ORIGINAL ARTICLE

The burden of healthcare-associated infection in Moroccan hospitals: Systematic review and meta-analysis

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DOI: 10.4081/jphia.2024.2641

Abstract. Healthcare-associated infections (HAI), also referred to as nosocomial infections, is defined as an infection acquired in a hospital setting. This infection is considered a HAI if it was not present or incubating at the time of admission. This includes infections acquired in the hospital but appearing after discharge, and also occupational infections among staff of the facility. HAI are a major patient safety measure to be considered in hospitals.

Introduction

HAI are considered to be the most frequent event threatening patient-safety in the world (3-5). According to WHO, more than 1.4 million people in the world are impacted by hospital contracted infections. Between 5 to 10% of patients admitted to hospitals in developed countries go on to contract one or more infections. This risk is 2 to 20 times higher in developing countries. In some developing countries, the proportion of patients impacted by HAI may surpass a rate of 25%, making HAI are a priority for the WHO (6). The significant subsequent healthcare associated costs of HAI are a great financial burden, especially for developing countries (7).

In Morocco, HAI represents a threat to public health due to the nature of their seriousness, emergence of resistance and the economic burdens caused by their direct and indirect expenses. Because of this Morocco joined the Global Antimicrobial Resistance Surveillance System (GLASS) by the end of 2018 (8).

When it comes to the prevalence of HAI at the global scale, there are few published statistics. A study conducted by the occupational medical services in 27 hospitals across

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Key words:

the Mediterranean region (Egypt, Italy, Morocco and Tunisia) has shown that the prevalence of nosocomial infections was 10.5%. When looking at Morocco specifically, various rates of HAI have been found across different healthcare centers; 17.8% (CHU Rabat, 2007), 10.3% (CHU Casablanca, 2016) and 6.7% (CHU Fes, 2010) (6,9,10). The risks of HAI are known in the literature, however the degree to which they are present continues to be imprecise.

The main objective of this systematic review and meta-analysis was to assess the prevalence of HAI in Morocco. This meta-analysis also demonstrates the variability in rates of HAI through time.

Methods

Protocol and registration. The meta-analysis was conducted in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (12) and the meta-analyses of observation researches in epidemiology (13). This protocol was registered in the international prospective register of systematic review protocols, PROSPERO number: CRD42017063897.

Design of the study and sources of the articles. We performed a systematic review and meta-analysis of prevalence. A multisource research strategy was used to retrieve all data published in complete text-form or in abstract-form, as well as non-published data (grey literature).

The research keywords and terms were used in the following data banks: Medline, Cochrane library, Scopus, Science Direct, Public Health Data Bank (BDSP), the published summaries as part of the congress, as well as scientific national researches like Doctorates or Masters, the WHO data bank and Google advanced research. Our research equation was constructed by using a combination of keyword (MeSH) terms and text.

Research strategy. The preliminary research strategy was elaborated by two investigators (LL,BA) and refined by a scientific librarian in order to identify new pertinent research terms.

Our bibliography research process led to the identification of cross-sectional studies identifying the point prevalence of HAI in Morocco. The research terms included various nosocomial infection types, namely urinary infections, surgical site infection, hospital acquired bacteremia and pneumonia. (See research equation in the appendix).

We applied the same research strategy in the regional medical database of the WHO and BDSP. We went through references summaries, which contain complete or partial data of nosocomial infection rates and relative proportions of each type, nosocomial urinary infections, bacteremia, hospital acquired pneumonia and the identified isolate of the microbiological etiology of the infection when it was reported.

The publication time was not limited. Data retrieval was supplemented by manually searching for the reference list of key reviews and references from retrieved studies. No language restriction was imposed.

Articles selection criteria. The inclusion criteria for the epidemiological studies were the following: studies reporting the prevalence of HAI in Morocco, regardless of the year or database.

Excluded studies were studies done on animals, review editorials, letters and comments, witness-case studies, case series, combined data studies, duplicated references, studies involving community acquired infections and publications mentioning identical data.

Judgement criteria: healthcare associated infection and nosocomial infection was defined based on the Center of Disease Control's definition (1,14).

Studies assessment and methodological quality. LL and BA independently reviewed and assessed articles after obtaining the integral text of potentially pertinent studies.

