A Major Reduction in Hospital-Onset Staphylococcus Aureus Bacteremia in Australia - 12 Years of Progress: An Observational Study

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Summary:
There have been efforts worldwide to reduce the incidence of hospital-onset *Staphylococcus aureus* bacteraemia (SAB). This longitudinal study demonstrates a nation-wide reduction in both methicillin-resistant and methicillin-susceptible SAB in Australia.
Abstract

**Background:** *Staphylococcus aureus* bacteraemia (SAB) is a serious cause of morbidity and mortality. This longitudinal study describes significant reductions in hospital-onset SAB (HO-SAB) in Australian hospitals over the past 12 years.

**Methods** An observational cohort study design was used. Prospective surveillance of HO-SAB in one hundred and thirty-two hospitals in Australia was undertaken. Aggregated data from all patients who acquired HO-SAB; defined as one or more blood cultures positive for *Staphylococcus aureus* taken from a patient who had been admitted to hospital for more than 48 hours. The primary outcome was the incidence of HO-SAB, including both methicillin-resistant (MRSA) and methicillin-susceptible (MSSA) strains.

**Results:** A total of 2,733 HO-SAB cases were identified over the study period giving an aggregate incidence of 0.90/10,000 patient days (95% CI, 0.86-0.93). There was a 63% decrease in the annual incidence, from 1.72/10,000 PDs in 2002 (95% CI, 1.50-1.97) to 0.64/10,000 PDs (95% CI, 0.53-0.76) in 2013. The mean reduction per year was 9.4% (95% CI, -8.1%, -10.7%). Significant reductions in both HO-MRSA (0.77 to 0.18 per 10,000 PDs) and HO-MSSA (1.71 to 0.64 per 10,000 PDs) bacteraemia were observed.

**Conclusion:** There was a major and significant reduction in incidence of HO-SAB caused by both MRSA and MSSA in Australian hospitals since 2002. This reduction coincided with a range of infection prevention and control activities implemented during this time. It suggests that national and local efforts to reduce the burden of healthcare associated infections have been very successful.
Background

In the past decade, efforts to decrease healthcare associated infections (HAIs), have increased worldwide. More than a decade ago, the landmark paper “To Err is Human: Building a Safer Health System” had a major impact on focussing the attention of policy makers, the public and healthcare workers (HCWs) on improving patient safety in healthcare facilities [1, 2]. In response HCWs, hospitals and health authorities across the world have increased efforts to keep people safe from potential harm associated with receiving health care [3, 4]. One infection of particular interest has been SAB. Worldwide, SAB is a serious cause of morbidity and mortality, with associated mortality rates of 20% to 50% [5-7] and a significant associated economic burden [8].

HAI surveillance programs have been established in numerous countries to monitor and control the occurrence of HAIs. The prevention of infection requires a multifaceted approach,[9] often making it difficult to determine the relative effect of each intervention. In the case of SAB, interventions to reduce its incidence include hand hygiene initiatives and improvements in the management of intravascular catheters [10-13]. Despite global concerns about serious HAIs such as SAB and the need to monitor the effect of interventions, international comparisons are limited. There are few longitudinal studies describing the incidence of SAB across a wide region [14]. The purpose of this longitudinal study is to describe significant reductions in hospital-onset SAB (HO-SAB) in Australian hospitals over the past 12 years.

Methods

The study presents an analysis of prospective surveillance of laboratory diagnosed HO-SAB cases according to agreed definitions [15]. The primary outcome was HO-SAB, which was defined as one or more blood cultures positive for S.aureus, taken from a patient who had been admitted to hospital for more than 48 hours. The term HO-SAB is defined as any case of SAB occurring more than 48
hours after admission. Only the first isolate per patient was counted, unless at least 14 days had passed without a positive blood culture, after which an additional episode was recorded. Surveillance data were collected and combined from 132 hospitals in four Australian States and Territories, representing 24% of all Australian hospitals who reported having one or more patient days in 2011-12. Of the 132 hospitals, 110 are publicly funded, the reminder are privately funded. In Australia, approximately 68% of all hospital beds are publicly funded [16]. Data from all admissions to inpatient wards or units within acute public hospitals, including psychiatric, rehabilitation and aged care admissions were included. For the period 1st January 2002 to 30th June 2013, HO-SAB surveillance and hospital bed day data were provided by the Australian Capital Territory (ACT), South Australia (SA), Tasmania (TAS) and Western Australia (WA) HAI surveillance units. All jurisdictions involved in this study have a system where laboratory data can be directly extracted and used for validation of reported cases. Data from the larger population states (NSW, Victoria and Queensland) were not available for the time period used for this study.

