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Secular trends of healthcare-associated infections at a teaching hospital in Taiwan, 1981–2007

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A R T I C L E   I N F O

Article history:
Received 10 September 2009
Accepted 7 May 2010
Available online 20 July 2010

Keywords:
Healthcare-associated infection
Infection control
Surveillance

S U M M A R Y

The National Taiwan University Hospital (NTUH) adopted international guidelines for surveillance and control of healthcare-associated infection (HCAI) in 1981. This report describes the secular trends in HCAI at the NTUH over the past 27 years according to site of infection, aetiological agents and control measures. Clinical and microbiological data were collected by infection prevention and control nurses using a standardised case-record form. Specific control programmes were implemented and/or intensified as needed. Poisson or negative binomial regression analysis was used to quantify time trends of the incidence of HCAI. The annual number of discharges increased from 25 074 to 91 234 with a parallel increase in the Charlson comorbidity index. Active HCAI surveillance and periodic feedback were associated with a marked decrease in surgical site infections from 1981 to 2007 (2.5 vs 0.5 episodes per 100 procedures, \(P < 0.0001\)). On the other hand, there was a 4.8-fold increase in bloodstream infections (BSIs) (0.39 vs 1.88 episodes per 100 discharges, \(P < 0.0001\)). The average annual increase of pathogen-specific HCAI incidence during 1981–2007 was 11.4% for meticillin-resistant Staphylococcus aureus (MRSA), 75.4% for extensively drug-resistant A. baumannii (XDRAB), and 7.5% for Candida albicans (\(P < 0.0001\), respectively). The infection prevention and control programme was upgraded in 2004 by implementing annual, intensive, project-based control programmes, and decreases in rates of HCAI, BSI, MRSA and XDRAB were observed. This long term study demonstrates the need to couple surveillance of HCAI with focused control programmes. Hospitals must invest in adequate manpower to accomplish these goals.

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I n t r o d u c t i o n

Ongoing surveillance of healthcare-associated infection (HCAI) is an essential component of hospital infection control programmes. The goals are to assess the burden of infectious diseases, identify important problems, monitor the efficacy of specific interventions and support rational hospital policies. The National Nosocomial Infections Surveillance System was established in the 1980s. HCAIs were reported to be significantly decreased in hospitals that adopted surveillance programmes. Hospital-wide surveillance programmes are highly labour intensive and tend to divert resources needed to implement control measures and prevention activities. Consequently, they are often of minimal interest to hospital policymakers except during major outbreaks such as severe acute respiratory syndrome (SARS). It has become increasingly apparent that hospital support for surveillance programmes needs to be justified by improved outcomes. To accomplish these goals they must be closely linked to effective intervention strategies.

The first infection prevention and control hospital-wide HCAI surveillance programme in Taiwan, based on international...
guidelines, was established at the National Taiwan University Hospital (NTUH) in 1981. A vigorous hospital-wide hand hygiene programme was initiated in 2004. This report describes the secular trends in HCAI at the NTUH during the past 27 years (1981–2007) according to site of infection, aetiological agents and control measures.

Methods

Hospital setting

The NTUH is a 2200-bed teaching hospital located in Taipei, Taiwan. It provides both primary and tertiary medical care, and served approximately 2000 inpatients, 7000 outpatients, and 300 emergency department visits daily in 2007. There are 220 intensive care unit (ICU) beds, 1866 beds in other acute care units, and 160 beds in a psychiatric day care unit. Among the acute care units are the following beds: 700 on medical wards, 800 on surgical wards, 200 on paediatric wards, 130 on gynaecology wards, and 100 on oncology wards. There are 68 negative pressure isolation rooms.

Infection prevention and control programme

The NTUH Infection Control Team currently consists of 10 full-time infection control nurses (ICNs), two full-time technicians and is supervised by two infection disease physicians. Prospective, hospital-wide on-site surveillance of HCAI was conducted by weekly visits of ICNs to all patient units. Hospital charts were reviewed to identify patients with HCAIs according to definitions of the Centers for Disease Control and Prevention with the help of infectious disease physicians at weekly meetings. The data were collected on standardised data collection forms (Appendix 1) and incorporated into the computer database by manual entry. The unit-specific incidences of HCAI (episodes per 100 discharges) including overall and site-specific infection rates were analysed monthly and compared with historical data. Feedback was provided to each service to stimulate intervention measures.