In this systematic review, the quality assessment performed on articles was based on JBI Critical Appraisal Checklist for Studies Reporting Prevalence Data (Edition 2017) (15). This checklist is made up of a grid of nine items which assesses the risks of bias in prevalence studies; for each of the nine items, assessing risk of bias is done so by marking either by yes, no, unclear or inappropriate. This critical appraisal was developed by Joanna Brigg's Institute at the faculty of health science at Adelaide university.

In this meta-analysis, the two investigators independently performed quality assessments on each pertinent study. Disagreement over the quotation was discussed and resolved by consensus or with a third member (AR).

The studies that received a scored of seven or more were considered to be of good quality, with a low risk of bias and were subsequently included in the meta-analysis (category A: Include), otherwise, they were classified in category B (seek further information if scored equal to, or below six). Studies classified under category B had a higher risk of bias.

Coefficient Kappa (K statistic was calculated to quantify the inter-observer concordance

Data extraction of studies that met inclusion criteria. Publication details collected: author(s), year of publication, language of publication, range of study, sample size, area where the study was conducted, tertiary institution or not, type

of patient population (neonatal, pediatric, adult), nosocomial infection type detected with definition used for diagnosis, and prevalence of infections identified.

Data collection. After in-depth examination of articles, which included contacting authors directly in case of missing data, we proceeded to data acquisition. Data acquisition consisted of acquiring and organizing data on prevalence rates of HAI and other covariables such as type of infection, type of patient population studied, etc.

Statistical analysis. Infection prevalence refers to the number of HAI infections among 100 patients present at the hospital at any given time.

Meta-analysis was conducted using a random effects model. Given the requirement for normalization of single rate in meta-analysis, a Double Arcsin of Freeman-Turkey for the original rate was performed to meet the requirement (16). Then the compiled results of the meta-analysis were represented in graphic form using a Forest Plot.

Statistical heterogeneity among the studies was estimated using a Chi-square test at the significance level of P<0.10 (17); heterogeneity was measured with the I² statistic (values of 25, 50, and 75% represented low, medium, and high heterogeneity, respectively). Publication bias was detected by Funnel Plot and by statistical methods suggested by Begg and Egger (P<0.05 was considered statistically significant) (20,21). R statistical software (package meta and metaphor) and Stata Statistical Version14 were used for all the calculations.

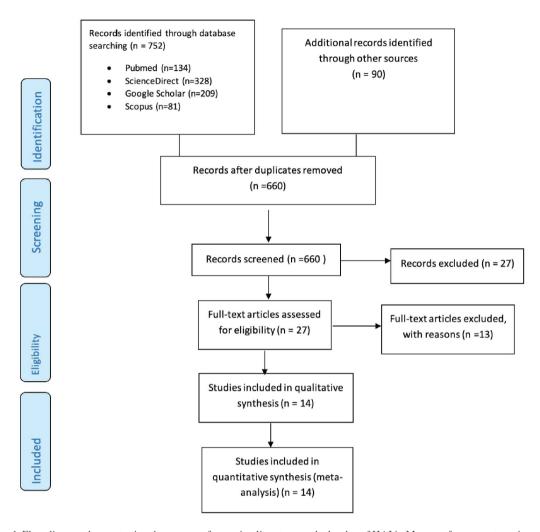
We did meta-regressions and subgroups analysis to investigate the association between outcomes, nosocomial infection types, tertiary hospital or not and quality of the study to explain possible effects on heterogeneity.

Sensitivity analysis: we identified the influence of each included study; aberrant values were excluded from the model in order to determine their effect on our estimation. The Trim and Fill method was additionally used. The Trim and Fill method is an iterative non-parametric method based on the asymmetry of a funnel plot that estimates an adjusted pooled effect; it is recommended to be used as a form of sensitivity analysis of the pooled estimate. Ultimately, this method aims to estimate the potential for missing studies, due to publication bias, in the funnel plot and adjust for this effect. The key assumption of the trim and fill method is that studies with the most extreme effect sizes are suppressed (22,23). The goal of incorporating this method is to reduce the impact publication bias can have on the validity of a meta-analysis.

Results

Our search was applied to several different data banks. A total of 687 studies (articles, theses, congress abstracts) were found. After the analysis of titles and summaries and the removal of identical works, 660 studies were excluded. Then after assessing the integral text, 14 articles met the outlined inclusion criteria.