All contributing hospitals used the HO-SAB definition as described earlier and provided bed-day denominator data to the HAI surveillance units. There were minor variations in the denominator used to calculate rates. ACT and WA used occupied bed-days for the entire study period, whilst SA used occupied bed-days from 2002 to June 2006, and then subsequently used patient-days [16]. Similarly, TAS used occupied bed-days from 2005 until June 2008 when patient days were subsequently used. The changes in denominators during the study period have negligible impact since the yearly variance between the two measures (“occupied” compared to “patient” days) is estimated to be <1%.[17] For convenience, we use the term patient-days (PDs) for the remainder of the paper.

Statistical analysis

Statistical analysis was conducted using IBM Statistics version 20.0. The incidence of HO-SAB per 10,000 PDs was calculated as: HO-SAB cases/number of PDs X 10,000; 95% confidence intervals (CI) were calculated for Poisson distributed counts. Monthly, quarterly and yearly incidence rates were obtained for HO-SAB. Monthly incidence of HO-SAB over the entire study period was tested
using time series analysis (regression analysis), to allow for autocorrelation between monthly measurements. Adjustment for seasonality was not undertaken.

To determine whether there was an issue of “dilution” of rates from the later inclusion of PDs from smaller hospitals with a much lower risk patient population and very few episodes, further analysis was undertaken. First, when new hospitals contributed data, comparisons of the mean HO-SAB rate before and after the addition of new hospitals were undertaken using analysis of variance (ANOVA). Second, monthly aggregate incidence of HO-SAB from the original 15 contributing hospitals and from larger more complex peer group hospitals (principal referral hospitals as defined by the Australian Institute of Health and Welfare) [18] was analysed separately over the entire study period using time series analysis.

**Ethical statement**

This study was approved by the human research ethics committee at Avondale College of Higher Education (H0013060).

**Results**

The number of hospitals contributing data to the state surveillance systems increased progressively from 15 in 2002 to 132 hospitals by 2011; this number was sustained until 2013. Of these 132 hospitals, 81 were from SA, 46 from WA, four from TAS and one from the ACT. A total of 2,733 HO-SAB cases were identified over the study period giving an aggregate incidence of 0.90/10,000 PDs (95%CI, 0.86-0.93). There was a 63% decrease in the annual incidence, from 1.72/10,000 PDs in 2002 (95% CI, 1.50-1.97) to 0.64/10,000 PDs (95%CI, 0.53-0.76) in 2013. Further descriptive HO-SAB data by year are presented in Table 1. Using time series analysis (regression) there was a mean reduction in the incidence of HO-SAB over the entire study period of 9.4% per year (95% CI, -8.1%, -10.7%) (Figure 1).
Over the study period the annual incidence of MRSA HO-SAB significantly reduced by 76% from 0.77 to 0.18 per 10 000 PDs (P <0.001). The proportion of HO-SAB that was caused by MRSA reduced from 44.7% to 28.0%. Cases of HO-SAB caused by both MRSA and MSSA significantly reduced during the study period (P<0.001) (see Table 1 and Figure 2). Aggregated data at the jurisdictional level also indicated a reduction in both MSSA and MRSA HO-SAB, consistent with trends reported in Table 1 and Figure 1. These data are not specifically reported, as to do so would potentially identify individual hospitals.

During the study period, the number of hospitals contributing data increased from 15 to 132. When new hospitals contributed data, a significant decrease in the mean incidence of HO-SAB only occurred when the number of contributing hospitals increased from 16 to 19 in June 2005 (P =0.02). There was no further significant change to the mean incidence of HO-SAB when additional hospitals contributed data.

