Archives of Gynecology and Obstetrics (2019) 300:1303–1316
https://doi.org/10.1007/s00404-019-05287-6

GENERAL GYNECOLOGY

Clinical relevance of colonization with antimicrobial-resistant bacteria (AMRB) and methicillin susceptible *Staphylococcus aureus* (MSSA) for mothers during pregnancy

A. H. Dammeyer[1] · S. Heinze[1,2] · A. C. Adler[3] · L. Nasri[4] · L. Schomacher[1] · M. Zamfir[1] · K. Heigl[1] · B. Karlin[5] · M. Franitza[4] · S. Hörmansdorfer[1] · C. Tuschak[1] · G. Valenza[1] · U. Ochmann[2] · C. Herr[1,2]

Received: 14 May 2019 / Accepted: 3 September 2019 / Published online: 17 September 2019
© Springer-Verlag GmbH Germany, part of Springer Nature 2019

Abstract

Purpose The impact of colonization with antimicrobial-resistant bacteria (AMRB) and methicillin-sensitive *Staphylococcus aureus* (MSSA) of healthy pregnant women is not described in detail in Germany. In this study, we screened for MSSA and AMRB, especially for methicillin-resistant *S. aureus* (MRSA) as well as extended-spectrum beta-lactamase (ESBL)-producing *E. coli*. Potential risk factors for colonization with AMRB/MSSA and the potential effects of colonization with these on the obstetric population were investigated.

Methods From October 2013 until December 2015 pregnant women were screened before birth for colonization with AMRB/MSSA from the mammillae, nose, perianal and vaginal area. Before birth, the expectant mother was administered a standardized interview questionnaire by a trained interviewer. Data from the hospital admission records were also included.

Results Samples from 651 pregnant women were analyzed. Colonization with MSSA was detected in 14.3% ($n=93$), AMRB in 3.5% [($n=23$); MRSA: $n=3$/ESBL: $n=20$]. Significantly more colonization of AMRB/MSSA could be detected in women who had previously given birth compared to women who were nulliparous ($p<0.05$). MSSA colonization was significantly associated with self-reported respiratory diseases during pregnancy ($p<0.05$), but AMRB/MSSA colonization was not statistically associated with other types of infection.

Conclusion Our results demonstrate a low overall rate of colonization with AMRB/MSSA, as well as a low percentage of colonized pregnant women who developed infections. Multiparous women are at higher risk for colonization with MSSA/MRSA or ESBL. Because the prevalence of AMRB/MSSA is low, this study suggests that general screening of pregnant women without risk factors is not recommended.

Keywords MRSA · MSSA · ESBL · AMR · AMRB · Pregnancy · Prevalence · Risk factors

Introduction

The colonization with microorganisms such as antimicrobial-resistant bacteria (AMRB) and methicillin-sensitive *Staphylococcus aureus* (MSSA) can lead to infections [1]. The consequences of AMRB and MSSA-related infections in healthy pregnant women may be prolonged hospital stays, additional hospital costs and more difficult treatment conditions [2]. Therefore, it is important to know the prevalence and clinical impact of colonization with antibiotic-resistant bacteria. The impact of colonization with AMRB and MSSA of healthy pregnant women is not described in detail in Germany. The increasing prevalence of infections as well as the reduced discovery of new drugs makes treatment more challenging [3]. It is questionable whether colonization with

✉ A. H. Dammeyer
antchen.d@gmail.com

1 Bavarian Health and Food Safety Authority, Munich/Oberschleißheim/Erlangen, Germany

2 Institute and Outpatient Clinic of Occupational, Social and Environmental Medicine, Clinic of the University of Munich, Munich, Germany

3 Bavarian State Ministry of Public Health and Care Services, Munich, Germany

4 Klinikum Augsburg, Women's Clinic, Augsburg, Germany

5 Rotkreuzklinikum München, Women's Clinic, Munich, Germany

AMRB and MSSA is relevant for pregnancy and childbirth and whether there is transmission from mother to child.

Prevalence of colonization

Methicillin-resistant *Staphylococcus aureus* (MRSA) as well as extended-spectrum beta-lactamase (ESBL)-producing microorganisms are some of the most common multiresistant bacteria [4, 5]. MSSA is often used as surrogate parameter for MRSA due to similar characteristics (e.g. in terms of PVL production), transmission pathways and caused infections. Similarly to MRSA, carriage of MSSA does not necessarily lead to infection; it is a facultative pathogen [6].

A study on the prevalence of ESBL-producing *E. coli* among infection control personal revealed a colonization rate of 3.5% [7] which continues to increase [1]. Furthermore, the number of ESBL-producing *E. coli* in German outpatient care increased from 2.7% in 2008 to 5.6% in 2012 [8]. Increases in ESBL-*E. coli* colonization in both hospital and community setting are an emerging threat [9].

In the German general population, MSSA was carried at least once in 40.9% [10] and in German hospitals MRSA prevalence decreased from 14.0% in 2010 to 9.0% in 2015 taken from swabs [11].

However, studies with the prevalence of AMRB in pregnant women are limited. It is difficult to find sources stating coherent prevalence of MSSA, MRSA and ESBL in Germany in the healthy, pregnant women population as most studies focus on high-risk populations. Therefore, most of the data available describe the prevalence of MSSA or MRSA in intensive care units [2], and colonization in the USA where prevalence rates in the obstetric setting are much higher than in the Western European region [12]. Various studies report MSSA colonization with 17–24.3% and MRSA colonization with 0.5–3.5% [12–14] in the USA in pregnant women. A literature review from 2010, which included the data of Medline, EMBASE and the Cochrane database, showed that the prevalence of MRSA in the obstetric population is generally low [15]. Exact numbers about the total incidence of MRSA and ESBL colonization in the obstetric population in Germany are not available. Given the limited availability of use of antibiotics, it is vital that research is focused on this particular risk group.

Infections

Evidence has been provided that shows an association between colonization with AMRB/MSSA and higher probability of infection [16]. MRSA or MSSA caused infections are not clinically distinguishable [5], but MRSA infection is associated with a higher mortality rate (36.4% with MRSA and 27% with MSSA in intensive care patients). The reason for that is not adequately clarified, but a possible explanation could be the delayed effect of antibiotics therapy or different pharmacokinetic properties of the antibiotic [5].

