# The prevalence of healthcare-associated infection in medical intensive care units in Tunisia. Results of the multi-centre NOSOREA1 study.

Prévalence des infections associées aux soins en réanimation médicale en Tunisie. Résultats de l'étude multicentrique NOSOREA1

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#### RÉSUMÉ

Objectifs: Déterminer la prévalence de l'Infection Associée Soins (IAS) en milieu de réanimation médicale, les facteurs de risque de ces infections et identifier les principaux micro-organismes en cause.

Méthodes : Il s'agissait d'une étude transversale de prévalence ponctuelle d'un jour au sein de tous les services de réanimation médicale de la Tunisie. Tous les patients hospitalisés depuis plus de 48 heures ont été inclus. Les IAS, le profil microbiologiques des germes identifiés et les potentiels facteurs de risques ont été relevés.

Résultats: Cent-trois patients appartenant à 15 services de réanimation médicale ont été colligés. La prévalence d'IAS était de 25,2 % IC 95% [15-35]. Il s'agissait principalement de pneumopathies nosocomiales (59%) et d'infections liées au cathéter (15%). Les facteurs de risque indépendants prédictifs d'IAS étaient : score d'IGS II ≥ 33 avec OR 1,047; IC 95% [1,015-1,077], p=0,003 et l'hospitalisation récente avec OR 4.14 CI 95% [1,235-13,889], p=0,021. Les germes non fermentants étaient prédominants au niveau de l'écologie des services participants, du portage des malades et des IASs. Conclusion: Les IASs sont fréquentes dans les services de réanimation médicale en Tunisie, ce qui accentue l'importance des mesures spécifiques de surveillance et du contrôle de l'infection chez les malades de réanimation. Implanter un système national de monitorage de l'IAS devrait figurer parmi les priorités de la santé publique en Tunisie.

# Mots-clés

Maladie iatrogène - Infection croisée - Unités de soins intensifs - Soins de réanimation - Prévalence - Facteurs de risque - Acinetobacter Baumanii

### SUMMARY

Objectives: To determine the prevalence of Healthcare-Associated Infection (HAI) in medical Intensive Care Unit (ICU), risk factors for these infections and identify the predominant infecting organisms.

Methods: A 1-day point-prevalence study within all medical ICUs in Tunisia, all patients occupying an ICU bed over a 48-hour period were included. Rates of HAI, resistance patterns of microbiological isolates and potential risk factors for HAI were recorded.

Results: One hundred and three patients were collected from 15 Tunisian medical ICUs. HAI prevalence was 25.2% CI 95% [15-35]. The most frequent HAIs were hospital acquired pneumonia in 19 cases (59%) and catheter related infection in 5 cases (15%). Independent factors associated with HAI occurrence were SAPSII score ≥ 33 with OR 1.047; CI 95% [1.015-1.077], p=0.003 and recent hospitalization with OR 4.14 CI 95% [1.235-13.889], p=0.021. Non-fermenting pathogens were the most frequent microorganisms reported in ICUs ecology, prior colonization and HAIs of the screened patients.

Conclusion: HAIs are frequent in medical ICUs in Tunisia, which emphasize the importance of specific measures for surveillance and infection control in critically ill patients. Implementing a national monitoring system of HAI should be a major priority of public health in Tunisia.

# **Key-words**

latrogenic Disease - Cross Infection - Intensive Care Units - Critical Care - Prevalence - Risk Factors - Acinetobacter baumannii

# انتشار العدوى المرتبطة بالرعاية الطبية في العناية المركزة تونس

# نتأئج دراسة NOSOREA1

ا**لأهداف:** تحديد مدى انتشار العدوى المرتبطة بالرعاية الصحية (HAI) في وحدة العناية المركزة الطبية، وتحديد مخاطر هذه العدوي والوقوف على أسبابها.