In order to test the possibility that dilution of rates was occurring by the addition of lower risk hospitals’ data, analysis of data from the original 15 contributing hospitals was undertaken for the entire study period. In these 15 hospitals there was a significant reduction in the incidence of HO-SAB of 6.5% (95% CI, -4.9%, -8.1%) per year, compared to 9.4% for the entire cohort of hospitals. When analysis was performed on data from the principal referral hospitals only [18], there was an annual mean reduction in the incidence of HO-SAB of 11.2% (95% CI, -9.2%, -13.2%). Therefore, it is unlikely that there was a significant “dilution” effect caused by progressive inclusion of many smaller hospitals to account for the observed results.
Discussion

Our study reports a major, sustained and significant reduction in HO-SAB in a large number of Australian hospitals since 2002. While other studies have also documented a reduction in national incidence of HO-SAB [11, 19-23] they have mostly focused on MRSA. None have reported such a large reduction in both MSSA and MRSA HO bacteraemia. Additionally, we report longitudinal data, a key strength of our study.

Comparisons of the incidence of HO-SAB between countries are difficult, given the variety of definitions for cases and denominator data. In England, “Trust Apportioned” cases (occurring after the 3rd day of admission) of MRSA bacteraemia have been collected since 2008. This has a close similarity to the HO-SAB definition used in our study. Their data suggests that a significant reduction in incidence of MRSA bacteraemia occurred between 2008-9 and 2012-13 from an incidence of 0.43 to 0.12 cases per 10,000 bed-days (P < 0.01) [21]. This latter figure in England is lower than that reported in our study for 2013 (0.18 per 10,000 PDs). It is not possible to determine whether a reduction in MSSA bacteraemia also occurred in England during the same period as these data are not available.

In a Scottish study, the prevalence of HO-SAB in an inpatient population reported a 41% decrease between 2006 and 2010, from 0.73 to 0.50 cases per 1000 acute occupied bed-days [19]. The incidence of HO-MRSA bacteraemia fell from 0.16 to 0.03 per 1000 acute occupied bed-days; however, unlike our study, the rates of HO-MSSA bacteraemia remained unchanged. Their reported incidence of HO-MRSA bacteraemia is higher than the incidence in the last year of our study (0.03 per 1,000 acute occupied bed days vs 0.18 per 10,000 PDs), assuming the calculation of bed-days is similar. The authors suggested that the introduction of a universal MRSA admission screening programme was associated with significant reductions in rates of MRSA bacteraemia but made no discernible impact on burdens from MSSA bacteraemia and declines occurred almost exclusively in
MRSA related disease [19]. There is no national mandate regarding MRSA or MSSA patient screening in Australia. Consistent with other studies, the Scottish study found that upward pressure on MSSA rates was not observed, and that MRSA appears to add to, rather than displace MSSA infection [20].

There is no national data from the United States on the incidence of HO-SAB, however some studies provide insight into trends. A study undertaken by Kallen and colleagues examined invasive healthcare associated MRSA infections in nine metropolitan areas [24]. In patients with an invasive HO-MRSA infection, the proportion of these caused by HO-MRSA bloodstream infections decreased slightly from 87% to 84% between 2005 and 2008 (P=0.06). A significant reduction in MRSA bacteraemia related to a device was also identified in Veteran Affairs hospitals, after the introduction of MRSA prevention and control bundle [23].

In the largest study of SAB to date, the incidence of SAB was compared in five countries, incorporating nearly 20,000 episodes [25]. During the nine years studied, several regions reported decreases in HO-MSSA, but in only two regions observed a significant decrease in both HO-MSSA and HO-MRSA bacteraemia (Copenhagen City, Sherbrooke). In a recent study from Victoria in Australia, data from 119 public and four private hospitals were analysed for a 3-year period (2010-2012) [26]. Healthcare associated SAB (i.e. any case associated with receiving healthcare) infection rates decreased from 1.4 to 0.7/10 000 OBDs (P < 0.001), whilst healthcare associated MRSA bacteraemia decreased from 0.4 to 0.1/10 000 OBDs (P < 0.001).