MRSA infections in the general population are often locally limited skin and soft tissue infection or recurrent abscess [17].

The prevalence of MRSA colonization in the obstetric population is comparable with the prevalence in the general population [18]. Most commonly it presents as skin and soft tissue infection (SSTI) with multiple sites and recurrences [18, 19].

Serious infectious syndromes have been reported [18] and can affect the obstetric population. Urinary tract infections (UTI) caused by ESBL colonization are one of the most frequent infections appearing during pregnancy [20]. The colonization with antibiotic-resistant bacteria complicates the treatment of these infections. Some epidemiologic reviews state, that the presence of an ESBL colonization is associated with a threefold increase in the risk to develop an urinary tract infection [21].

Risk factors

Various sources show different potential risk factors for colonization with AMRB or MSSA. Among the generally known and well described risk factors are hospitalization [22–25] contact with the health care setting [26, 27] chronic diseases or comorbidities [3, 27, 28] and previous antibiotic use [3, 23, 24].

There is no immediate risk of infection after colonization for healthy people. At risk for infection after AMRB colonization are people with chronic wounds, skin lesions, chronic diseases like diabetes or undergoing immunosuppressive therapy [3, 5, 29].

Another potential risk factor for AMRB colonization and spread could be travelling or time spent abroad [30, 31]. Studies determined that a colonized family member is also a high-risk factor for colonization with AMRB/MSSA (intra-familial transmission) [32, 33]. In this context, Kellie shows that contact with children in day-care could be a further cause of MRSA acquisition [18]. Further risk groups for a MRSA colonization are pregnant women who had a cesarean section or who are multiparous [19].

A potentially higher risk for colonization with livestock-associated MRSA (LA-MRSA), are also persons either coming in direct contact with industrial livestock or via inhalation of contaminated barn dust [34]. The actual number of ambulant LA-MRSA infections in Germany is unknown [35]. LA-MRSA is not less virulent than other MRSA but can be differentiated in its epidemics in health care institutions [36].

Objective

Thus, it is particularly relevant to find how colonization with AMRB affects the obstetric population. So far there are scarcely any research results on the clinical relevance and risk factors for the colonization with MSSA, MRSA or ESBL in the obstetric population.

The aim of this study was to detect the prevalence of colonization of healthy pregnant women with AMRB/MSSA as well as its clinical relevance and corresponding risk factors.

Methods

Population

Participants from two large Bavarian clinics were recruited from October 2013 until December 2015 to participate in this (cross-sectional) study. Therefore, they had to sign an informed consent form, be at least 18 years of age and have a planned vaginal delivery. Primary, selected or emergency caesarean section, outpatient birth, multiple pregnancies or cervical incompetence (pessary, cerclage) were excluded from the study. Data from participants who withdrew their consent or moved to another health care facility were removed from the study. All the collected data and the microbiological samples were pseudo-anonymized via an internal encryption code which did not contain the name, initials or date of birth. The methodology has already been described in detail in the work of Adler et al. and Zamfir et al. [37, 38].

The study was developed by the Bavarian Health and Food Safety Authority, Munich and was funded by the Bavarian State Ministry for Public Health and Care Services. The Institutional review board of Ludwig-Maximillians-University Munich approved the study.

Data collection

Before birth, the expectant mother was administered a standardized in-person interview questionnaire by a trained interviewer. The expectant mother answered questions regarding potential contact with fomites, exposure to known risk factors or persons belonging to a group with higher prevalence of AMRB. The questions in the questionnaire were designed to assess prospectively designated selected risk factors for AMRB/MSSA-colonization. Of particular importance were the issues of occupational activity, infections and hospital stays during pregnancy. The mother's medical history and medication intake were self-reported during this interview (Fig. 1). Data from the hospital admission records such as delivery date, weight and size of the mother were also included. The child's birth data, possible complications and the discharge from the hospital were collected from medical records. After about six weeks, a follow-up Computer Assisted Telephone Interview (CATI) was conducted concerning any infection the child or the mother developed after hospital leave.

Screening

Before birth, four samples were taken from the woman. In prevention service U1 and prevention service U2 a total of 5 samples were taken from the newborn. In total, samples were taken from the following sites: Mother: mammillae, nose, vaginal, perianal; infant (U1): nose, perianal; infant (U2): nose, perianal, umbilical. All samples were screened for MSSA, MRSA and ESBL-*E. coli.* Antibiotic resistance screening for MRSA and ESBL was performed. The isolates were tested for antibiotic susceptibility, for detailed description see the article by Zamfir et al. [37].

Statistical methods

To compare categorical variables, the χ^2-test and Fisher's exact test were used. A logistic regression model building was done with the potential factors with influence on colonization status selected a priori. A p value < 0.05 was considered as statistically significant. All statistical analyses were performed using SPSS 23.0 (IBM).

Results

Descriptive statistics and prevalence

This study analyzed data from 651 pregnant women. Out of initially 763 participating pregnant women, 112 were excluded due to missing questionnaires. 62.5% ($n = 406$) of data were collected in clinic 1 as well as 37.6% ($n = 245$) in clinic 2. Post-delivery 420 women were interviewed per follow-up CATI.

The average age of pregnant women at hospital admission was 32 years (SD = 4.8). The underlying average BMI before pregnancy was 23.7 (SD = 6.0) with a minimum of 12.9 and a maximum of 51.3. A summary of the socio-demographic data is given in Table 1. AMRB/MSSA colonization was detected in 17.4% ($n = 113$), whereof MSSA was found in 14.3% (n = 93) and AMRB in 3.5% ($n = 23$) (MRSA: $n = 3$; ESBL $n = 20$) of the pregnant women.

Analysis of risk factors and clinical relevance

Different potential risk factors for infections were analyzed to examine an association between the colonization with AMRB/MSSA and clinical relevance.

