RESEARCH LETTER

Methicillin-Resistant *Staphylococcus Aureus* Colonization and Mortality Risk Among Community Adults Aged 40-85

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Introduction: **The objective of this study was to assess the 11-year mortality risk of methicillin-resistant *Staphylococcus aureus* (MRSA) colonization in community-dwelling adults aged 40 to 85 years.**

Methods: **The study analyzed the National Health and Nutrition Examination Survey (NHANES) 2001 to 2004 linked to the National Death Index through December 31, 2015. Our cohort of community adults aged 40 to 85 years was 6085 participants (representing 118 718 486 adults). Mortality risk from MRSA colonization was examined with an 11-year follow-up.**

Results: **The 11-year mortality rates were 35.9% (95% CI, 25.4%- 46.4%) for MRSA-colonized and 17.8% (95% CI, 16.4%- 19.2%) for non-colonized participants. After adjusting for potential confounders the hazard ratio for mortality among those colonized with MRSA was 1.75 (95% CI, 1.12-2.73).**

Discussion: **MRSA colonization in middle-aged and older adults in the community is associated with a significantly increased mortality risk. Considering that this effect was in the community and not in hospitalized patients, this finding of increased mortality risk is especially troubling. (J Am Board Fam Med 2021;34:439–441.)**

Keywords: **Cohort Studies, Methicillin-Resistant Staphylococcus Aureus, Mortality, NHANES, Population Health**

Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) infections are associated with significant morbidity and mortality.[1] Several cohort studies have examined MRSA colonization, not an infection, on downstream mortality risk with some focusing on hospitalized or nursing home patients and others focusing on community adults.[2,3] These studies have yielded different findings with only some yielding an increased mortality risk.[2–4] One study using a national cohort of colonized community adults as young as 18 years found no significant effect, which was likely due to the low general mortality risk of young adults.[3] The mortality risk of middle-aged and older community adults colonized with MRSA is currently unclear.

Methods

We analyzed the National Health and Nutrition Examination Survey (NHANES) 2001 to 2004 linked to the National Death Index through December 31, 2015. The NHANES uses a stratified multistage probability sample design to be representative of the United States (US) population. These are not patients but rather individuals in the community. This 2001 to 2004 baseline NHANES included 6270 participants aged 40 to 85 years. MRSA colonization was measured by nasal swabs plated on mannitol salt agar. Those that were *S. aureus* positive isolates were tested for resistance to oxacillin (MRSA). Individuals with missing MRSA colonization or mortality follow up information were excluded from the analysis, reducing the size of our analyzed cohort to 6085 participants. As a population-based cohort with a complex survey design and appropriate weighting a population

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Table 1. Baseline Characteristics of the Cohort (N = 6085; Weighted N = 118, 718 486)

	Staph Colonization	Staph Non-Colonized	MRSA Colonization	MRSA Non-Colonized
Weighted N	32, 735 000	85, 983 486	1, 793 186	116, 925 300
	%	%	%	%
Percentage of deaths	16.7	18.6	35.9	17.8
Sex				
Male	49.8	46.6	38.2	47.6
Female	50.2	53.4	61.8	52.4
Race/ethnicity				
Non-Hispanic White	80.9	76.4	83.6	77.5
Non-Hispanic Black	7.0	10.8	8.2	9.8
Hispanic	8.4	8.6	3.9	8.6
Other race/ethnicity	4.3	4.2	4.2	4.1
Poverty-to-income ratio > 1	83.9	84.9	75.8	84.8
No health insurance	9.1	11.5	5.1	10.9
Hospitalization in the past 12 months	12.8	11.8	25.4	11.9
Heart disease	9.2	10.4	18.0	10.0
Diabetes	11.5	10.6	14.7	10.8
Asthma	11.6	11.2	18.6	11.2

MRSA, methicillin-resistant *Staphylococcus aureus*.

Table 2. All-Cause Mortality Hazard Ratios for Methicillin-Resistant *Staphylococcus aureus* Colonization a 11-Year Period

	Crude HR (95% CI)	*P* value	Adjusted HR* (95% CI)	*P* value
MRSA colonization	2.30 (1.61-3.29)	< .001	1.75 (1.12-2.73)	.014
Staph colonization	0.90 (0.75-1.06)	.206	0.91 (0.75-1.11)	.348

CI, confidence interval; HR, hazard ratio; MRSA, methicillin-resistant *Staphylococcus aureus*.
*Model adjusted for sex, race/ethnicity, poverty-to-income ratio, lack of health insurance coverage, hospitalization in the previous 12 months, and the presence of heart disease, diabetes, and asthma.

estimate representative of the noninstitutionalized US population allows the sample to represent 118 718 486 adults. The mortality status for each participant was censored at 11 years to create consistency among follow-up lengths between members of the different NHANES cohorts.

Unadjusted Cox proportional hazards models were used to compare the 11-year mortality risk between MRSA colonized and non-colonized individuals. Cox regression analyses adjusted for the potential confounders of gender, race/ethnicity, health insurance, poverty-income ratio, hospitalization in the previous 12 months, and doctor diagnosis of heart disease, diabetes, and asthma in a forced inclusion model predicting mortality between MRSA colonized and non-colonized individuals. Cox proportional hazards models were also applied to assess the 11-year mortality risk of *S. aureus* colonization. All analyses were conducted using the survey package in R 3.6.3 to account for the complex NHANES sampling design and make population estimates.

Results

Table 1 shows the characteristics of the cohort. In the US population aged 40 to 85 years, 1.5% (95% CI,1.1%- 2.0%) were MRSA colonized. The 11-year mortality rate for *S. aureus* colonization was 16.7% (95% CI, 14.5% -18.9%) and 18.6% for those not colonized (95% CI, 16.8%- 20.3%). The

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11-year mortality rates were 35.9% (95% CI, 25.4%-46.4%) for MRSA-colonized and 17.8% (95% CI, 16.4%-19.2%) for non-colonized participants. Table 2 indicates that *S. aureus* colonization was not associated with mortality in an unadjusted or adjusted analysis while MRSA colonization was associated with increased mortality risk in both unadjusted and adjusted survival analyses.

Discussion

MRSA colonization in middle-aged and older adults in the community is associated with a significantly increased mortality risk. *S. aureus* colonization is not associated with increased mortality, which is consistent with previous research.[5]

Although this cohort study is based on a nationally representative population estimate of community dwellers, there are some limitations. Limitations include the lack of an ability to determine the length of colonization or whether high-risk patients were likely re-colonizers. Second, the public use data in the National Death Index lists deaths into specified categories with no category for deaths associated with infectious disease.

Our observation of increased mortality risk among MRSA colonized individuals invites further investigation into the risks of MRSA colonization. Considering that MRSA colonization among adults in the community was examined rather than MRSA infection in hospitalized patients, this finding of increased mortality risk is especially troubling. It is important to emphasize that current evidence is unclear whether MRSA decolonization of colonized individuals in the community would have a positive benefit in decreasing the mortality risk.

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