Received: 28 July 2022 | Accepted: 4 March 2023

DOI: 10.1111/dme.15081

DIABETIC Medicine

RESEARCH: COMPLICATIONS

Reduction in the prevalence of methicillin-resistant *Staphylococcus aureus* in tissue and wound swab samples taken from outpatients attending a specialist diabetic foot clinic 2005–2021

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Abstract

Aims: To assess annual change in prevalence of methicillin resistant *Staphylococcus aureus* (MRSA) from tissue and wound swab samples from foot ulcers (DFUs) in people with diabetes between 2005 and 2021.

Methods: A retrospective analysis of everyone with MRSA positive wound or tissue swabs taken from our specialist multidisciplinary foot clinic between July 2005 and July 2021.

Results: A total of 406 MRSA positive isolates from DFU swabs were identified from 185 individuals attending the foot clinic. There were 22 hospital-acquired infections (HAIs) and 159 community-acquired infections (CAIs). Fifty-two per cent ($n = 37$) of these individuals from 2010 to 2021 ($n = 71$) had presence of at least three risk factors for MRSA. The total number of swabs sent was 6312 from 1916 individuals living with diabetes. Annual MRSA DFU prevalence peaked in 2008 at 14.6% ($n = 38$), decreased in 2013 to 5.2% ($n = 20$) and did not exceed 4% ($n = 6$) from 2015 to 2021. Hospital MRSA was lowest in 2021 ($n = 211$), a 76% fall from 2007 ($n = 880$). Incidence of MRSA HAI from 2015 to 2021 ranged from 5.4% ($n = 14$) in 2020 to 11.5% ($n = 41$) in 2018.

Conclusions: Prevalence of MRSA in DFU infections treated as outpatients is decreasing in line with falls in hospital acquired blood-borne infections and with overall hospital MRSA incidence. This is likely a reflection of the combination of interventions, including stringent antibiotic prescribing and decolonisation strategies. Reduction in prevalence should have positive impact on outcomes in people living with diabetes, reducing the complication of osteomyelitis and necessity for long-term antibiotic administration.

KEYWORDS

diabetes mellitus, foot ulceration, methicillin-resistant *Staphylococcus aureus*

1 | INTRODUCTION

Diabetes-related foot ulcers (DFUs) are a common complication of diabetes mellitus, that are associated with significant morbidity and mortality.[1] They are the most common reason for hospital admission for a diabetes-specific complication.[2] Optimal management requires a dedicated multidisciplinary approach, often relying on inpatient and outpatient care. The economic burden of DFUs is well documented, with estimated annual costs in the United Kingdom approaching £1 billion or 1% of the National Health Service (NHS) budget.[3] In developing countries, the financial implications are even greater, with the direct impact of DFUs in Barbados conservatively estimated at 6% of government healthcare budget.[4]

There is great diversity in the organisms causing infection in DFUs, including gram positive and negative aerobes as well as anaerobes in deeper seated infections.[5] A recent meta-analysis suggested that the most commonly isolated organism from infected DFUs was *Staphylococcus aureus* of which 18% were methicillin-resistant *Staphylococcus aureus* (MRSA).[6]

The prevalence of MRSA in the diabetic foot clinic has been looked at in previous retrospective studies from 1998 and 2001, showing an increase in prevalence correlating with rises in overall hospital MRSA incidence.[7,8] We wanted to assess if these trends had changed, and if they remained in keeping with trends in hospital MRSA incidence. This study looked at MRSA positive tissue and wound swabs taken from the multidisciplinary specialist diabetic foot clinic at the Norfolk and Norwich University Hospital (NNUH) from 2005 to 2021.

What's new?

What is already known on this topic

Incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) bacteraemia has decreased in UK hospitals. Diabetes-related foot ulcers (DFUs) infected with MRSA are associated with worse clinical outcomes than those infected by methicillin-sensitive *Staphylococcus aureus* (MSSA).

What this study adds

This study is the first to show a reduction in prevalence of DFUs infected with MRSA which is in keeping with the falling levels of hospital- and community-associated MRSA infections.

How this study might affect research, practice or policy

Reduction in prevalence of DFUs infected with MRSA should have positive outcomes in people living with diabetes. However, while levels have decreased, MRSA remains a clinical challenge in DFU infections and further studies will be required to continue monitoring prevalence as resistance profiles change over time.

2 | AIMS

To assess the annual change in prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) from tissue and wound swab samples from foot ulcers (DFUs) in people with diabetes between 2005 and 2021.