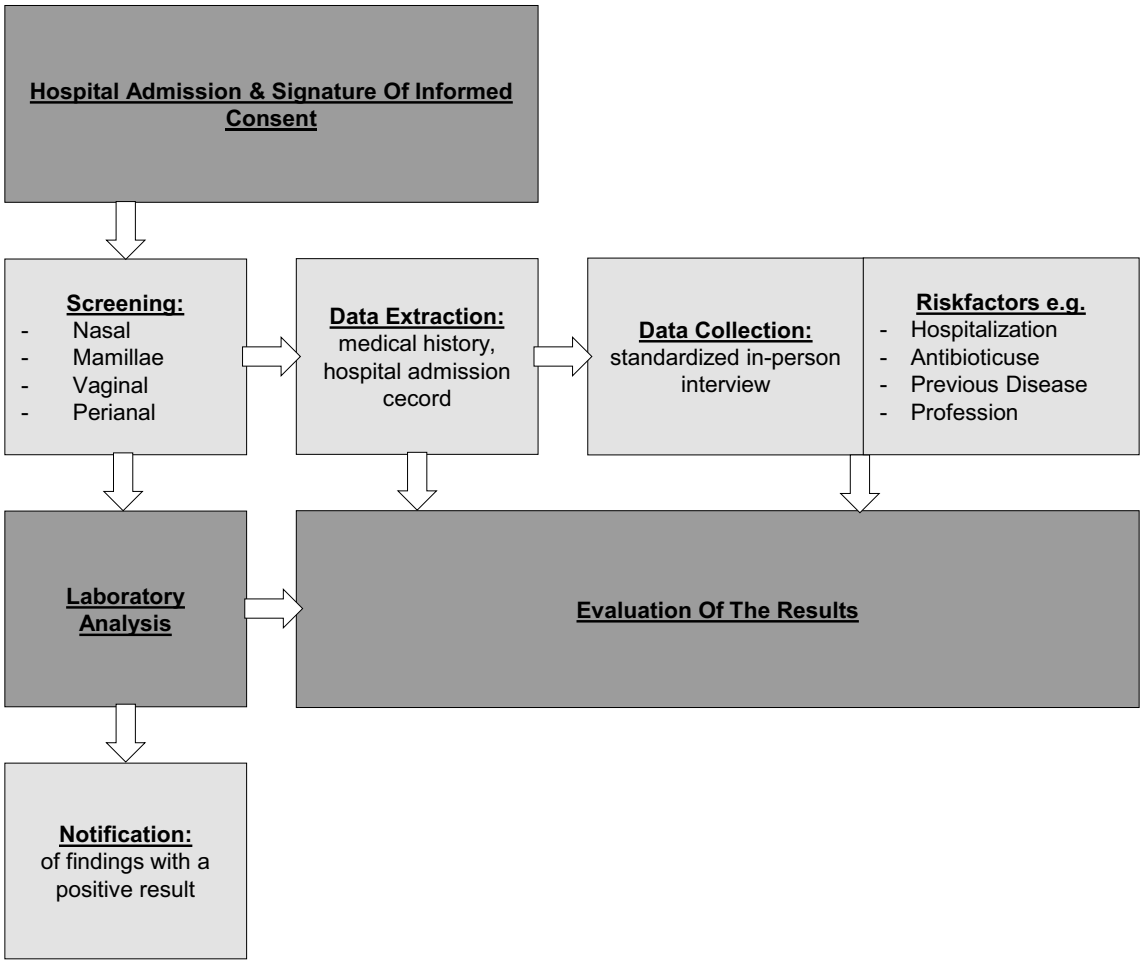

Fig. 1 Data collection

Table 1 Sociodemographic characteristics of pregnant women

	Total ($N=651$)		Clinic 1 ($N=406$)		Clinic 2 ($N=245$)	
	n	%	*n*	%	*n*	%
Age in years						
18–29	197	30.6	114	28.5	83	34.2
30–34	253	39.3	156	39.9	97	39.9
> 34	193	30.0	130	32.5	63	25.9
BMI						
Underweight (< 19)	47	7.2	29	7.1	18	7.4
Normalweight (19–25)	400	61.4	246	60.6	154	62.9
Overweight/Adipositas (≥ 25)	186	28.6	119	29.3	67	27.4
Previous birth						
Nulliparous	433	66.5	290	71.4	143	58.4
Multiparous (1)	165	25.4	82	20.2	83	33.9
Multiparous (2)	40	6.1	25	6.2	15	6.1
Multiparous (3 or more)	13	2.0	9	2.2	4	1.6

Regarding the delivery mode, 79% ($n=514$) of the pregnant woman had a vaginal delivery. The remaining 21% ($n=137$) delivered with a secondary Cesarean Section due to different unpredictable reasons. The mode of delivery did not predict colonization with AMRB/MSSA.

Another factor considered was previous pregnancies. About one third (33.5%; $n=218$) of the women were multiparous. From them, 16.9% ($n=37$) were colonized with MSSA, 0.9% ($n=2$) with MRSA and 4.1% ($n=9$) with ESBL-*E. coli*. From the woman who were nulliparous (66.5%; $n=433$), MSSA colonization could be detected in 12.9% ($n=56$), MRSA colonization in 0.2% ($n=1$) and 2.5% ($n=11$) colonization was detected with ESBL-*E. coli.* Consequently, significantly more colonization of MRSA/MSSA and ESBL-*E. coli* could be detected in women who had previous birth compared to women who were nulliparous ($p<0.05$).

Differences due to hospital location were not significant (Clinic 1: $n=12$; 2.4% ESBL-*E. coli*/Clinic 2: $n=8$; 3.2% ESBL-*E. coli*). 258 (40%) women reported travelling abroad during their pregnancy. Overall, no significant increase was detected in the colonization with MRSA ($n=0$; 0%), MSSA ($n=38$; 15%) or ESBL-*E. coli* ($n=5$; 2%) (Table 2). Of the women who traveled abroad, 5% ($n=12$) reported having had contact with health care facilities (2 as guests and 10 as patients). From the 651 mothers included in the study, 10 mothers reported having had contact with the medical services outside the country as patients (3 stationary) and 2 were visitors. The factors "professional activity in the healthcare sector" and "leisure/professional activity within agriculture or with animals" showed no statistically significant differences with regard to AMRB/MSSA colonization.

Furthermore, pregnant women self-reported preexisting diseases (long-term medication, cardiovascular diseases, kidney or thyroid diseases, hypertension and diabetes) in 16.9% of the cases and medical conditions during pregnancy (gestational hypertension, gestational diabetes) in 8.9%. Both factors did not predict AMRB/MSSA colonization. Likewise, antibiotic use did not predict AMRB/MSSA colonization during pregnancy. When looking at hospitalization, it was found that the median hospital stay was four days. The days were not significantly different when the mother was colonized with MSSA, MRSA or ESBL-*E. coli.* The odds ratio of colonization with AMRB for pregnant woman who were hospitalized was 0.87 (CI 0.11–6.96) and 0.42 (CI 0.16–1.17) for pregnant woman who travelled abroad after adjusting for clinic and antibiotic use in the logistic model. The odds ratio without adjusting were 0.70 (CI 0.09–5.33) and 0.55 (CI 0.20–1.51), respectively.