There are several potential explanations for the reduction in HO-SAB described in our study. Australian States and Territories have had a long history of implementing state-wide infection prevention and control initiatives. At a national level, the work undertaken by the Australian
Commission on Safety and Quality in Health Care (an independent statutory authority) in the area of HAI prevention is notable [27]. The Commission has led several major HAI prevention initiatives that were additional to those from state and local hospital initiatives. These initiatives included the development of national surveillance programs for HAIs, national evidence-based guidelines, training and support for improved clinician capacity in infection prevention and control, development of a national hand hygiene initiative, and new accreditation standards. Hospitals who contributed data to this study were involved in these national initiatives, in addition to local and jurisdictional HAI prevention initiatives. The reduction in SAB observed in this study is unique, given the reduction in both MSSA and MRSA HO-SAB. We believe a major factor was that national, jurisdictional and local interventions did not just focus on MRSA, but on all cases of healthcare associated SAB and an overall effort reduce all HAIs [10, 12, 26-28].

Regardless of how the data in our study is analysed, a significant downward trend in the incidence of HO-SAB, including MRSA and MSSA is seen (Figure 3). To determine whether the observed reduction in HO-SAB was simply offset by increased healthcare delivery in the community and a subsequent increase in non-inpatient healthcare associated SAB, we examined two further pieces of data. First, we explored hospital activity data and found there was only a 0.7% reduction in the average number of hospital beds per 1000 population in Australia between 2007-8 and 2011-12 [29]. We also identified a 2.7% increase in overnight admissions in Australian hospitals over the same period [29]. Second, we examined non-inpatient healthcare associated SAB data for the four last years of our study period in all jurisdictions. We found no evidence of an increase in non-inpatient SAB during this time. Consequently, we are confident that the decrease in HO-SAB observed in our study was not offset by increases in non-inpatient SAB or changes in the at risk population.

Our study is unique because we identified a significant decrease in both MRSA and MSSA HO-SAB over the course of the study and are unaware of any nation reporting similar findings in a longitudinal manner. Of the limited Australian population based studies available, data suggests that the overall
incidence of SAB (including HO and community-onset cases) has not significantly increased or decreased in two regions within Australia [25, 30]. Put simply, in Australia, reductions in HO-SAB have not been driven by an overall reduction in the incidence of SAB or reductions in either HO-MRSA or HO-MSSA bacteraemia individually, a point of distinction from other notable studies [5, 11, 19].

A strength of this study is the application of a consistently applied internationally recognised definition for HO-SAB, and that data were captured for an extended period (12 years). However, a limitation of using this definition is that not all cases of healthcare associated SAB will be captured. For example, cases of SAB occurring within 48 hours of hospitalisation but associated with prior healthcare interventions such as intravascular devices or surgery will not be included [31]. Previous studies suggest that using a timeframe of 48 hours post admission will fail to identify approximately 30% of cases [26, 30]. It was not possible to obtain longitudinal data using a more comprehensive healthcare associated SAB definition as this approach did not commence in all states in Australia until 2010. Further limitations of our study included our inability to collect data on comorbidities, strain typing and treatment data, which may have been helpful to explain observed differences in incidence over long time periods.

All jurisdictions involved in this study have had a history of making data publically available on SAB and the data presented in our study is consistent with and significantly builds on previously published work [12, 25, 30]. We report an incidence of HO-SAB in 2002 of 1.73 per 10,000 PDs. If this rate remained constant during the entire study period, 5,274 cases of SAB would have potentially occurred in the contributing jurisdictions. This suggests that there were about 2,500 less cases of HO-SAB across the study period from the participating hospitals. As a result, assuming a mortality of 21%, 500 or more lives were saved over the study period, as a result of the reduction in HO-SAB incidence [7].
We commend those responsible for infection prevention and control initiatives at a local, jurisdictional and national level. The Australian experience showing reductions in both MSSA and MRSA HO-SAB, highlights the need to tackle HAIs in a multifaceted manner, with a strong national focus, supported by local interventions. Policy makers should not focus prevention strategies on one organism or infection, whilst researchers should, where possible, consider the value of examining multiple HAI outcomes to evaluate infection prevention initiatives.

Notes

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Conflict of interest: We declare we have no conflicts of interest. All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.
Author contributors: The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication. BM and PC were involved at every stage from the literature search, planning and design of the study, data collection, data analysis, data interpretation, and writing. RM, IW and AW were involved data collection, data interpretation, and writing. BM and PC are the guarantors. All authors had full access to the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. All authors were involved in the drafting the work or revising it critically for important intellectual content and final approval of the version to be published.

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