3 | METHODS

This retrospective study identified everyone with MRSA positive wound or tissue swabs taken from the diabetic foot clinic at NNUH over a 17-year period, from July 2005 to July 2021. All were attendees at appointments at the foot clinic for review by podiatrists specialising in diabetes-specific foot care. Samples were taken from the ulcer base following debridement if clinically manifesting infection in accordance with 2004 guidelines.[9] Then from 2012 onwards following updated Infectious Diseases Society of America (IDSA) guidelines which considered additional signs such as foul odour, non-purulent secretions and friable granulation tissue.[10] A subsequent data set of all wound or tissue swabs taken over the same time period was obtained to facilitate calculation of proportionality.

The UK Health Security Agency (HSA) (previously Public Health England) attribution definition was used to calculate Healthcare Acquired Infection (HAI) and Community Acquired Infection (CAI). HAI is classified as first new MRSA specimen taken on day 2 of admission or later (admission counting as day 0), and CAI being first new MRSA specimen taken before day 2 of admission. Admission dates were compared with date of first positive MRSA sample to enable this calculation.

Individual participant data were obtained from the Telepath Laboratory Information Management System (LIMS), (DXC Technology Services, Virginia, USA), using requesting location and requesting clinician. These data were filtered to show MRSA positive samples. Duplicate samples were excluded by name and date of birth to determine incidence.

The MRSA infection data at NNUH was provided by the Infection Prevention and Control Department Information Officer and collated from laboratory data sent to the department's Infection Control System (ICNET, Baxter) between 2006 and 2021. GraphPad Prism v8.2, was used for graphical construction.

Participant data including clinical characteristics and risk factors were obtained through Integrated Clinical Environment (ICE) v7.1.8, 710 (CliniSys).

4 | RESULTS

A total of 406 cases of MRSA positive isolates from DFU swabs, were identified over the 17-year period, from 185 individuals attending the foot clinic. The total number of swabs sent during same period totalled 6312 from 1916 individuals living with diabetes. The annual percentage of MRSA positive swabs is shown in Table 1. There is a gradual decrease in proportion of all samples being MRSA positive from 2005 at 12.6% ($n = 37$), before dramatically dropping off in 2014 to 4.7% ($n = 13$) since when it has remained at or below 2%.

Table 1 also shows the prevalence of MRSA in individuals with a DFU. Multiple positive isolates from the same individual were excluded, allowing each person to be counted once per year. There was a peak in 2008 at 14.6% ($n = 38$) which gradually decreased in 2012 to 9% ($n = 20$) before steeply declining and not exceeding 5.2% ($n = 6$) from 2015 to 2021.

Table 2 shows the distribution of the attribution of first MRSA infection from all the individuals with positive isolate from a DFU. From 185 individuals from 2005 to 2021, there were 22 HAI and 159 CAI. There were four exclusions due to the absence of discharge records which prevented calculation of attribution.

The annual incidence of total MRSA cases in the hospital from 2007 to 2021 was plotted against new positive MRSA foot swabs in diabetic foot clinic in Figure 1. Duplicate samples from same individual were excluded and a person was only counted for the first year of positive swab, to give number of annual first positive MRSA cultures. The numbers from 2005 were excluded as 2004 data were unavailable. New hospital MRSA infections showed a slight fall then plateaued before showing a 44% decrease from 2013 to 2014. Numbers continued to fall until

TABLE 1 Showing the total number of swabs taken in clinic with the total number of MRSA positive swabs and their percentage by year. Also shown are the number of individuals swabbed annually with the number of MRSA positive individuals and their percentages. All swabs taken met Infectious Diseases Society of America clinical criteria for infection. MRSA, Methicillin-resistant *Staphylococcus aureus*.

Year	Total wound and tissue swabs taken in clinic	Total MRSA positive wound and tissue swabs	Percentage of MRSA positive swabs in total swabs taken in foot clinics %	Number of individuals swabbed	Prevalence of MRSA positive swabs from DFUs	Percentage of individuals with MRSA positive isolates %
2005	294	37	12.6	166	25	15
2006	469	45	10.4	230	24	10.4
2007	515	56	10.9	246	32	13
2008	611	60	9.8	261	38	14.6
2009	551	40	7.3	260	24	9.2
2010	432	47	10.9	248	26	10.5
2011	397	36	9.1	203	20	9.9
2012	442	37	8.4	223	20	9
2013	357	12	3.4	174	9	5.2
2014	277	13	4.7	154	8	5.2
2015	266	5	1.9	156	5	3.2
2016	289	1	0.3	184	1	1
2017	316	5	1.6	184	3	2
2018	392	6	1.5	211	6	2.9
2019	257	0	1.5	177	0	0
2020	242	2	0	164	2	1.2
2021	205	4	2	149	4	2.7
Total	6312	406				