From the 113 (17.4%) women positive for MRSA/MSSA or ESBL colonization during pregnancy, 8.8% had a vaginal infection, 5.3% had a urinary tract infection (UTI), 0.9% a soft tissue infection and 11.5% a respiratory disease such as bronchitis, sinusitis or otitis, as indicated in Table 3.

Figure 2 compares the infections of patients with AMRB/MSSA colonization and without. Patients suffering from a self-reported respiratory disease had a higher percentage of AMRB/MSSA colonization. Thus, MSSA colonization was significantly associated with respiratory diseases ($p<0.05$), but MRSA, MSSA or ESBL colonization were not statistically associated with other types of infections.

The data from the post-survey were evaluated and can be found in Table 4. There is no significant evidence that AMRB/MSSA induced infections after delivery are higher than infections that are not due to colonization, based on data of colonization before birth.

With regards to the antibiotic resistance of the bacterial isolates, 100% of MSSA isolates were resistant to penicillin. MRSA isolates were 100% resistant to cefoxitin, imipinem, oxacillin and penicillin. In ESBL isolates, amoxicillin, ampicillin, cefotaxime, cefuroxim, piperacilin and tazobactam resistance was found in all isolates (Fig. 3).

Discussion

Our results demonstrate a low overall rate of colonization with MSSA (14.3%), MRSA (0.5%) and ESBL-*E. coli* (3.1%). Other sources reported comparable results with a MSSA prevalence of 17–24.3% [13], MRSA prevalence of 0.5–3.5% [12–14] and ESBL-*E. coli* prevalence of 6.3–8.6% [26, 39]. The colonization with AMRB/MSSA was not significantly associated with any demographic or obstetrical

Table 2 Travelling

	Total ($N=258$)		MSSA ($N=38$)		MRSA ($N=0$)		ESBL ($N=5$)	
	n	%	*n*	%	*n*	%	*n*	%
North-/West Europe	59	22.9	9	23.7	0	0.0	0	0.0
East-/South Europe	166	64.3	22	57.9	0	0.0	4	80.0
North America	10	3.9	1	2.6	63	0.0	0	0.0
Central-/South America	10	3.9	1	2.6	0	0.0	0	0.0
Asia	15	5.8	4	10.5	0	0.0	1	20.0
Africa	3	1.2	1	2.6	0	0.0	0	0.0

Table 3 Analysis of risk factors and clinical relevance

	Total ($N=651$)		AMRB + SA pos ($N=113$)		AMRB + SA neg ($N=23$)		MRSA ($N=3$)		SA ($N=93$)		ESBL ($N=20$)	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Mode of delivery												
Vaginal	514	79.0	89	78.8	20	87.0	3	100.0	71	77.2	17	85.0
Cesarean[c]	137	21.0	24	21.2	3	13.0	0	0.0	21	22.9	3	15.0
Previous pregnancy												
Nulliparous	433	66.5	65*	57.5	12	55.2	1	33.3	55	60.0	11	55.0
Multiparous	218	33.5	48	42.5	11	47.9	2	66.6	37	40.0	9	45.0
Risk factors												
Stay Abroad	252	38.7	43	38.1	5	21.7	0	0.0	38	41.0	5	25.0
Profession Healthcare	28	4.3	5	4.4	0	0.0	0	0.0	5	5.4	0	0.0
Profession Agriculture	173	26.6	31	27.4	4	17.4	1	33.3	27	29.4	3	15.0
Previous disease[a]	110	16.9	19	16.8	2	8.7	0	0.0	17	17.9	2	10.0
Disease during pregnancy[b]	58	8.9	10	8.8	1	4.3	0	0.0	9	9.5	1	5.0
Antibiotic use	80	12.3	15	13.3	1	0.2	0	0.0	14	14.7	1	0.2
Hospitalzation	46	7.1	10	1.5	1	0.2	0	0.0	9	1.4	1	0.2
Infections in pregnacy												
Vaginal	57	8.8	10	8.8	4	17.4	0	0.0	6	6.3	4	20.0
Urinary tract	43	6.6	6	5.3	0	0.0	0	0.0	6	6.5	0	0.0
Purupent Skin	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Soft tissue	14	2.2	1	0.9	0	0.0	0	0.0	1	1.1	0	0.0
Otitis	6	0.9	1	0.9	0	0.0	0	0.0	1	1.1	0	0.0
Respiratory[d]	41	6.3	12**	10.6	1	4.4	0	0.0	11***	12.0	1	5.0
Operation	5	0.8	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

*p 0.026

**p 0.038

***p 0.016

[a]Long-term medication/cardio vascular/kidney, thyroid/hypertension/diabetes I, II

[b]Gestational hypertension/diabetes

[c]Only secondary C-section (not emergency or primary)

[d]Respiratory = sinusitis, bronchitis

variable except increased parity and self- reported respiratory infections during pregnancy.

Comparing our results with the available data is opaque due to methodological differences, as well as sampling from different skin regions and at different time points.

Infections and diseases

Different determinants like the ability to spread, as well as virulence factors (e.g. pathogenity, resistance and factors from the environment like hygiene) influence whether colonization leads to infection or not [40]. Our study showed, that only a small percentage of colonized pregnant women also have infections. It can also be mentioned that colonized women are more susceptible to later reinfections [41]. Huang et al. [41] found that about 29% of patients developed MRSA reinfections.

A previously reported association between chronic disease or comorbidities and higher incidence of AMRB/MSSA colonization [3, 42] could not be detected in our study. Self-reported preexisting or chronic medical conditions were not significantly associated with colonization (Table 3).

With respect to acute infections, AMRB/MSSA colonization resulted in more respiratory infections in pregnant women. MSSA colonization in particular, which is used as a surrogate parameter for MRSA due to similar characteristics, was associated with respiratory diseases, as confirmed by Lowy [3]. A point prevalence survey reported lower respiratory tract infections as the most frequent documented nosocomial infection [43]. Respiratory infection is one of the major consequence of MRSA colonization, with the more serious results of MRSA induced pneumonia [35].

