



ORIGINAL ARTICLE

Prevalence of methicillin-resistant *Staphylococcus aureus* in complicated skin and soft tissue infections and the outcome among patients with diabetes in Bahrain Defence Force Hospital, Bahrain

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Received date: January 22, 2017; Accepted date: July 27, 2017; Published date: July 31, 2017

Abstract

Background and objectives: There is no data regarding the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) complicated skin and soft tissue infections (cSSTI) in the Kingdom of Bahrain despite its rapidly growing existence worldwide. This study aims to ascertain its prevalence at Bahrain Defence Force Hospital between 2010 and 2015. Since Bahrain is considered one of the top ranking countries with Diabetes Mellitus (DM), we aim to establish the percentage of patients with DM in MRSA cSSTI. Diabetic foot infections constitute a major complication of DM and contribute to the risk of amputation. We intend to identify the rate of MRSA cSSTI infections in the foot and the rate of amputation in patients with and without DM.

Methods: Retrospective cohort study of an electronic medical chart review of in- and outpatients who had documented swab collection for cSSTI.

Results: Out of 16,189 swabs collected, 702 were positive for MRSA cSSTI. The prevalence rate of MRSA in cSSTI was 4.3%. Out of 439 patients, 43% were positive for DM. There were higher odds of MRSA cSSTI occurring in the foot in patients with DM (OR = 5.2, 95% CI 3.1 to 8.6; $P < 0.0001$) compared to patients without DM (RR = 3.6, 95% CI 2.4 to 5.4; $P < 0.0001$). There were higher odds of patients with DM foot MRSA cSSTI undergoing amputation (OR = 46.1, 95% CI 2.7 to 786.1; $P < 0.05$) compared to patients without DM (RR = 25.1, 95% CI 1.6 to 395.9, $P < 0.05$).

Conclusion: This will be the benchmark study for the prevalence of MRSA in cSSTI in Bahrain to establish the awareness of its association with DM and its disease burden.

Keywords: Bahrain, MRSA, cSSTI, Prevalence, Diabetes, Foot, Amputation

Introduction

First recognized in the 1960s, methicillin-resistant *Staphylococcus aureus* (MRSA) was considered to be a medical oddity; however, today, it is considered to be the leading cause of a nosocomial infection in most parts of the world.¹⁻⁴ MRSA infection is commonly associated with complicated skin and

soft tissue infections (cSSTI) hospitalization for which there is a substantial clinical and economic burden.⁵⁻⁷

Not only is the initial variant of MRSA (hospital-acquired MRSA) still constituting a large part of the problem, a newer and very rapidly spreading type of MRSA (community-acquired MRSA) has

recently evolved in the community setting and in a healthy population.⁸ With this contributing to major health implications, and given the fact that, to the best of our knowledge, there are no data regarding prevalence of MRSA among patients admitted with cSSTI in the Kingdom of Bahrain, we initially sought out to obtain the prevalence of MRSA in cSSTI at Bahrain Defence Force (BDF) Hospital between 2010 and 2015, to assist in identifying the extent and significance of this disease within our hospital.

Furthermore, Bahrain is one of the top ranking countries in the Gulf Cooperation Council (GCC) for diabetes mellitus (DM)^{9,10} and it is suffice to say that DM is a risk factor for multiple infections, MRSA and cSSTI included. Diabetic foot infections, most of which come under the spectrum of cSSTI, constitute a major complication of DM and also contribute to the risk of amputation. The lifetime risk for foot ulceration among patients with DM is 15%. Foot ulcers, frequently complicated by infection, are responsible for more prolonged hospitalization than any other complication of DM and the most common cause of lower extremity amputation.^{11,12} DM increases the risk of foot ulcer admissions by 11 fold, accounting for more than 80% of all amputations.¹³ Hence, we aimed to establish the percentage of patients with DM in MRSA cSSTI in BDF Hospital, the rate of MRSA cSSTI located in the foot, and subsequently the rate of amputation for patients with DM as compared to patients without DM. We intended to see if there were major differences in outcome between patients with DM versus patients without DM, predicting that a greater number of those with DM MRSA cSSTI will have MRSA isolated from the foot and that the rate of amputation will be higher in the DM foot MRSA cSSTI group compared to the non-DM MRSA cSSTI group.

Materials and methods

This was a retrospective study. An initial cross-sectional approach was applied to determine the prevalence of MRSA in cSSTI in BDF Hospital. The study was conducted between 2010 and 2015, after which a cohort methodology was used for its completion. Ethical approval was obtained from the BDF Ethical Committee.