	Individuals with MRSA positive isolate from DFUs
HAI first MRSA specimen taken on day 2 or later of admission	22
CAI First new MRSA specimen taken before day 2 of admission	159
Exclusions	4
Total	185

TABLE 2 Showing the distribution of the attribution of the first MRSA infection from individuals with positive DFU MRSA isolate from 2005 to 2021 as either HAI or CAI. Calculated using definition set by UK Health Security Agency. MRSA, Methicillin-resistant *Staphylococcus aureus*; CAI, Community-acquired infection; HAI, Hospital-acquired infection; DFU, Diabetes-related foot ulcer.

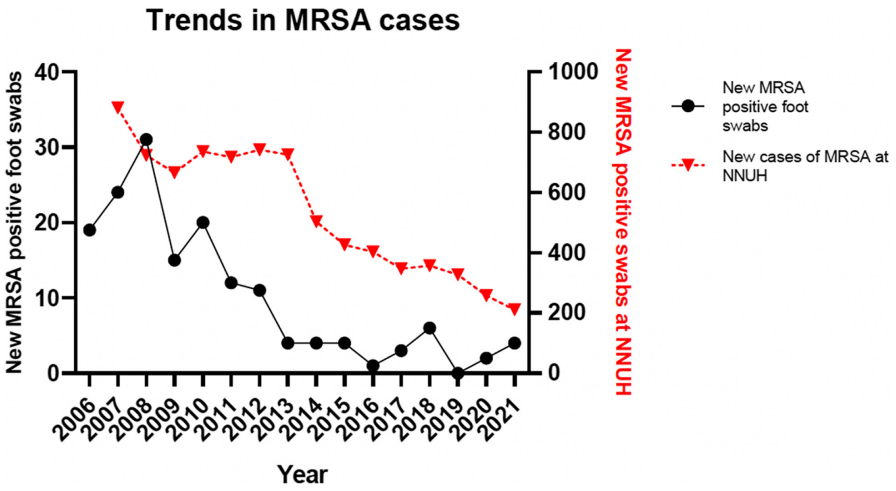

FIGURE 1 Graph showing incidence of MRSA positive foot swabs by year and total number of new MRSA positive cases by year. MRSA, Methicillin-resistant *Staphylococcus aureus*.

Year	New cases MRSA at NNUH attributed to CAI	New cases of MRSA at NNUH attributed to HAI	Percentage of new cases of MRSA at NNUH attributed to HAI
2015	384	42	9.9
2016	362	41	10.2
2017	324	23	6.6
2018	316	41	11.5
2019	307	20	6.1
2020	244	14	5.4
2021	192	19	9

TABLE 3 Showing incidence of the new MRSA cases at NNUH from 2015 to 2021 with attribution to CAI or HAI. Calculated using definition set by UK Health Security Agency. Also shown are the percentage of new MRSA infections attributed as HAI. MRSA, Methicillin-resistant *Staphylococcus aureus*; NNUH, Norfolk and Norwich University Hospital; CAI, Community-acquired infection; HAI, Hospital-acquired Infection.

reaching a low in 2021, a 76% fall from the 2007 figures (from $n = 880$ to $n = 211$). Incidence of MRSA in DFUs interestingly shows a similar downward trend following a peak of ($n = 31$ new cases) in 2008. Table 3 shows incidence of the new MRSA cases from 2015 to 2021 with attribution to CAI or HAI. The percentage of HAI ranges from 5.4% ($n = 14$) in 2020 to 11.5% ($n = 41$) in 2018. Figure 2 shows the number of blood stream MRSA infections by year with indication of those attributed to CAI or HAI. It showed a peak of ($n = 48$ cases) in 2006/07 then fell annually, having reduced by two thirds ($n = 16$) in 2011/12 with a solitary case reported in 2021/22.