There was a total of 6,532 patients represented in the 14 studies that met the inclusion criteria. Out of the 14 studies, one concerned only surgical wound infections and four were



 $Figure\ 1.\ Flow\ diagram\ demonstrating\ the\ process\ of\ assessing\ literature\ on\ the\ burden\ of\ HAI\ in\ Morocco\ for\ our\ systematic\ review.$

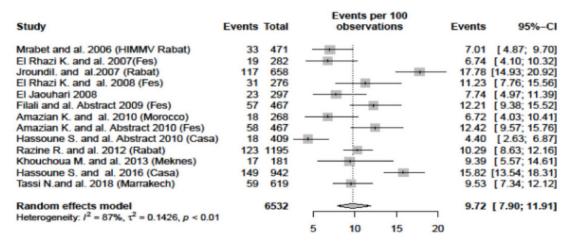


Figure 2. Morocco HAI pooled prevalence (Forest Plot).

published in bibliographical data. The remaining eight studies corresponded to congress abstracts or grey literature.

The below chart includes eligible article characteristics, namely authors, year of publication, place where the study took place (tertiary hospital or not), the number of patients having developed HAI during the study, total number of patients

included in the study and the prevalence of HAI identified by the authors. The last search was conducted during May 2022.

Methodological quality assessment. The average methodological quality score was 6.8 among the 14 eligible studies, 6 met criteria to be considered in category A (score equal to

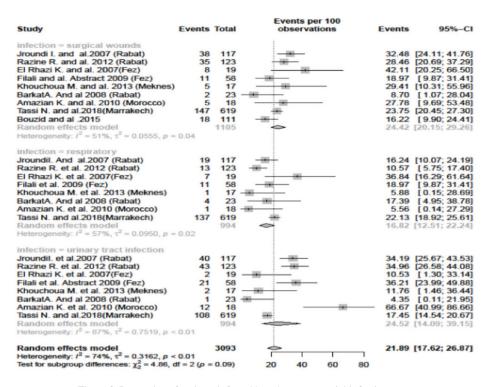


Figure 3. Proportion of patients infected based on nosocomial infection type.

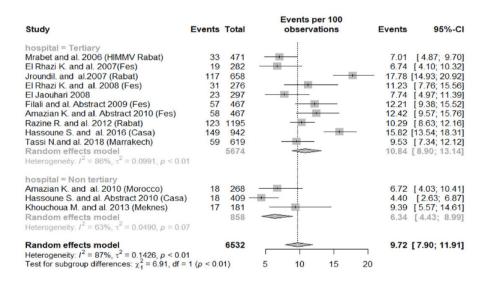


Figure 4. Pooled prevalence of HAI sub-group analysis in tertiary hospitals and non-tertiary hospitals.

or greater than 7); this means 54% of studies had a low risk of bias. A coefficient Kappa (K) statistic was calculated to quantify the inter-observer concordance.

Methodological quality assessment of the studies. Questions considered in the Methodological Quality Assessment of the Studies

Was the sample frame appropriate to address the target population?:

Were study participants sampled in an appropriate way?:

Was the sample size adequate?:

Were the study subjects and the setting described in detail?:

Was the data analysis conducted with sufficient coverage of the identified sample?:

Were valid methods used for the identification of the condition?:

Was the condition measured in a standard, reliable way for all participants?:

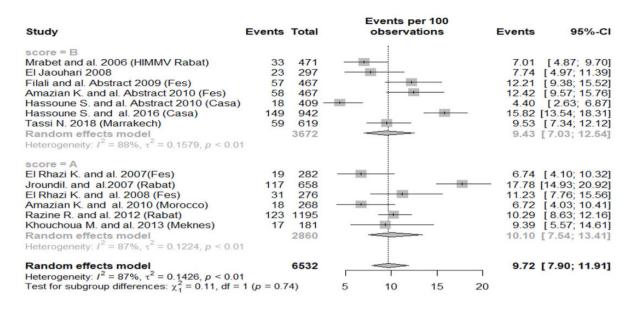


Figure 5. Prevalence sub-group analysis depending on study quality.