We systematically collected data from the electronic medical records of all patients (inpatients and

outpatients) aged more than 14 years. Patients presented to BDF Hospital between 1st of January 2010 and 31st of December 2015 having either a primary or secondary diagnosis of cSSTI, and documented swab collection from that cSSTI were included in the study. cSSTI was defined as deep/extensive cellulitis, infected wound or ulcer, major abscess, or other skin/soft tissue infection requiring substantial surgical intervention.¹⁴

Patients aged less than 14 years (considered as pediatric), patients transferred to and from another hospital, admissions for scheduled amputation, cSSTI acquired during current hospitalization, or diagnosis of burn, gangrene, animal or human bite, or osteomyelitis were excluded from the study.¹⁵

The samples analyzed in the study involved swabs collected from wounds, ulcers, abscesses, bedsores, tissues, sternum, wound aspirates etc. A second search was established to further narrow down the number from all cSSTI-positive swabs to MRSA cSSTI-positive swabs, hence, all microbiologically proven MRSA swabs were identified. Further to authenticate sample collection strategy, a third search was established by cross-checking all MRSA cSSTI-positive swabs with patient records (subjective, objective, assessment, and plan (SOAP) notes if outpatient and admission/discharge; summaries if inpatient) to certify that inclusion and exclusion criteria were met.

Each swab positive for MRSA was counted as a positive isolate as long as it was collected from a different site or from the same site on a different day regardless if it was from the same patient, enabling us to calculate the prevalence of MRSA in cSSTI.

Once prevalence was calculated, the total number of patients that accounted for all MRSA cSSTI-positive swabs was established. This number was then divided into two groups: those with DM and those without DM. A patient was labeled as diabetic if there were records to confirm the diagnosis (SOAP notes, inpatient/discharge notes, e-Prescription showing patient was on treatment for DM) or if the patient had a documented HbA1c level consistent with DM within the hospital's records. Each group was further divided into two groups: those with foot MRSA cSSTI and those with MRSA cSSTI occurring elsewhere. Each foot MRSA cSSTI (DM or non-DM) was further divided into two groups: patients who underwent amputations and those

who did not. Figure 1 is a summarized flowchart to represent the above information.

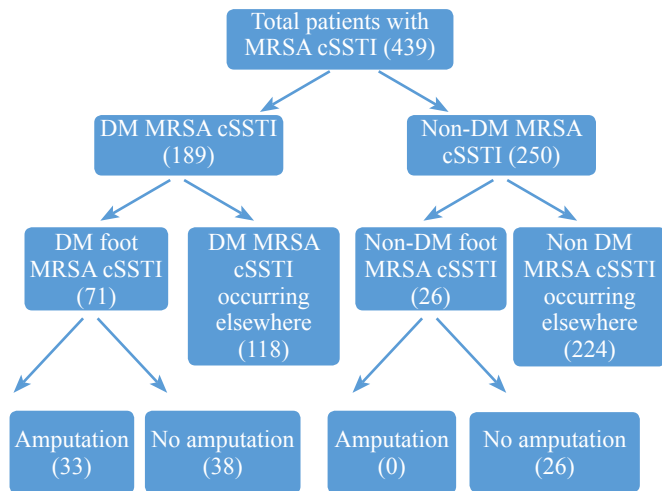


Figure 1: Summary of results

During this study, we also sought to recognize:

- The most common age distribution of patients documented to have MRSA cSSTI
- The most common site from which MRSA was isolated
- The average HbA1c in patients with DM MRSA cSSTI
- The average HbA1c in patients who underwent amputation secondary to DM foot MRSA cSSTI
- The percentage of MRSA cSSTI that were treated as inpatients versus those treated as outpatients

Descriptive analyses were provided for all study population. IBM SPSS Statistics Version 23, a statistical software, was used for all statistical analyses. Odds ratio and relative risk were calculated for all hypotheses between the two main groups of study population, DM MRSA cSSTI and non-DM MRSA cSSTI, for both location of MRSA and rate of amputation. For categorical or ordinal outcomes, Pearson’s chi-square tests were used for bivariate statistical testing.

Results

A total number of 16,189 swabs were collected from all documented cSSTIs in BDF Hospital between January 1st, 2010 and December 31st, 2015. Out of 16,189 swabs, 11,595 were positive for any organism, including MRSA. This was subsequently narrowed down to 702 swabs, which were documented to be positive for microbiologically proven MRSA cSSTIs (as shown in Table 1). Hence, the prevalence

rate of MRSA in cSSTI at BDF Hospital between 2010 and 2015 was calculated to be 4.3%.