Infection prevention and control events and interventions

Multiple special infection prevention and control events and interventions occurred during the study period. Prevention and control measures for surgical site infection (SSI) included intensified surveillance of SSI with feedback to the surgeons during March to June 2003. The number of acute care beds was 1846 in 1990 in HCAI with admission, as defined by Charlson comorbidity index, are shown in Figure 1A. The number of acute care beds was 1846 in 1999 and 2212 in 2007. The number of discharges was 25 074 in 1981 and 91 234 in 2007. The average length of patient stay decreased from 11.3 in 1993 to 7.3 days in 2007. This was accompanied by an increasing proportion of patients admitted with multiple underlying conditions.

Secular trends in annual rates of overall infections

The annual number of discharges and the severity of underlying diseases on admission, as defined by Charlson comorbidity index, are shown in Figure 1A. The number of acute care beds was 1846 in 1999 and 2212 in 2007. The number of discharges was 25 074 in 1981 and 91 234 in 2007. The average length of patient stay decreased from 11.3 in 1993 to 7.3 days in 2007. This was accompanied by an increasing proportion of patients admitted with multiple underlying conditions.

Secular trends in the distribution of infections according to site

The major sites of HCAIs over the entire study period are shown in Figure 1D. The average annual change (95% confidence interval) for bloodstream infection (BSI) was 6.4% (5.5% to 7.4%, P < 0.0001); urinary tract infection (UTI), 1.9% (1.2% to 2.5%, P < 0.0001);
Changes in the distribution of pathogens

The proportions of infections by pathogens in 1981 and 2007 are shown in Table I. Gram-negative bacteria were about twice as common as Gram-positives during both time periods. There was an 8.7-fold increase in fungal infections (mainly *Candida* spp.) from 1981 to 2007 (*P* < 0.0001). Rate of *C. difficile* infection increased from 0.004 episodes per 100 discharges in 1983 to 0.037 in 2007 (*P* = 0.008).

Secular trends in the major pathogens

Annual percentage changes in the incidences of pathogens causing all HCAI during 1981–2007 are shown in Table II. The average annual increase of pathogen-specific HCAI incidence during 1981–2007 was 11.4% for MRSA, 7.5% for *C. albicans*, and 75.4% for XDRAB (*P* < 0.0001, respectively).

The incidences for all BSI pathogens increased significantly (Table III). The secular trends of pathogen-specific BSI rates closely mirrored the overall rates of HCAIs, except for an aerobes. The secular trends of the major pathogens causing BSI are shown in Figure 2A. Fungi (mainly *Candida* spp.) were rare in the 1980s and increased rapidly in later years. Note the decrease in BSI caused by *S. aureus, Acinetobacter* spp., and *C. albicans*, but not *Escherichia coli* after the implementation of a hand hygiene programme.

Secular trends for *S. aureus* infections

The secular trends of the annual incidence of *S. aureus* and MRSA are shown in Figure 2B. *S. aureus* steadily increased over the study period, peaked in 2001 and fell thereafter (year 2003 vs 2007: *P* < 0.0001). The incidence of MRSA paralleled that of all *S. aureus* infections and accounted for 69.2% of *S. aureus* infections at their peak in 2000.

Secular trends for *Acinetobacter* infections

The secular trends of the annual incidence of *Acinetobacter* and XDRAB are shown in Figure 2C. XDRAB began to appear in 1999, increased rapidly and peaked in 2005. XDRAB markedly decreased...
in association with the hand hygiene programme and possibly with other interventions between 2003 and 2007 (P < 0.0001).

Changes in the distribution of the five most common pathogens

There were modest place changes of the leading pathogens causing any HCAI, BSI and UTI during five-year intervals from 1981 to 2007. The leading pathogen causing BSI was Klebsiella spp. (18.6%) in 1981, E. coli (20.9%) in 1986, Candida spp. and other yeasts (18.6%) in 1996, S. aureus (12.7%) in 2001, and Klebsiella spp. (11.0%) in 2007.