Table 4 shows the presence of risk factors for MRSA infection in individuals with positive MRSA isolate from a DFU from 2010 to 2021 ($n = 71$). Seventy-six per cent ($n = 54$) of cases were >65 years old, 61% ($n = 43$) had been hospitalised in the previous 6 months, and 44% ($n = 31$) had a length of stay in excess of a week. Sixty-two per cent ($n = 44$) of people had been exposed to antibiotics in the past 2 years with a course lasting over a week. Nasal colonisation with MRSA preceded infection in 25% ($n = 18$) of cases. Only 5.6% ($n = 4$) did not have a risk factor and 52% ($n = 37$) had the presence of at least three risk factors.

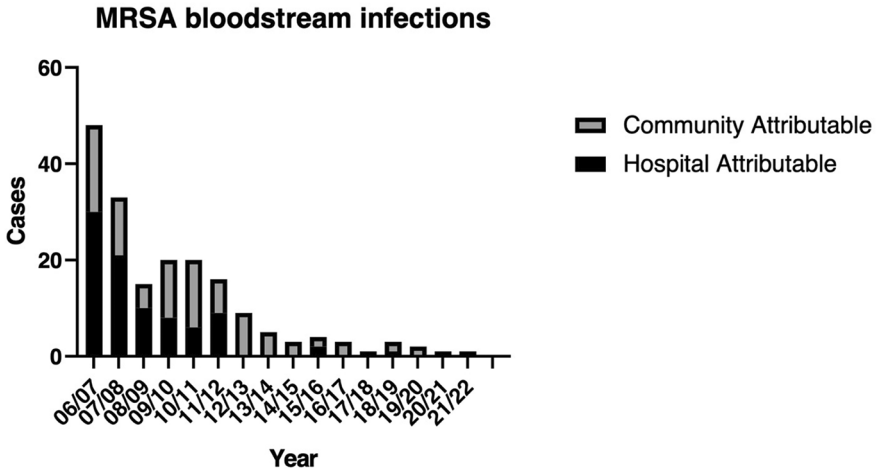

FIGURE 2 Graph showing community and hospital attributable MRSA bloodstream infections by year. MRSA, Methicillin-resistant *Staphylococcus aureus*.

TABLE 4 Showing number of cases in individuals with positive MRSA isolate from a DFU from 2010 to 2021 with risk factors for MRSA infection and their percentages. Risk factors include age >65 years old, MRSA nasal colonisation, previous antibiotic usage in past 2 years with duration >7 days, previous hospital admission within 6 months and admissions lasting longer than a week. MRSA, Methicillin-resistant *Staphylococcus aureus*; DFU, Diabetes-related foot ulcer.

Risk factor for MRSA	Number of individuals with positive MRSA isolate from DFU from 2010 to 2021 with risk factor	Percentage (%) of individuals with positive MRSA isolate DFU from 2010 to 2021 with risk factor
Recent hospitalisation, admission within 6 months	43	61
Recent hospitalisation in past 6 months lasting more than 7 days	31	44
Age > 65 years	54	76
Prior nasal colonisation with MRSA	18	25
Previous antibiotic use in past 2 years lasting > 7 days	44	62

5 | DISCUSSION

Our retrospective single-centre study has shown that the prevalence of MRSA in diabetes-related foot ulcer infections is decreasing in line with falls in hospital acquired blood-borne infections and with overall hospital MRSA incidence. In addition, it has shown most MRSA infections in individuals with DFUs are community associated, which was expected considering the outpatient nature of the clinic and is in keeping with the overall incidence of MRSA CAI. The current UK HSA guideline for the calculation of infection attribution does not consider recent discharge or prior surgery which are included in the WHO definition, this is likely to contribute to the degree of predominance of CAI in this study.

People with diabetes are at higher risk of colonisation with MRSA than people living without diabetes. Greater interaction with healthcare, increased likelihood of prior treatment with antibiotics and higher native carriage rates of *S. aureus* on skin are thought to contribute to this increased prevalence.[11,12] Older age is considered an indirect risk factor to MRSA infection as an age of >65 years old is a risk factor for hospitalisation.[13] Our study has found high levels of these risk factors in MRSA positive cases. MRSA nasal carriage has also been shown to be associated with increased risk of MRSA infection of DFUs.[14] The relatively low rates of MRSA nasal carriage in our study are not surprising as likely reflect the outpatient setting, where individuals are not routinely screened for MRSA when attending clinic. Furthermore, the chronicity of DFUs have been shown to be an independent risk factor for MRSA colonisation.[15] This is in keeping with a previous review showing *S. aureus* as the predominant pathogenic organism in DFU infections with MRSA incidence at 12%–30%.[9] In addition, a meta-analysis reported a similar MRSA prevalence of 16.8% in DFUs.[11,16] MRSA-infected DFUs have been thought to have worse clinical outcomes with prolonged antibiotic treatment duration, delayed healing and increased need for amputation.[8,11] Interestingly, a subsequent literature review suggested that this may not be the case, with the authors finding no significant differences in outcomes compared with methicillin-sensitive *Staphylococcus aureus* (MSSA).[17] However, a recent study looking at

radiological evidence has shown a significant association between MRSA and incidence of osteitis in DFUs.[18] This lends support to the traditional thought of MRSA leading to greater morbidity than MSSA in DFUs.