Table 1: Breakdown of total swabs collected, total positive swabs, and swabs positive for MRSA cSSTI per year

Year	Swabs taken from cSSTIs, n	Positive swabs, n (%)	Swabs positive for MRSA cSSTIs, n (%)
2010	2362	1707 (72.3)	96 (4.1)
2011	2571	1812 (70.5)	69 (2.7)
2012	2666	1906 (71.5)	130 (4.9)
2013	2605	1891 (72.6)	105 (4.0)
2014	2799	1976 (70.6)	133 (4.8)
2015	3186	2303 (72.3)	169 (5.3)
Total	16189	11595 (71.6)	702 (4.3)

We next had to establish the total number of patients who had MRSA cSSTI to determine the relevance of our hypotheses. The 702 swabs that were positive for MRSA cSSTI belonged to 439 different patients (as shown in Table 2).

Table 2: Data of the number of patients per year found to have MRSA cSSTI and the number of cases with MRSA cSSTI treated as inpatients versus outpatients)

Year	Patients with MRSA cSSTI, n	Cases per year with MRSA cSSTI, n	Cases admitted per year with MRSA cSSTI, n	Cases with MRSA cSSTI treated as outpatients per year
2010	52	53	29	24
2011	40	44	26	18
2012	80	84	46	38
2013	78	84	32	52
2014	86	97	37	60
2015	103	114	41	73
Total	439	476	211	265

We next determined how many MRSA cSSTI-positive patients were treated as inpatients versus outpatients per year. Given that some patients were admitted multiple times between 2010 and 2015, their admissions per year were accounted for differently. For example, if one of the 439 patients was admitted twice but in a different year, this was accounted for as two admissions. Hence, from an

initial total of 439 patients, a total number of 476 cases were established, out of which 211 were treated as inpatients whereas 265 were treated as outpatients (Table 2).

As exemplified in Figure 2, there was a near equal distribution of age over the years, with no one particular group standing out to be the most common age category to develop MRSA cSSTI.

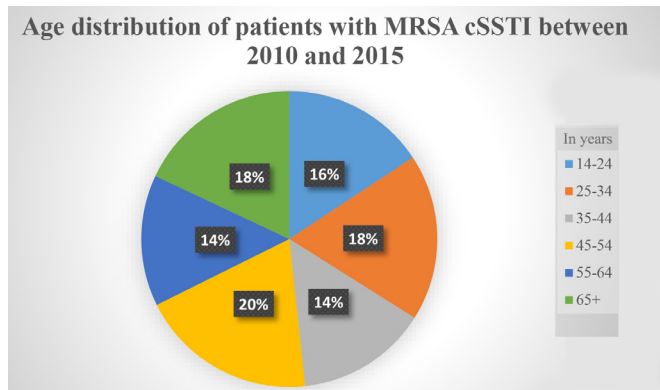


Figure 2: Age distribution of patients with MRSA cSSTI between 2010 and 2015

As shown in Table 3, the most common site of diagnosed MRSA cSSTIs was foot (27.1%) followed by the lower extremities including the hip, thigh, and knee (22.6%). Miscellaneous swabs include those, which were taken from a source noted to be cSSTI but not labeled correctly in terms of exact location.

Table 3: Distribution of sites of swabs confirmed to be positive for MRSA cSSTI

Sites	Swabs isolated, n (%)
Head and neck	45 (6.4)
Axilla/upper limbs/hand	66 (9.4)
Chest/sternum/breast	36 (5.1)
Abdomen and groin	61 (8.7)
Back/sacrum/gluteal/bedsore	86 (12.3)
Hip/thigh/knee/lower limbs	1159 (22.6)
Foot	190 (27.1)
Genital and perianal	42 (6)
Miscellaneous	17 (2.4)
Total	702 (100)

Figure 3 shows that out of the 439 MRSA cSSTI-positive patients between 2010 and 2015 at BDF Hospital, 189 (43%) had DM. Whereas, 250 (57%) patients had no records or proof of having the condition. The mean HbA1c in patients with DM MRSA cSSTI was 8.62%.

Out of the 189 patients with DM MRSA cSSTI, 71 had MRSA isolated from the foot, that is, the probability of MRSA cSSTI occurring in the foot in patients with DM MRSA cSSTI was 37.6%. Out of the 71 patients with DM foot MRSA cSSTI, 33 underwent amputation, that is, the risk of amputation in DM foot MRSA cSSTI is 46.5%.