Table I
Incidence of healthcare-associated infections and the proportion by site and pathogen at the National Taiwan University Hospital, 1981–2007

| Parameters | 1981 | 2007 | Average annual change, % (95% CI) | P-value*
|------------|------|------|-----------------------------------|--------
| Total no. of discharges | 25,074 | 91,234 | | |
| Total no. of infections | 1002 | 4125 | | |
| Total no. of pathogens | 1181 | 5081 | | |
| Overall incidence, per 100 discharges | 4.00 | 4.52 | 0.3 (–0.1 to 0.7) | 0.1621
| Site-specific infection | | | | |
| Surgical site | | | | |
| No. of episodes | 374 | 279 | | |
| Incidence, per 100 procedures | 2.5 | 0.5 | –6.1 (–7.2 to –5.0) | <0.0001
| Proportion (%) | 37.3 | 6.8 | | |
| Urinary tract | | | | |
| No. of episodes | 208 | 1340 | | |
| Incidence, per 100 discharges | 0.83 | 1.47 | 1.9 (1.2 to 2.5) | <0.0001
| Proportion (%) | 20.8 | 32.5 | | |
| Respiratory tract | | | | |
| No. of episodes | 100 | 347 | | |
| Incidence, per 100 discharges | 0.40 | 0.38 | –1.0 (–1.7 to –0.3) | 0.0083
| Proportion (%) | 10.0 | 8.4 | | |
| Bloodstream | | | | |
| No. of episodes | 98 | 1714 | | |
| Incidence, per 100 discharges | 0.39 | 1.88 | 6.4 (5.5 to 7.4) | <0.0001
| Proportion (%) | 9.8 | 41.6 | | |
| Others | | | | |
| No. of episodes | 222 | 445 | | |
| Incidence, per 100 discharges | 0.89 | 0.49 | –3.6 (–5.1 to –2.1) | <0.0001
| Proportion (%) | 22.2 | 10.8 | | |
| Pathogens | | | | |
| Gram-positive aerobic bacteria | | | | |
| Incidence, per 100 discharges | 0.016 | 0.153 | 4.0 (2.9 to 5.0) | <0.0001
| Proportion (%) | 0.6 | 6.8 | | |
| Gram-negative aerobic bacteria | | | | |
| Incidence, per 100 discharges | 0.024 | 0.217 | 7.7 (6.3 to 9.1) | <0.0001
| Proportion (%) | 0.8 | 41.6 | | |
| Anaerobic bacteria | | | | |
| Incidence, per 100 discharges | 0.048 | 0.166 | 5.2 (3.7 to 6.8) | <0.0001
| Proportion (%) | 0.2 | 6.8 | | |
| Fungi | | | | |
| Incidence, per 100 discharges | 0.016 | 0.066 | 3.0 (1.2 to 4.8) | <0.0001
| Proportion (%) | 0.6 | 2.8 | | |

CI, confidence interval.
* Negative binomial regression was used to model the secular trends of the annual incidence.

Table II
Time trends of pathogen-specific healthcare-associated infections at the National Taiwan University Hospital during 1981–2007

| Pathogen | Incidence (per 100 discharges) | Average annual change, % (95% CI) | P-value*
|-----------|---------------------------------|-----------------------------------|--------
| Staphylococcus aureus | 0.199 | 0.404 | 3.1 (1.9 to 4.3) | <0.0001
| Meticillin-resistant | 0.028 | 0.272 | 11.4 (8.3 to 14.6) | <0.0001
| Meticillin-susceptible | 0.164 | 0.132 | –2.8 (–3.9 to –1.7) | <0.0001
| Enterococcus spp. | 0.004 | 0.452 | 0.2 (–1.8 to 2.2) | 0.8463
| Escherichia coli | 0.634 | 0.650 | –0.2 (–1.3 to 0.9) | 0.719
| Klebsiella spp. | 0.447 | 0.552 | 0.5 (–0.6 to 1.5) | 0.5883
| Enterobacter spp. | 0.209 | 0.356 | 0.0 (–0.6 to 0.6) | 0.9234
| Pseudomonas aeruginosa | 0.538 | 0.516 | –1.7 (–2.4 to –1.0) | <0.0001
| Acinetobacter spp. | 0.227 | 0.393 | 2.4 (1.4 to 3.4) | <0.0001
| Extensively drug-resistant | 0.000 | 0.105 | 75.4 (46.9 to 109.3) | <0.0001
| Candida albicans | 0.016 | 0.272 | 7.5 (5.3 to 9.6) | <0.0001

CI, confidence interval.
* Negative binomial regression was used to model the secular trends of the annual incidence.