ا**لطريقة:** تم إجراء دراسة للتعرف على مدى انتشار العدوى طيلة يوم واحد في جميع وحدات العناية المركزة الطبية في تونس، وشملت جميع المرضى الذين يشغلون سريراً في وحدة العناية المركزة لمدّة لا تقلّ عن 48 ساعة. وقد وقع تسجيل معدلات HAI وأنماط مقاومة العزلات الميكروبيولوجية وعوامل الخطر المحتملة لـ HAI.

النتائج: تم جمع مائة وثلاثة مرضى من 15 وحدة عناية مركزة طبية تونسية. كان انتشار 35-15 ٪ OI 25.2 . [HAI 25.2 . العوامل المستقلة المرتبطة بحدوث HAI كانت AAI كانت SAPSII ≤ 33 OR 1.047 ؛ 95 p = 0.003 95 . [1.015-1.07] ٪ CI والمستشفى الأخير بـ P = 0.021 4.14 ، [1.235-13.889] ، OR . كانت مسببات الأمراض غير المتخمرة هي الكائنات الدقيقة الأكثر شيوعًا التي تم الإبلاغ عنها في علم بيئة وحدة العناية المركزة ، وحاملي المرض سابقاً و HAI للمرضى الذين تم فحصهم.

**الاستنتاج:** إن HAIs موجودة بصفة متلازمة في وحدات العناية المركزة الطبية في تونس ، والتي تؤكد على أهمية اتخاذ تدابير محددة للمراقبة ومكافحة العدوى خصوصاً لدى المرضى ذوي الحالات الحرجة. كما ينبغي أن يكون تنفيذ نظام رصد وطني لهيئة HAI بين أولويات الصحة العامة في تونس.

**الكلمات الرئيسية:**مرض علاجي المنشأ - العدوى المتصالبة - وحدات العناية المركزة - الرعاية الحرجة - الانتشار - العوامل المؤثرة - Acinetobacter baumannii

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### INTRODUCTION

Healthcare-associated infection (HAI) represents a major public health concern worldwide. The burden of HAI in developing countries is high [1]. According to the World Health Organization, a limited number of studies in these settings have been published in the scientific literature, so prevalence of HAI in low-and middle-income countries and regular monitoring occurrence may be unfeasible at national level [2]. In Tunisia, there is no national or regional monitoring system of HAI. It is worth noting that HCAIs in intensive care unit (ICU) are more common and life threatening than in general ward because of the frequent use of invasive procedures and multiple therapies [3]. Controlling this fatal scourge should begin with greater awareness of HAI frequency and ICU ecology. That is why conducting multi-center Tunisian studies is necessary to quide control measurements against HAI and to improve surveillance and infection-control practices. We aimed to determine the prevalence of HAI in medical Tunisian ICUs. Secondary endpoints were to identify the predominant infecting microorganisms and evaluate independent risk factors of HAIs.

#### **METHODS**

It was a one-day point-prevalence study (September 26<sup>th</sup>, 2017). All medical ICUs across Tunisia were invited to participate, excluding cardiologic and paediatric care units. All patients occupying an ICU bed over a 48-hour period were included. In every participating ICU, a referred physician chosen for the study received 2 Word documents to fill up:

 Service data: hospital, ICU beds' capacity, most reported microorganism in the ecology of the ICU, occupation rate, ratio nurse/patients, ratio caregiver/patients and ratio Physiotherapist/patients during the study day; mechanical ventilation support and invasive devices present at the survey day.

 Patients' data: demographic characteristics, severity scores, comorbidities, prior multidrug resistance (MDR) colonization, recent hospitalization and reason for actual ICU admission. All suspected or confirmed HAI present at the survey day were reported. HAI types, sites and resistance patterns of microbiological isolates were recorded.

Healthcare-Associated Infection (HAI): infection occurred after hospital admission ( $\geq$ 48 h) that was neither present nor incubating on admission was considered as HAI [4].