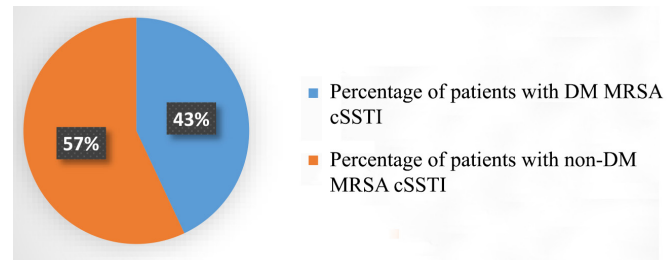


Figure 3: Patients with DM MRSA cSSTI vs. patients with non-DM MRSA cSSTI

The mean HbA1c in patients with DM foot MRSA cSSTI that led to amputation was 8.73%. All patients who had amputation were aged more than 45 years. The most common age-group was 65+ years (16 patients out of 33).

Out of the 250 patients with non-DM MRSA cSSTI, 26 had MRSA isolated from the foot, that is, the probability of MRSA cSSTI occurring in the foot in patients with non DM MRSA cSSTI was 10.4%. Out of the 26 patients with non-DM foot MRSA cSSTI, none underwent amputation, that is, the risk of amputation in non-DM foot MRSA cSSTI was 0%. These results are summarized in Figure 1.

We calculated the odds ratio and relative risk with the above results to target our hypotheses.

We established that having DM is associated with higher odds of having MRSA cSSTI in the foot. The odds of MRSA cSSTI occurring in the foot in patients with DM MRSA cSSTI is five times the odds of MRSA cSSTI occurring in the foot in patients with non-DM MRSA cSSTI (OR = 5.2, 95% CI = 3.1–8.6; $P < 0.0001$). Patients with DM were more likely to get MRSA cSSTI in the foot than those who were not diabetic (RR = 3.6, 95% CI = 2.4–5.4; $P < 0.0001$). The chi-square statistic without Yates correction was 46.1 with first degree of freedom ($P < 0.0001$).

We also were able to conclude that having DM foot MRSA cSSTI was associated with higher odds of having an amputation. The odds of amputation in patients with DM foot MRSA cSSTI was 46 times the odds of amputation in patients with non-DM foot MRSA cSSTI (OR = 46.1, 95% CI 2.7–786.1,

$P=0.0081$). Patients with DM foot MRSA cSSTI were more likely to undergo amputation compared to patients with non-DM foot MRSA cSSTI (RR=25.1, 95% CI 1.6–395.9, $P=0.0219$). The chi-square statistic was 18.3. This result was significant at $P<0.05$.

Discussion

This will be, to the best of our knowledge, the first prevalence study of MRSA in cSSTI in Bahrain. Considering MRSA is a leading cause of nosocomial infections and a growing cause of community-acquired infections, there was a need to establish such a study in the Kingdom. Moreover, with DM being so prevalent in the GCC countries, it was anticipated that there would be an association between DM and MRSA cSSTI. Hence, the reason for this study to further assess the outcome of DM MRSA cSSTI in our hospital.

Initially, it was surprising to note that patients with MRSA cSSTI were spread out evenly throughout all age categories. This concludes that the assumption, MRSA cSSTI predominantly occurs in patients of older age, is erroneous. MRSA cSSTI, in fact, occurs across all age-groups, which makes it a health-related issue. This should remind us to be more vigilant with cSSTI in people of all ages to prevent the complications of MRSA. MRSA cSSTI was more commonly found in the lower extremities and feet (49.7%), with 27.1% of the swabs isolated from the feet solely.

In this study, 44% of patients were treated as inpatients whereas 56% were treated as outpatients for MRSA cSSTI. This indicates that the treatment of MRSA cSSTI is both a burden for inpatient and outpatient facilities. Hence, future studies are needed to determine appropriate choice of antibiotic therapy and to see if an early switch from intravenous to oral therapy or early discharge will help benefit patients in the long run and will help reduce costs. In the meantime, cSSTI therapy should be tailored on the basis of local resistance patterns, origin, type and extent of infection. Additionally, it is prudent to provide therapy with MRSA coverage, especially if and when local prevalence is high.

Also, 43% of MRSA cSSTI-positive patients were known to have DM. This is consistent with our assumption that there will be an association between MRSA cSSTI and DM particularly since DM is a risk factor for multiple infections, MRSA, and cSSTI, and it is prevalent in this part of the world.