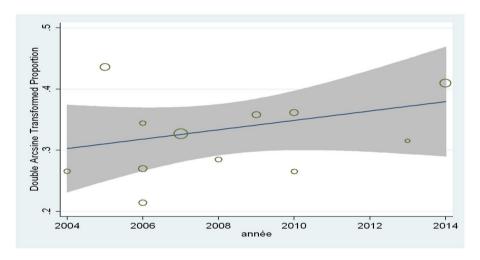


Figure 6. Mate regression demonstrating prevalence of HAI over years.

Was there appropriate statistical analysis?:

Was the response rate adequate, and if not, was the low response rate managed appropriately?:

Overall appraisal

Include ☐ Exclude ☐ Seek further info ☐

Pooled prevalence of HAIs in Morocco. Pooled prevalence of HAI was found to be 10% (95% CI: 8-12). By using I_2 statistic, a high heterogeneity effect of 87% was found, hence the choice of a random effect model.

Sub-group analysis. In order to explain this heterogeneity, we proceeded to perform a subgroup analysis on infection types (Fig. 3), prevalence of HAI in tertiary hospitals vs. non-tertiary hospitals, (Fig. 4) and quality of the study (Fig. 5).

The sub-group analysis performed to identify proportions of infection type among patients demonstrated that the most common HAI were nosocomial urinary tract infections (24.52%, CI 95%:14.09-39.15, I_2 =87%). This proportion was followed closely by surgical wound infections at 24.42% (CI 95%: 20.15-29.26, I_2 =51%). Respiratory infections accounted for 16.82% (CI 95%: 12.51-22.24, I_2 =57%) of the HAI.

Of the 14 selected studies, 10 were conducted in tertiary hospitals and the remaining three in non-tertiary hospitals. Pooled prevalence of HAI in tertiary hospitals was 11% (CI of 95%, 8.90-13.14); in non-tertiary hospitals it was 6.34% (CI of 95%, 4.43-9). There was no statistical difference in pooled prevalence of HAI in tertiary hospitals when compared to non-tertiary hospitals (P=0.08).

After performing the sub-group analysis based on the methodological quality of the studies, it was identified that studies rated higher in quality (less biased), reported, on average, a greater prevalence of HAI (10.10%, CI 95%)

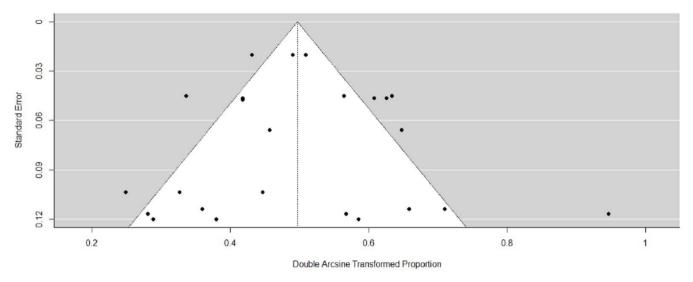


Figure 7. Funnel Plot assessing Publication bias.

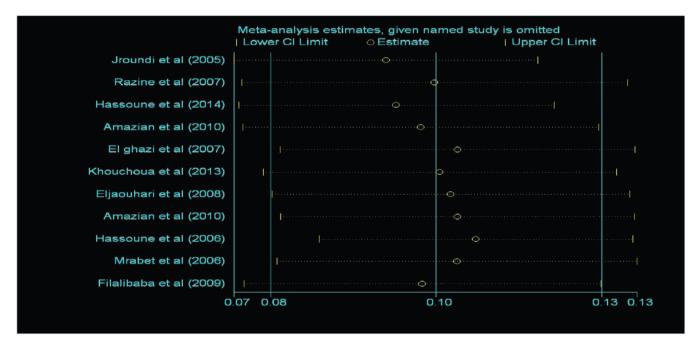


Figure 8. Sensitivity study by deletion.

7.54-13.41) when compared to studies rated lower in quality (9.43%, CI 95% 7.03-12.54).

By using meta-regression, it was identified that HAI prevalence increased from 2004 through 2014 with a beta of 0.05, confidence interval 95%: -0.07 through 0.16. Then, from 2014 to present, there was a slight increase in HAI prevalence however it was not statistically significant (P-value=0.9).

Publication bias exploration. The publication bias was assessed by using a graphic method (Funnel Plot) and statistical method (Begg and Egger tests).