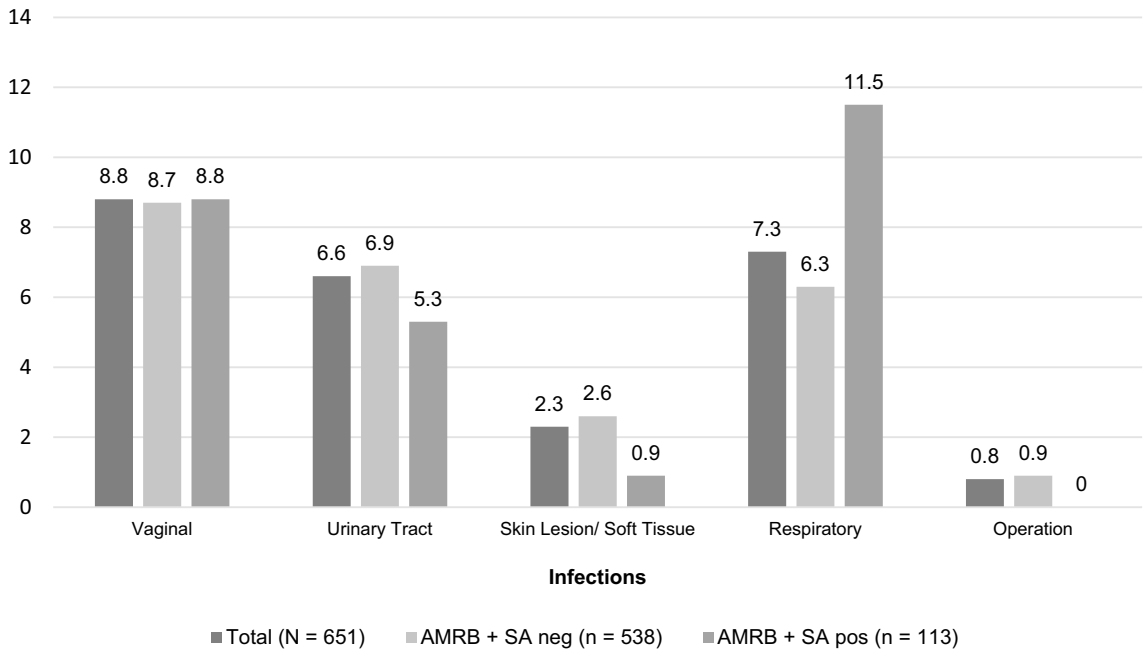

Fig. 2 Infections of pregnant women with/without colonization

Clinically, the most common result of MSSA/MRSA colonization is skin and soft tissue infection [17, 28, 44]. Numerous studies suggested that colonization with AMRB/MSSA correlates with a higher risk of postpartum infections like increased risk for postoperative or post-cesarean wound infections as well as postpartum mastitis [45]. Other studies stated that there is no higher risk of infection through MRSA colonization [13], which was coherent with our results. In our study population only 15 cases of SSTI (2.4%) were found, from them only 1 case (6.7%) was colonized with MSSA and none with MRSA. Similar results were found for postoperative condition—in our study sample, only 5 women had surgical intervention during pregnancy. A larger study population would have been needed to reliably detect comparable results.

UTI is one of the most common nosocomial infections [43] and presents a particular problem for pregnant women and their children since they are the most frequent infections appearing during pregnancy [20]. Most frequently they are due to colonization with gram-negative pathogens [27]. Studies show that the numbers of community-acquired UTI with ESBL-*E. coli* keep increasing [4, 46, 47]. Ascending microorganisms in the vaginal tract can lead to possible problems during pregnancy, for example ascending ESBL-*E. coli* in the urinary tract. In our sample 6.6% ($n=43$) self-reported having had an UTI, 5.3% ($n=6$) of them also having colonization with ESBL-*E. coli* or MSSA (none with MRSA). This is comparable to the incidence of bacteriuria in pregnancy as reported by the German Society of Urology [48].

Pregnant women are more inclined to develop a vaginal or urinary tract infection due to hormonal and physiologic changes [20]. Vaginal infection was the most self-reported infection in our sample during pregnancy. 8.8% ($n=57$) of women, from them 17.5% ($n=10$) being colonized with ESBL-*E. coli* or MSSA. In the literature, incidence bacterial vaginosis (bacterial disturbance of the vaginal flora) is reported to be 5 to 20% in pregnancy [49, 50].

Risk factors

Risk factors for infections have been analyzed in studies before, but scarcely in the combination of MSSA/MRSA and ESBL-*E. coli*. Well known risk factors like hospitalization, antibiotic use, chronic disease and contact with health care have been associated with AMRB infection [3, 22–24, 24, 26, 27]. However, other studies found that traditional risk factors do not predict MRSA carriage in pregnant women [45]. Reusch [14] investigated risk factors (prior abscess, afterschool/daycare program, antibiotic use, hospitalization) for colonization with MRSA in pregnancy and could not identify statistically significant risk factors [12].

In our study, there are several possible explanations for the weak associations between traditional risk factors and colonization with AMRB/MSSA. Particularly the low prevalence of colonization with AMRB/MSSA restricted our statistical power. On the other hand, the low prevalence was expected, as the majority of pregnant women without additional risk factors are healthy individuals who rarely

Table 4 Questionnaire follow up

Infections before delivery	Present (see Table 3)					Non-existent (see Table 3)				
Infections after delivery	Uncolonized		Colonized		*p*	Uncolonized		Colonized		*p*
	n	%	*n*	%		*n*	%	*n*	%	
Vaginal infections	*N* = 320		*N* = 61		0.52	*N* = 34		*N* = 5		0.58
Negative	310	96.9	60	98.4		32	94.1	5	100.0	
Positive	10	3.1	1	1.6		2	5.9	0	0.0	
Skin infections	*N* = 354		*N* = 66		0.82	*N* = 0		*N* = 0		–
Negative	345	97.5	64	96.9		0	0.0	0	0.0	
Positive	9	2.5	2	3.1		0	0.0	0	0.0	
Urinary tract infections	*N* = 326		*N* = 61		0.29	*N* = 28		*N* = 5		0.67
Negative	318	97.5	58	95.1		27	96.4	5	100.0	
Positive	8	2.5	3	4.9		1	3.6	0	0.0	
Respiratory infections	*N* = 326		*N* = 57		0.05*	*N* = 28		*N* = 9		0.57
Negative	324	99.4	55	96.5		27	96.4	9	100.0	
Positive	2	0.6	2	3.5		1	3.6	0	0.0	
Overall infections	*N* = 270		*N* = 51		0.40	*N* = 84		*N* = 17		0.54
Negative	247	91.5	43	87.8		75	89.3	16	94.1	
Positive	23	8.5	6	12.2		9	10.7	1	5.9	

Fig. 3 Antibiotic resistance

need inpatient treatment. Other investigations have shown similar results [12].