The probability of MRSA cSSTI occurring in the foot of patients with DM MRSA cSSTI was found to be 37.6% when compared to 10.4% in patients with non-DM MRSA cSSTI. The risk of amputation in DM foot MRSA cSSTI was 46.5% compared to 0% in non-DM foot MRSA cSSTI.

This confirmed that the risk of amputation in DM foot MRSA cSSTI is significantly higher compared to those with non-DM foot MRSA cSSTI, especially when none in the latter group underwent amputation. The majority of patients with non-DM foot MRSA cSSTI were secondary to trauma (road traffic accidents, fractures etc.). Hence, amputation was not indicated. Additionally, upon calculation of odds ratio, this result was statistically significant; however, the CI was very broad, as this particular subset of sample size was small, hence, point estimate was imprecise. We can thereby conclude that even though this result was statistically significant for this sample size, larger studies are needed to reduce the level of uncertainty.

Patients with DM foot MRSA cSSTI who underwent amputation were of older age, as it is commonly expected and known that complications of DM and vascular disease worsen with duration of disease, particularly with inadequate control.

What is surprising is that the mean HbA1c of patients with DM foot MRSA cSSTI who underwent amputation was not very high (8.73%) compared to those who did not require amputation (8.62%). This was lower than expected, as it was an assumption that patient who require amputation will have poorer glycemic control. This may be due to presence of few extremes of HbA1c, which may have contributed to the result hence, this was a limitation of this study.

With a total of 16,189 swabs to begin with, results can be drawn with greater precision and statistical power. As the subset of sample population that included only foot MRSA cSSTI and amputation rate within that particular group was small, larger studies are needed in that respect to ensure greater validity and reliability of results in order to lessen the uncertainty.

As this study was a retrospective medical chart review, some limitations were inherent to the design. Information was dependent on or was estimated on the basis of previous medical records. We aimed to crosscheck all data gathered with multiple reference

points within the electronic medical records for all patients; however, not all data were complete. Electronic medical charts for all patients were only used after 2012, the unavailability of certain information such as HbA1c results for a minority of patients, or the exact location of the MRSA cSSTI, was a limitation of this study.

Furthermore, we recommend that better, more detailed labelling of swabs should be done before sending the sample to the laboratory, as we found that not all swabs were labeled as thoroughly as we had hoped for. Hence, exact location of MRSA cSSTI was not determined in certain cases.

We did not limit the population to who had a culture result within 24–48 h of admission, as this was not typical of or not feasible in general clinical practice. Cultures were usually taken either on admission or during admission (depending on if it is a primary or secondary diagnosis of cSSTI). Also, globally, laboratories usually take more than 24–48 h to document an organism with antibiotic sensitivity. In addition, limiting the study population to the above would not ensure in a large enough sample size and would not aid in calculating the true prevalence of MRSA in cSSTI in our hospital.

Collectively, the findings have implications for more awareness in early identification, early treatment, and early control of both diabetes and MRSA cSSTIs. Further studies are needed to generalize these results to other hospitals in the region.

We recommend to establish awareness of DM in the general population in Bahrain and to enforce doctors to adhere to stringent control of diabetes in patients to help reduce the disease burden and lessen its complications related to cSSTI.

Furthermore, we recommend enhancing the knowledge and gaining insight into the cost of hospital stay, choice of antibiotics based on the local predominant pathogens, and comparative study to see if early switch from intravenous to oral therapy or early discharge in the case of inpatients will help benefit the patients in the long run.

Conclusion

This is a benchmark study for the prevalence of MRSA in cSSTI at BDF Hospital, Bahrain. Our data suggest that DM is highly associated with cSSTI, MRSA in particular, as studied in this research. As shown in this study, 43% of patients positive for

MRSA cSSTI were known to have DM and the mean HbA1c in this group was 8.62%.

The probability of MRSA cSSTI occurring in the foot in patients with DM MRSA cSSTI was found to be 37.6% as compared to 10.4% in patients with non-DM MRSA cSSTI. The risk of amputation in patients with DM foot MRSA cSSTI was 46.5% compared to 0% in those with non-DM foot MRSA cSSTI.

It is therefore evident that the risk of having foot MRSA cSSTI in patients with DM is higher than having foot MRSA cSSTI in patients without DM. It is also concluded that having foot MRSA cSSTI in patients with DM led to a higher rate of amputation than in patients without DM.

Acknowledgements

We would like to thank Ms. Ruchi Sharma and Ms. Alya Thulaj for their assistance in the statistical analysis.

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