**Data analysis**: Continuous variables are presented as mean ± standard deviation, and categorical variables are shown as percentages. The prevalence of HAI (defined

as the number of infected patients divided by the total number of patients) and the constituent ratio of a specific HAI (defined as a specific type of HAI divided by the total number of HAI) were assessed. The 95 % confidence intervals (CI) for each parameter were also estimated. For potential risk factors, variables with a P-value of less than 0.05 in a univariate analysis were selected and included in a multivariate logistic regression model. Odds ratio (OR) and 95 % CI were evaluated to assess associations between risk factors and HAI. Statistical analyses were performed using SPSS 23.0; P-value less than 0.05 was considered as statistically significant. This observational study did not affect the clinical course of treatment, and all the data were analysed anonymously.

#### RESULTS

On the study day, 103 patients were collected from 15 ICU all around the country of Tunisia, with a mean occupation rate of 66%. General characteristics of the included ICUs are detailed in table I. Seven ICUs performed without caregivers and 3 without physiotherapist. Among patients included, 53% were invasively ventilated and only 9% required noninvasive mechanical ventilation. The most reported microorganism in the ecology of the ICUs was *Acinetobacter spp* in 66% of cases. The mean age of the included patients was 46±20 years, 60% were male. The mean SAPSII and APACHE II score on admission were respectively 33±19 and 13±8. The mean SOFA score on the study day was 5±5. Main reason for ICU admission was respiratory failure. Baseline characteristics of the patients are detailed in table II.

 Table 1: General characteristics of the 15 included medical ICUs

 on the study day (September 26<sup>th</sup>, 2017) in Tunisia

	15 ICUs
Invasive mechanical ventilation, n (%)	55 (53)
Noninvasive mechanical ventilation, n (%)	9 (9)
Central venous catheter, n (%)	56 (54)
Central arterial catheter, n (%)	29 (9)
Urinary catheter, n (%)	79 (76)
Caregivers, n	8
Physiotherapists, n	12
Mean nurse/patient ratio	1/2.4
Acinetobacter Baumanii*, n (%)	10 (66)

\*most prevailing pathogen in ICU ecology

Table 2 : Baseline characteristics of 103 patients within 15medical ICUs on the study day (September 26th, 2017) in Tunisia

	N=103
Age, n (%), years	46±20
Sex	
Male, n (%)	62 (60)
Female, n (%)	41 (40)
SAPSII, mean ± SD	33±19
APACHEII, mean ± SD	13±8
Comorbidities, n (%)	
Hypertension	23 (22,3)
Diabetes	17 (16,5)
Immunosuppression	9 (8,7)
COPD	8 (7,8)
Reason for admission, n (%)	
Respiratory failure	30 (29,1)
Neurologic failure	24 (23,3)
Burns	11 (10,7)
Trauma	9 (8,7)
Shock	8 (7,8)
Prior MDR colonization, n (%)	29 (28,3)
CRAB	11 (10,6)
Pseudomonas aeruginosa	12 (11,6)
MRSA	9 (8,7)
Klebsiella pneumonia	11 (10,6)
Recent hospitalization, n (%)	25 (24,3)
Individual ICU room stay, n (%)	61 (59,2)
SOFA on the study day, mean ± SD	5±5

SD: Standard Deviation; SAPS II: Simplified Acute Physiology Score; APACHE II: Acute Physiologic and Chronic Health Evaluation II; SD: standard deviation; COPD: chronic obstructive pulmonary disease; MDR: multidrug resistant; CRAB: carbapenem-resistant *Acinetobacter Baumanii*; MRSA: methicillin resistant *staphylococcus aureus*; SOFA: Sequential Organ Failure Assessment

HAI was recorded in 32 cases giving a prevalence of 25.2% CI 95 % [15-35]. Among these HAI, 21 (66%) were confirmed with microbiological documentation and 11 (34%) were suspected on the study-day. The most frequent HAIs were hospital-acquired pneumonia in 19 cases (59%) and catheter related infection in 5 cases (15%). The remaining HAIs were: Blood stream infections (n=3), Urinary tract infections (n=3), skin infection (n=1) and peritonitis (n=1).