These amongst others are reasons why the risk of MRSA acquisition and thus infection for healthy pregnant is not increased compared to the general population [5]. There are studies stating antibiotic use as a risk factor for colonization with MSSA or MRSA [51]; but there are also studies stating the contrary [29, 32].

Hospitalization is regarded as a strong risk factor for AMRB acquisition, but our results do not confirm this statement. Woman, who were hospitalized during pregnancy did not show a higher incidence of AMRB acquisition. In addition, the hospital stay for the delivery has been looked at and like Saiman et al. [22], we conclude that the days were not significantly different when the mother was colonized with MSSA, MRSA or ESBL-*E. coli.*

In this context, we noted that women who are multiparous show statistically significantly higher prevalence of AMRB/MSSA colonization ($p < 0.05$) compared to woman without previous deliveries. This variable is significant but a weak risk factor. Other studies point out that a risk of colonization is increased with multiparity [19, 52, 53]. Prior studies showed that multiparous women and women who have had a cesarean delivery were more likely to have CA-MRSA (community-acquired MRSA) infections [19].

A possible explanation could be recent visits to outpatient medical facility like visits at the gynecologist, prenatal care and visits at the emergency department. There the risk is higher for AMRB/MSSA colonization [45, 54]. Another reason could be more exposure with AMRB/MSSA for multiparous women who were previously hospitalized for the births of the first children.

Another variable considered was travelling or rather time spent abroad. From the 258 women (40%) travelling during pregnancy, no significant increase was detected in the colonization with MRSA.

Trips to areas with high AMRB prevalence or increased contact with potentially contaminated surfaces (e.g. airports) [30] could be risk factors [35]. Further studies showed that rectal colonization with ESBL-producing Enterobacteriaceae was associated with travelling [26]. Maier et. al. [31] showed that an increased number of MRSA cases were associated with travelling or contact with persons originating from countries with high MRSA prevalence. Similar results were found in the Netherlands or Sweden, where after return from Asia approximately 30% of individuals were colonized with ESBL [30, 55]. These findings are similar to our data where 33% ($n = 5$) of the women travelling to Asia ($n = 15$) were colonized (7% with ESBL-*E. coli* and 27% with MSSA).

Based on our study, local differences in prevalence can be traced between the two participating clinics. The difference between the two clinics in the prevalence of MSSA and ESBL-*E. coli* illustrates that prevalence is dependent on regional and local conditions and the way institution-specific factors are influencing the spread of bacteria.

Professional activity in health care was also considered as a risk factor influencing AMRB acquisition. Studies show that with 1–5% MRSA colonization, health care employees have considerably higher prevalence [43]. Contact with the health care setting is particularly also a known risk factor for ESBL infection [27]. We cannot confirm these results, but our dataset is too small to make an accurate statement. Therefore, additional special protection measures in the context of maternity protection seem to be unnecessary.

In some studies, the contact with agriculture is handled as another risk factor [35]. Köck et. al. [26] demonstrated, that people with agricultural livestock were 31 times more likely to acquire MRSA. Although frequently acquired, colonization was tested negative within 24 h [56]. The main reservoir of LA-MRSA is agricultural livestock which can be transmitted from animals to humans. A possible threat would be the introduction from the colonized human to the hospital setting [35]. Because we had so few mothers colonized with AMRB in our study population, the variable "contact with agriculture" could not clearly highlight a risk factor. The value of MRSA outside the hospital gains in importance and becomes a new challenge.

Antibiotic resistance

The therapy for MSSA and MRSA has to be differentiated. Up to 80% of MSSA strains are resistant to all penicillins. This is also reflected in our data. The therapy has to be adapted to the antibiogram and to the clinical picture [57]. According to recommendations of the Robert Koch Institute, infections with MSSA are treated with „penicillinase-resistant penicillin (e.g. flucloxacillin) as well as 1st generation cephalosporins and inhibitor-protected penicillin. Alternatives are combinations with rifampicin [40]. For skin and soft tissue infections as well as penicillin allergy a therapy with clindamycin is recommended. The total duration of treatment depends on the clinical course, but it should at least be 7–10 days [57].

In the case of an MRSA infection, the treatment will be more selective because MRSA is a variant of Staphylococcus aureus with the formation of an additional penicillin-binding protein PBP2a which has a low affinity for beta-lactam antibiotics and that results in resistances to almost all antibiotics in the beta-lactam group [40]. Vancomycin from the glycopeptide group was long time first-line therapy, but the resistances in hospitals are increasing and alternative antibiotics have to be used. This was not reflected in our data, we found 100% susceptibility for vancomycin (Fig. 3). In case of uncomplicated bacteraemia, it is still used as a standard. A series of antibiotics are available as alternative

therapy. Clindamycin, for example, is rarely effective in nosocomial MRSA infections. It is often effective in community acquired MRSA, but our data showed 33% resistance for clindamycin. Further alternatives to vancomycin are available; Teicoplanin is another representative of glycopeptides or linezolid as well as daptomycin or tigecycline can also be used [58]. Our data do also reflect 100% susceptibility in these alternative antibiotics.

In the event of a gram-negative infection, ESBL formers are considered. Extended-spectrum β-Lactamase is a beta-Lactamase with an extended-spectrum, which inactivates penicillin and cephalosporins, which are highly resistant to many antibiotics. Data from a study in France found an increasing resistance from 2001 to 2016 in the third generation of cephalosporin group for invasive *E. coli* strains [59]. Our data also showed resistance to this group, ESBL-*E. coli* was susceptible with only 19% to ceftazidim. Further resistances exist for amoxicillin, ampicillin, piperacillin and tazobactam, cefepim, ceftazidim, cefotaxim and cefuroxim. Equally, substances from the group of flouroquinolones (ciprofloxacin and levofloxacin each up to 35%) as well as substances from the groups of glycosides (azithromycin 73%) and aminoglycosides (gentamicin 42%) show resistances. Today, this might constitutes a greater therapeutic problem in Europe than MRSA [60]. Currently, available therapy options are beta-Lactamase inhibitors in combination with a penicillin or cephalosporin as well as temocillin, carbapenems, colistin, fosfomycin and tigecycline [60]. Resistance to fosfomycin and tigecycline are very rare until now.