Table III
Time trends of pathogen-specific healthcare-associated bloodstream infections at the National Taiwan University Hospital during 1981–2007

| Pathogen | Incidence (per 100 discharges) | Average annual change, % (95% CI) | P-value*
|-----------|---------------------------------|-----------------------------------|--------
| Staphylococcus aureus | 0.092 | 0.617 | 8.4 (7.0 to 9.8) | <0.0001
| Meticillin-resistant | 0.024 | 0.203 | 10.3 (8.1 to 12.5) | <0.0001
| Meticillin-susceptible | 0.000 | 0.138 | 23.4 (16.9 to 30.2) | <0.0001
| Enterococcus spp. | 0.000 | 0.180 | 7.85 (6.3 to 9.3) | <0.0001
| Escherichia coli | 0.291 | 1.137 | 5.4 (4.7 to 6.1) | <0.0001
| Klebsiella spp. | 0.048 | 0.180 | 3.3 (2.3 to 4.3) | <0.0001
| Enterobacter spp. | 0.076 | 0.246 | 5.8 (4.6 to 7.0) | <0.0001
| Pseudomonas aeruginosa | 0.016 | 0.153 | 4.0 (2.9 to 5.0) | <0.0001
| Acinetobacter spp. | 0.040 | 0.217 | 7.7 (6.3 to 9.1) | <0.0001
| Extensively drug-resistant | 0.000 | 0.045 | 62.1 (37.7 to 90.8) | <0.0001
| Anaerobic bacteria | 0.004 | 0.052 | 2.1 (1.0 to 3.6) | 0.0005
| Fungi | 0.008 | 0.213 | 15.0 (9.9 to 20.4) | <0.0001
| Candida albicans | 0.000 | 0.105 | 13.5 (8.7 to 18.4) | <0.0001

CI, confidence interval.
* Negative binomial regression.
* Poisson regression.
in 2007. Gram-negative bacilli accounted for 60% of healthcare-associated BSI in 2007. Among the leading five pathogens causing UTI, *E. coli* was the first or second most common pathogen followed by *C. albicans* and other yeasts, *Enterococcus* spp. *Enterobacter* spp., *Pseudomonas aeruginosa* and *Klebsiella* spp.

**Discussion**

This report describes the secular trends of HCAIs over the course of a 27 year prospective hospital-wide surveillance programme in a large university hospital in Taiwan. The major findings are similar to those in tertiary care hospitals in western countries. Among the leading five pathogens causing UTI, *E. coli* was the first or second most common pathogen followed by *C. albicans* and other yeasts, *Enterococcus* spp. *Enterobacter* spp., *Pseudomonas aeruginosa* and *Klebsiella* spp.. There was a gradual increase in admissions of patients with severe underlying disease. The overall rate of the HCAI increased slowly and has fluctuated at approximately 4.5 episodes per 100 discharges. This is in the high range reported by other tertiary care facilities. The time trend of overall infection rates tended to obscure the substantial changes in SSI rates, a 4.8-fold increase in BSI, an increase in UTI, the appearance of XDRAB and MRSA, and an 8.7-fold increase in fungal infections.