Prevalence of MRSA bacteraemia has been declining in developed countries; in the UK 2020–21 figures showed an 84.4% decrease from 2007 to 8.[19] This coincides with regional and national infection control campaigns initiated in the last decade, such as mandatory reporting of MRSA cases, although falls have reached a plateau.[20,21] Moreover, a large observational study has shown a decline in community onset skin and soft tissue infections due to MRSA, with healthcare-associated community-onset infections making up the greatest proportion of infections.[22] People with community-onset MRSA infections frequently have other co-morbidities such as diabetes.[23] Notably, these results are in keeping with findings from a recent Ghanaian study which found a far lower MRSA prevalence of 6% in DFUs, which was postulated to reflect the low overall MRSA prevalence in the country.[24]

It is unclear what has been the driving force behind the decrease in prevalence. The COVID-19 pandemic may have influenced the low rates recorded in 2020–2021 which may have resulted in reduced individual contacts in the community, reduction in hospital admissions and in length of stay. However, it is likely to be a result of a combination of interventions such as more stringent antibiotic prescribing and decolonisation strategies. This has led to a fall in community MRSA and subsequently in high-risk groups such as people living with diabetes. While levels have decreased, MRSA remains a clinical challenge in DFU infections and further studies will be required to continue monitoring prevalence as resistance profiles change over time.

Our study has a number of strengths. First, in being a single-centre study with a small number of podiatrists observing the same sampling technique it would reduce chances of variability in sampling technique. The CODIFI study highlighted the significance of centre-based differences of tissue collection and specimen processing as well as differences in laboratory processing in yielding isolates from DFUs.[25] In addition, in using a single microbiology laboratory with a single data set, it eliminated potential inconsistencies in obtaining data by using the same search criteria. Lastly, our data reflect what has been shown elsewhere and thus we believe that despite, our limitations, our results remain valid. Our study was limited by the inability to retrieve participant data preceding the introduction of electronic documentation at our institution. This restricted further analysis including epidemiological characteristics, clinical outcomes and other risk factors such as antibiotic treatment regimes, duration of diabetes and success of glycaemic control. In addition, it prevented identification of cases which were successfully treated and those possibly complicated by recurrence, which may have been caused by different organisms or varying strains of MRSA. We were able to access records from 2010 to 2021 to provide association with MRSA positive cases and risk factors, although without a control group of MSSA cases, significance could not be determined, and this is beyond the scope of this paper.

In summary, we have shown that between 2005 and 2021, there has been a reduction in the prevalence of MRSA in those with diabetes-related foot ulcers.

AUTHOR CONTRIBUTIONS

CG, RS and KD developed the initial idea for the study. JM, CG and KD made substantial contributions to the conception and design of the study. JM conducted data analysis, interpretation and drafted the manuscript. JM and KD critically reviewed and revised the manuscript for important intellectual content. All authors read, amended and approved the final manuscript.

ACKNOWLEDGEMENTS

We are very grateful to Claire Stuart and Graham Verbrugge who supplied data used in study. We thank Emma Bull and Helen Popov for support in data analysis and graphical presentation.

FUNDING INFORMATION

None.

CONFLICT OF INTEREST STATEMENT

The authors have no financial or competing interests that impact on their responsibilities towards the scientific value or potential publishing activities associated with the study.

DATA AVAILABILITY STATEMENT

The datasets generated and/or analysed during the current study will be made available from the corresponding author on reasonable request, provided appropriate credit is attributed to the original authors and the data source.

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

Did not require ethical approval, no participant identifiable information included.

CONSENT FOR PUBLICATION

Not applicable.

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How to cite this article: Moore J, Gooday C, Soliman R, Dhatariya K. Reduction in the prevalence of methicillin-resistant *Staphylococcus aureus* in tissue and wound swab samples taken from outpatients attending a specialist diabetic foot clinic 2005–2021. *Diabet Med*. 2023;40:e15081. doi:10.1111/dme.15081