Non-fermenting pathogens were the most frequent microorganisms isolated in 12 cases among them *pseudomonas aerogenosa* was observed in 10 cases and *acinetobacter baumanii* in 2 cases. Carbapenem resistant pathogens were isolated in 4 cases. The enterobacteriacae microorganisms were recorded in 7 cases with *Klebsiella pneumonia* isolated in 4 cases, *proteus mirabilis* in 2 cases and *citrobacter freundii* in one case. These enterobacteriacae were bata-lactam resistant in 4 cases and carbapenem resistant in only one case. Fungi were isolated in 3 cases and Gram positive cocci in 2 cases.

Univariate analysis comparing the HAI group and the non-HAI group showed that HAI group had higher severity scores on admission and SOFA score on the study day, experienced more hypertension and recent hospitalization, and needed more isolation (table III). Independent factors associated with HAI occurrence in multivariate analysis are show in table IV.

**Table 3**: Univariate analysis comparing HAI group versus non-HAI group among 103 patients within 15 Tunisian medical ICUs on the study day (*September 26th, 2017*)

	HAI group N=26	Non-HAI group N=77	р
Age, mean ± SD (years)	49±20	45±20	0.363
Male gender, n (%)	15 (57)	47 (61)	0.763
SAPSII	46±15	28±19	<10 <sup>-3</sup>
APACHEII	18±5	12±8	0.001
SOFA (on study day)	7±4	4±4	0.017
Hypertension, n (%)	10 (38)	13 (17)	0.022
Diabetes, n (%)	6 (23)	11 (14)	0.296
COPD, n (%)	2 (7)	6 (8)	0.987
Immunosuppression, n (%)	1 (4)	8 (10)	0.307
Recent hospitalization, n (%)	12 (46)	13 (17)	0.003
Isolation, n (%)	11 (42)	9 (11)	0.001

SD: standard deviation; SAPS II: Simplified Acute Physiology Score; APACHE II: Acute Physiologic and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment; COPD: Chronic Obstructive Pulmonary Disease.

**Table 4**: Independent factors associated with HAI occurrencein multivariate analysis among 103 patients within 15 Tunisianmedical ICUs on the study day (September 26<sup>th</sup>, 2017)

	Odds Ratio	95% CI	р
SAPSII > 33			0.003
SAPS II ≤ 33	1	-	
SAPS II > 33	1.047	[1.015-1.077]	
Recent hospitalization			0.021
No	1	-	
Yes	4.14	[1.235-13.889]	

SAPS II: Simplified Acute Physiology Score

### DISCUSSION

Through a transversal 1-day point prevalence study, we aimed to determine the prevalence rate of HAI in Tunisian medical ICUs which was of the order of 25.2% CI 95% [15-35]. This was the first multicentre Tunisian study focusing on HAI in ICUs. This concern is insufficiently studied in Tunisia and the Maghreb arena. Between 1995 and 2010,

the World Health Organization declared a prevalence of HAI of 17.9 % in Tunisia and 17.8 % in Morocco. It also highlighted the paucity of available data in all low-and middle-income countries, making these values possibly under- or overestimated [2]. According to the same report, the proportion of patients with ICU-acquired infection in low-and middle-income countries was as high as 35.2% CI 95% [24.2-48.0] (pooled cumulative incidence).

Within the Maghreb arena, different authors report different HAI prevalence rates among ICU patients. In a prospective survey in a 22-bed medical surgical ICU in a teaching hospital in Sfax (Tunisia), reported HAI rate was 21.1/100 hospitalizations [5]. During 2013, Trifi A. et al reported within a 8-bed medical ICU (RABTA teaching hospital in Tunis) a HAI incidence of 66.4 episodes/1000 days of hospitalization [6]. Other studies focused on hospital HAI prevalence, all wards combined: it was of 6.7% within Hassan II teaching hospital of Fès, Morocco [7] and 16.2% within Bab el Oued teaching hospital of Alger, Algeria [8]. A yearly survey of nosocomial infection prevalence was carried from 2001 to 2005 in the university hospital of Blida (Algeria) to evaluate the impact of a program against HAI implemented in 2001. A total of 1,362 patients were included in the five surveys. From 2001 to 2005, the prevalence of nosocomial infections decreased from 9.8 to 4% (p < 0.001) [9].