The remarkable decrease in SSI may result from improvements in surgical prophylaxis, active surveillance and periodic feedback, and changes in surgical practice including the increasing shift to ‘day surgery’ which led to decreased detection of SSIs in a system which depended on ICNs going through inpatient charts. However, there was no PDS apart from those patients readmitted for

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**Figure 2.** (A) Annual incidence (per 100 discharges) of the major pathogens causing healthcare-associated bloodstream infections during 1981–2007. (B) Annual incidence (per 100 discharges) of healthcare-associated infections due to *Staphylococcus aureus* and meticillin-resistant *S. aureus* (MRSA) during 1981–2007. (C) Annual incidence (per 100 discharges) of healthcare-associated infections due to *Acinetobacter* spp. and extensively resistant *Acinetobacter baumannii* during 1981–2007. XDRAB, extensively drug-resistant *A. baumannii*. 
A notable decrease was observed in the overall HCAI rates since 2004 when a hospital-wide hand hygiene programme was launched. However, due to a limited postintervention period, it is not possible to attribute the decrease to the hand hygiene programme. Therefore further analysis is required by expanding the follow-up periods which might make the formal statistical inference possible.

Regarding pathogens causing healthcare-associated BSI, a multicentre study in the USA [Surveillance and Control of Pathogens of Epidemiological importance (SCOPE)] from 1995 to 2002 showed that Gram-positive organisms accounted for 65% of cases and the leading pathogens were coagulase-negative staphylococci, S. aureus, and enterococci. Furthermore, the proportion of healthcare-associated BSI due to Gram-positive cocci increased gradually. Most of the studies showed coagulase-negative staphylococci were the leading cause of healthcare-associated BSI. However, in this study, Gram-negative bacilli accounted for 60% of healthcare-associated BSI in 2007, and the leading pathogen was Klebsiella spp., which is very unusual in Europe and North America. Therefore when considering HCAs, regional factors should be considered. Despite these achievements we have not as yet been able to achieve our goal to reduce overall infection rates below 4.5%. It may be impossible to reduce the rate in a structurally and immunocompromised patient population that requires aggressive antimicrobial therapy for endogenous infections. A third of patients had one or more malignancies. This hospital also maintains very active organ and bone marrow transplantation programmes and ICUs. Rates of infection are more meaningful when adjusted for major underlying diseases and disease severity, such as the Charlson comorbidity index, the McCabe–Jackson criteria and Acute Physiological Assessment and Chronic Health Evaluation (APACHE) score. It is apparent from these observations that there needs to be a major shift in hospital infection prevention and control measures from passive surveillance to focused control programmes of proven efficacy. The CDC 12-step campaign to prevent antimicrobial resistance in healthcare settings provides a good start. Some of the key measures optimise conditions that prevent infections, e.g. removing an unnecessary device, minimising broad spectrum antibiotics, avoiding long term antimicrobial prophylaxis, treating infection rather than colonisation, and preventing transmission. Our major successes were achieved when we adopted some of these measures.

Time-trend analysis performed in this study can be considered a screening tool to decide whether a more intensive investigation into underlying causes is justified. Also regression analysis allows us to state the annual changes in HCAI rates. However, there are limitations to this study from the methodological viewpoint. This study has demonstrated that changes in HCAs were due to multiple factors which occurred in different time periods. Thus, the underlying trend might not be continuously increasing or decreasing. Also, the time trends might not be the same for overall HCAI rate, site-specific or pathogen-specific HCAI rates. The model used in our study to quantify the linear trend could not account for other variations such as possible serial correlation. However, a longer time period of one year was used in our analysis, to minimise the correlations between adjacent periods.

In conclusion, this long term prospective hospital-wide surveillance study indicates what needs to be addressed to prevent and control HCAI. There needs to be a shift in the paradigm from surveillance with feedback to implementation of proven, control measures using focused surveillance to monitor efficacy. This will require a greater investment on the part of hospitals, if we want to reduce HCAI to the minimum and thus improve the quality and safety of patient care.

Acknowledgements

We are grateful to members of the Center for Infection Control for the contribution of the hospital-wide healthcare-associated infection surveillance programme and all the staff in the hospital for their commitment to improving patient safety and reducing healthcare-associated infection. We are also grateful to members of the Biostatistics Laboratory, College of Public Health, National Taiwan University Taipei for contributing to the statistical analysis. The authors are indebted to Prof. C. Kunin and Prof. W.-C. Hsieh for their critical reviewing and comments.

Conflict of interest statement

None declared.

Funding source

Y.-C. Chen received grants from the Center for Disease Control, Department of Health, Taiwan (DOH96-DC-1010, DOH97-DC-1005).

Appendix. Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.jhin.2010.05.001.

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