As presented by the Funnel Plot, there was a slight dissymmetry in favor of small-sized studies; also, larger-sized studies were among those that found the highest prevalence of HAI.

Begg and Egger tests were non-significant (P>0.05). There was no evidence of publication bias using this test.

Sensitivity analysis

Assessing the influence of studies through deletion. A sensitivity study consists of a process of recalculating outcomes based on removing inputs to help in determining the relative impact of each study on the reported findings.

The sensitivity study allows for the individual separation of each study's impact on the results. This individual impact is presented graphically and helps in identifying the influence of each study on the reported pooled prevalence estimation.

Based on the sensitivity study, it was found that no study was particularly influential on the reported findings. In other words, when studies were removed one by one, the pooled

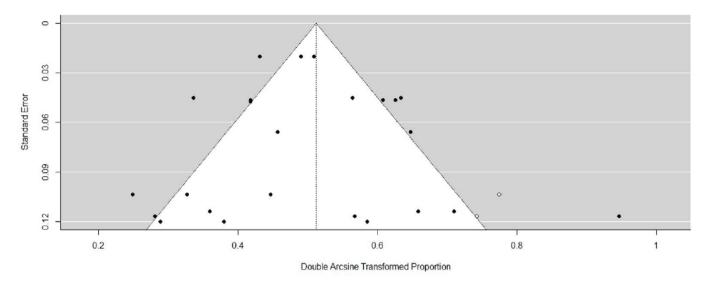


Figure 9. Missing studies by Trim and Fill method.

prevalence remained near the 10% value demonstrating the estimation in the prevalence of HAI.

Trim and Fill method. The Trim and Fill method showed that one study, with a large sample size, was missing; once included, the pooled prevalence changed from 10 to 8%.

Discussion

This is the first systematic review and national meta-analysis to estimate the prevalence of HAI in Morocco.

A meta-analysis that tackles HAI epidemiology in developing countries found a similar pooled prevalence of 10.1% (CI at 95%, 8.4-12.2). It also similarly raised the issue of heterogeneity among studies; they reported that 41% of their included studies met criteria to be considered good methodological quality. For the reported proportion in the various infections types, there was a variance in their results compared to our study. Their meta-analysis found the proportion of HAI to be 29% for surgery site infections, followed by the urinary infections at 24% and then respiratory infections at 15% of the total infected patients (35,36).

Another multicentric transversal study estimated the prevalence of nosocomial infections to be 10.5% (26).

The diagnosis criteria for HAI are not the same across all studies, which may help explain the level of heterogeneity and the variations in the reported estimated prevalence of HAI.

This makes comparisons with other meta-analyses, including those from developing countries, difficult, especially when considering the limited number of capable laboratories, which are a necessity when confirming nosocomial infections.

According to Zaidi *et al* (37). HAI frequency was 3-20 times higher in countries with limited resources when compared to industrialized countries. In Europe, according to the European center for disease prevention and control, HAI prevalence is 7.1% (38).

Most studies assessing HAI in Morocco have small sample sizes with a very limited scope. Other studies have been conducted but were not published for a variety of reasons, as portrayed by the two national investigations which have never been published.

In our meta-analysis, the Funnel plot was slightly asymmetrical whereas the Begg and Egger tests did not find any publication bias. It is possible these findings are due to the limited number of studies that met the inclusion criteria; these tests would not be powerful enough to detect a possible publication bias.

Conclusion

In Morocco, assessing the prevalence of HAI is an essential part of infection control and prevention. This meta-analysis identified that the pooled prevalence of HAI was 10%. The most common HAI were nosocomial urinary tract infections (24.52%), followed by surgical wound infections (24.42%), and respiratory infections (16.82%). This meta-analysis also found that HAI have been increasing over time since 2014, however this increase was not statistically significant (P-value=0.9).

Overall, HAI are a public health concern and a financial burden for Morocco. There are few published studies assessing the prevalence of HAI in Morocco, and of these few, most have a small sample size. More studies are required to assess the prevalence of HAI in Morocco and to aid in identifying effective strategies aimed to reduce HAI.

Supplementary information

The online version of this article (10.4081/jphia.2023.2641) contains supplementary material, which is available to authorized users.

Received: 5 Apr 2023; accepted XXXXX; published online: 5 Jan 2024.

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