The overall prevalence of HAIs in ICU patients in this multicenter study was 25%, which is substantially higher than that described in the ECDC surveillance report for European Union countries. In Europe, HAI prevalence among patients admitted to ICU was 19.5 % [10]. Several factors can explain this difference. Besides lack of monitoring system of HAI, nurses work burden was notably important in our ICUs as evidenced by the nurse/patients ratio and the absence of caregivers in half-screened ICUs. Importance of vascular and urinary devices and invasively ventilated patients also contribute to promote HAI emergence.

SAPSII score  $\geq$  33 and recent hospitalization were identified as independent factors associated with HAI occurrence. These factors inquire about patients' severity level. Previous hospitalization was already reported by Saïdani M et al. as a risk factor for carbapenem resistance acquisition [11]. Kallel et al. demonstrated that SAPS II > 35 is an independent risk factor for mortality in ICU among patients with HAI [5]. HAP was the most frequently identified HAI (59 %). Kallel H. et al conducted an ICU prospective observational cohort study in Sfax (Tunisia) and reported 34.7 HAI/1000 days of hospitalization from which 58.2 % were HAP [5]. In 2016, another prospective cohort study carried out in a surgical (26 beds) and medical (5 beds) ICUs of the Tunisian University hospital of Sahloul (Sousse) found 53.7% of HAP among HAI [12]. BSI was the third HAI site reported in our study. EI Kettani A. et al conducted a prospective longitudinal study on patients admitted to the Ibn Rochd University Hospital ICU of Casablanca (Morocco) to determine incidence of acquired healthcare-associated bacteremia, which ranged from 7.3 to 13.7/1,000 hospital days [13].

In the present study, non-fermenting pathogens were the most frequent microorganisms reported. Notably, Acinetobacter Baumanii was the most frequent pathogen on the ICUs ecology (66 %) and also responsible of prior colonization of the screened patients. In Tunisia, production of OXA-23 was the important mechanism of resistance to carbapenem among Acinetobacter Baumanii [14]. In 2018, a recent study focusing on 246 carbapenemresistant Acinetobacter Baumanii isolates from a teaching hospital in Sousse (Tunisia) evidenced the dissemination of a single clone of NDM-1-producing Acinetobacter Baumanii. Authors highlighted that North Africa countries may constitute a significant reservoir for NDM-1-producing Acinetobacter Baumanii [15]. This multidrug resistant bacteria is among the biggest concern for Tunisian ICUs because of limited therapeutics and poor prognosis [6, 16]. The enterobacteriacae were the second most frequent microorganisms isolated. The emergence of ESBLand carbapenemase-producing enterobacteriaceae in Tunisian and Libyan hospitals is already reported [17]. In 2012, the emergence of five OXA-48 carbapenemaseproducing Enterobacteriaceae was described within a Tunisian hospital. Authors underlines the necessity of enhanced surveillance and rapid detection of this resistance mechanism to prevent its further spread [6, 11]. In 2016, Chabah M. et al reported a prevalence of enterobacteriacae infections of 12.2 % and carbapenemase-producing enterobacteriacae infections of 2.6 % in the neonatal ward and ICU of the Abderrahim El Harrouchi Children hospital of Casablanca (Morocco) [18]. This study focused only on medical and adult Tunisian ICUs. Its findings need to be enhanced with bigger sample including surgical, pediatric and neonatal ICUs.

#### CONCLUSION

In this first multicenter Tunisian study, HAI prevalence among Tunisian medical ICUs was of 25.2 %. These findings reinforces that HAI is a global public health issue, so implementing a national monitoring system of HAI should be a major priority in Tunisia. HAI surveillance is a highly demanding and challenging task, but should be the first step of actions against this epidemiological threat.

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