeck *et al.*, 2011) (for VAP, 4/1000DD and for CLABSI, 3/1000DD), these values still appear to be much lower than the figures for developing economies in a statistically significant correlation. Accordingly, VAP and CLABSI is directly associated and affected by the economic status of the country under study.

Indwelling urinary catheters are common in healthcare settings outside the ICU and are far more researched, so CAUTI prevention steps are better known and better followed by healthcare professionals. Also, there is limited interest among ICU researchers to investigate this subject and then to employ scientific literature recommendations as the current relatively low infection rates are judged acceptable. This is reflected in the fact that only seven out of the 14 articles reviewed studied CAUTI rates, and the low infection rates reported in both developed and developing economies. The highest reported CAUTI rate comes from Belgium(Mertens, Morales and Catry, 2013) at

5.5/1000DD and the best result is reported from Japan(Watanabe *et al.*, 2011) (2.4/1000DD). The mean CAUTI rate among developed economies is 5.31(SD. 3.18) while the median is 2.38(IQR. 1.7-11.95).

In developing economies, there is significantly greater interest among researchers with regard to CAUTI rates. Of the 24 reviewed articles from developing economies, 22 measured CAUTI incidence rates in their hospitals. The highest reported CAUTI rate came from Egypt(Rasslan *et al.*, 2012) (34.2/1000DD) and the lowest result was reported from India(Mehta *et al.*, 2016) (2.1/1000DD). Mean and median were found to be 9.02(SD. 3.66) and 8.94(IQR. 5.75-12.75) respectively. There was no statistically significant correlation in the comparison of the mean and median values although much higher rates of incidence were found in developing economies. Accordingly, country of origin may associated with high or low CAUTIs rates, but it cannot be considered as the only cause of positive or negative results.

In general, the incidence rate of infections related with invasive devices usage is higher in developing than in developed economies. In comparison, the mean and median values of all DA-HAI rates in developing economies are 50% - 60% higher than those of developed economies, verifying the World Health Organization's findings(World health Organization, 2015).

Conclusions

There are many gaps in bibliography when it comes to aggregating results per ICU and per country as most studies are multicentered, and sometimes even from multiple countries so conclusive results cannot be extracted on a per country or per ICU basis.

When it comes to correlations between developed and developing economies DA-HAI rates, we concluded that the economic status of countries tend to be associated with marked variations in DA-HAI rates.

The most practical way to separate DA-HAIs rates for comparison is by considering the economic status of the article's originating country (as per the International Monetary Fund classification), as it is more likely for limited resource ICUs from

developing economies to have higher DA-HAIs rates as compared with ICUs from countries with developed economies and therefore resources.

Limitations

Grey literature was not included in the study.

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