Prevention and screening

The Hospital-Infections-Surveillance-System (KISS), a German surveillance system for nosocomial infections, proposes a focus on the improvement of prevention instead of treatment [2].

Basic hand hygiene represents a very important factor. In most cases the bacteria are transferred through the hands of medical staff (nurses and physicians). In the case of nasopharyngeal colonization, the transmission occurs via skin and can then spread further [40]. In medical institutions, the hands of employees are the most important transmission way for infections [5], a good established and consequent basic hygiene is, therefore, the basis to prevent infections and spread of bacteria [61].

Another aspect to be considered is the careful handling of antibiotics. Kallen et al. [62] showed that a uniform and transparent approach to the use of antibiotics is essential to measure the qualitative and quantitative use of antibiotics and to ensure reliable use [62]. Any use of antibiotics should be subject to a strict indication to prevent the rise of new antibiotic resistance [63].

Commission for Hospital Hygiene and Infection Prevention (KRINKO) recommends that universal screening in pregnant is ineffective [64], the prevalence is low, resulting in massive costs without additional benefits [12, 18, 65]. Our results support this approach, that there is no dependence between AMRB/MSSA colonization and associated infections.

In the case of MRSA colonization, a local eradication/decolonization is a useful prevention strategy to prevent colonization [15, 66–68].

Further, we have to mention that there is no danger for the pregnant and their unborn because Staphylococcus does not pass the placental barrier. In the situation of MRSA carriage, it is recommended to take swabs and to apply a local eradication/decolonization to prevent wound infections of the newborn [40]. Standard procedure for the eradication on skin is body washings of intact skin with antiseptic solutions, nasal eradication therapy is mupirocin treatment [40].

However, we also have to say that MRSA is rare and the burden is modest but decolonization is still recommend when the risk for infections needs to be minimized [12].

For patients colonized with ESBL-*E. coli*, it was found that ESBL will stay for some month and will then disappear in the majority of cases [63]. There are only weak data for eradication therapy, which did not give satisfying results. The appropriateness of eradication has not yet been conclusively clarified and it is not advisable so far [63].

Limitations and future studies

As previously noted, we could not demonstrate strong risk factors predicting AMRB/MSSA colonization and consequent infections. The low prevalence of colonization provided limited statistical power to determine a large number of risk factors. We recognize that there may have been many potential risk factors that could have been evaluated given a larger sample size. The analysis of risk factors reveals the multitude/variety of conflicting results. In relation to the study population, geographical location and the different strains, a variety of different aspects were considered. Samples were collected in two hospitals from two different cities from the same federal state; therefore, we can assume that the population is not fully representative for the whole German obstetric population. However, a comparison of two hospital populations is possible, with one of them in a more rural area and one with urban population.

Conclusion

Summarizing, AMRB/MSSA colonization rates in expectant mothers were low and concordant with the general population. Increased parity can be a risk factor for colonization with MSSA/MRSA or ESBL.

The colonization with MSSA/MRSA or ESBL of healthy pregnant woman did not seem relevant for infections during pregnancy. As the percentage of infections is similar in colonized and uncolonized healthy pregnant women, this study suggests that routine screening is not necessary in a population with low prevalence, when no complicated pregnancy conditions are given. Prophylactic screening or further investigations should be considered individually for every case. Awareness should be raised on problems surrounding AMRB spread, colonization and infection. Information and medical consultation of the patient are of special interest. Early detection of resistant isolates is getting more and more important because that is the only way to prevent spreading in hospitals and the community.

Author contributions AHD: Data Collection, Data Analysis, Manuscript writing. SH: Protocol/project development, Manuscript editing. ACA: Protocol/project development, Laboratory work, Data Collection, Manuscript editing. LN: Data Collection, Protocol development. LS: Data Collection, Protocol development. MZ: Data Collection, Data Analysis, Laboratory work, Manuscript editing. KH: Manuscript editing. BK: Protocol/project development, Data Collection. MF: Protocol/project development, Data Collection. SH: Laboratory work. CT: Laboratory work. GV: Laboratory work. UO: Protocol/project development. CH: Protocol/project development, Manuscript editing.

Funding This study was funded by the Bavarian State Ministry of Public Health and Care Services.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Research involving human participants Ethical approval was provided by the Ludwig-Maximilians-University, Munich, Germany. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent: Informed consent was obtained from all individual participants included in the study.

References

1. (2015) ECDC publishes 2014 surveillance data on antimicrobial resistance and antimicrobial consumption in Europe. Eurosurveillance 20(46) (**Epub 2015/11/27**)
2. Geffers C, Gastmeier P (2011) Nosocomial infections and multidrug-resistant organisms in Germany: epidemiological data from KISS (the Hospital Infection Surveillance System). Deutsches Arzteblatt International 108(6):87–93 (**Epub 2011/03/05**)
3. Lowy FD (1998) *Staphylococcus aureus* infections. N Engl J Med 339(8):520–532 (**Epub 1998/08/26**)
4. Coque TM, Baquero F, Canton R (2008) Increasing prevalence of ESBL-producing Enterobacteriaceae in Europe. Eurosurveillance 13(47):19044
5. Ruscher C. [Not Available]. Bundesgesundheitsblatt, Gesundheitsforschung, Gesundheitsschutz. 2015;58(6):654. Epub 2015/05/06. Erratum zu: Empfehlungen zur Pravention und Kontrolle von Methicillin-resistenten Staphylococcus aureus-Stammen (MRSA) in medizinischen und pflegerischen Einrichtungen : Empfehlung der Kommission fur Krankenhaushygiene und Infektionspravention (KRINKO) beim Robert Koch-Institu.
6. van Belkum A, Verkaik NJ, de Vogel CP, Boelens HA, Verveer J, Nouwen JL et al (2009) Reclassification of *Staphylococcus aureus* nasal carriage types. J Infect Dis 199(12):1820–1826 (**Epub 2009/05/08**)
7. Meyer E, Gastmeier P, Kola A, Schwab F (2012) Pet animals and foreign travel are risk factors for colonisation with extended-spectrum beta-lactamase-producing *Escherichia coli*. Infection 40(6):685–687 (**Epub 2012/09/14**)
8. Eckmanns T, Richter D, Feig M. [MRSA and ESBL in outpatient: development from 2008 up to 2012 and socio demographic differences]. Berliner und Munchener tierarztliche Wochenschrift. 2014;127(9–10):399–402. Epub 2015/04/15. MRSA und ESBL in der ambulanten Versorgung: Entwicklung in den Jahren 2008 bis 2012 sowie soziodemografische Unterschiede.
9. Danino D, Melamed R, Sterer B, Porat N, Hazan G, Gushanski A, et al. (2018) Mother to child transmission of extended spectrum beta-lactamase producing Enterobacteriaceae. J Hosp Infect 100:46 (Epub 2018/01/14).
10. Becker K, Schaumburg F, Fegeler C, Friedrich AW, Kock R (2017) *Staphylococcus aureus* from the German general population is highly diverse. Int J Med Microbiol 307(1):21–27 (**Epub 2016/12/27**)
11. Walter J, Noll I, Feig M, Weiss B, Claus H, Werner G, et al. (2017) Decline in the proportion of methicillin resistance among Staphylococcus aureus isolates from non-invasive samples and in outpatient settings, and changes in the co-resistance profiles: an analysis of data collected within the Antimicrobial Resistance Surveillance Network, Germany 2010 to 2015. BMC Infect Dis 17(1):169 (Epub 2017/02/25).
12. Gray JW, Suviste J (2012) Three years' experience of screening for meticillin-resistant *Staphylococcus aureus* in obstetrics. J Hosp Infect (0).
13. Beigi RH (2011) Clinical implications of methicillin-resistant *Staphylococcus aureus* in pregnancy. Curr Opin Obstet Gynecol 23(2):82–86 (**Epub 2010/12/24**)
14. Reusch M, Ghosh P, Ham C, Klotchko A, Singapuri S, Everett G (2008) Prevalence of MRSA colonization in peripartum mothers and their newborn infants. Scand J Infect Dis 40(8):667–671 (**Epub 2008/11/04**)
15. Gray J, Patwardhan SC, Martin W (2010) Meticillin-resistant *Staphylococcus aureus* screening in obstetrics: a review. J Hosp Infect 75(2):89–92 (**Epub 2010/04/13**)
16. Stenehjem E, Rimland D (2013) MRSA nasal colonization burden and risk of MRSA infection. Am J Infect Control 41(5):405–410 (**Epub 2012/12/25**)
17. Layer F, Cuny C, Strommenger B, Werner G, Witte W. [Current data and trends on methicillin-resistant Staphylococcus aureus (MRSA)]. Bundesgesundheitsblatt, Gesundheitsforschung, Gesundheitsschutz. 2012;55(11–12):1377–86. Epub 2012/11/02.

Aktuelle Daten und Trends zu Methicillin-resistenten Staphylococcus aureus (MRSA).
18. Kellie. Methicillin-resistant Staphylococcus aureus (MRSA) in pregnancy: epidemiology, clinical syndromes, management, prevention, and infection control in the peripartum and post-partum periods.
19. Laibl VR, Sheffield JS, Roberts S, McIntire DD, Trevino S, Wendel GD Jr (2005) Clinical presentation of community-acquired methicillin-resistant *Staphylococcus aureus* in pregnancy. Obstet Gynecol 106(3):461–465 (**Epub 2005/09/02**)
20. Connolly A, Thorp JM Jr (1999) Urinary tract infections in pregnancy. Urol Clin N Am 26(4):779–787 (**Epub 1999/12/10**)
21. Zilberberg MD, Shorr AF (2013) Secular trends in gram-negative resistance among urinary tract infection hospitalizations in the United States, 2000–2009. Infect Control Hosp Epidemiol 34(9):940–946 (**Epub 2013/08/07**)
22. Saiman L, O'Keefe M, Graham PL 3rd, Wu F, Said-Salim B, Kreiswirth B et al (2003) Hospital transmission of community-acquired methicillin-resistant *Staphylococcus aureus* among postpartum women. Clin Infect Dis 37(10):1313–1319 (**Epub 2003/10/30**)
23. Graffunder EM, Venezia RA (2002) Risk factors associated with nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) infection including previous use of antimicrobials. J Antimicrob Chemother 49(6):999–1005 (**Epub 2002/06/01**)
24. Mahamat A, MacKenzie FM, Brooker K, Monnet DL, Daures JP, Gould IM (2007) Impact of infection control interventions and antibiotic use on hospital MRSA: a multivariate interrupted time-series analysis. Int J Antimicrob Agents 30(2):169–176 (**Epub 2007/06/15**)
25. Kock R, Winner K, Schaumburg F, Jurke A, Rossen JW, Friedrich AW (2014) Admission prevalence and acquisition of nasal carriage of meticillin-resistant *Staphylococcus aureus* (MRSA) in German rehabilitation centres. J Hosp Infect 87(2):115–118 (**Epub 2014/05/06**)
26. Kock R, Werner P, Friedrich AW, Fegeler C, Becker K (2016) Persistence of nasal colonization with human pathogenic bacteria and associated antimicrobial resistance in the German general population. New Microbes New Infect 9:24–34 (**Epub 2016/02/11**)
27. Eppes CS, Clark SL. Extended-spectrum beta-lactamase infections during pregnancy: a growing threat. American journal of obstetrics and gynecology. 2015. Epub 2015/03/17.
28. Wertheim HF, Melles DC, Vos MC, van Leeuwen W, van Belkum A, Verbrugh HA et al (2005) The role of nasal carriage in *Staphylococcus aureus* infections. Lancet Infect Dis 5(12):751–762
29. Herrmann M, Petit C, Dawson A, Biechele J, Halfmann A, von Muller L et al (2013) Methicillin-resistant *Staphylococcus aureus* in Saarland, Germany: a statewide admission prevalence screening study. PloS One 8(9):e73876 (**Epub 2013/09/17**)
30. Ostholm-Balkhed A, Tarnberg M, Nilsson M, Nilsson LE, Hanberger H, Hallgren A (2013) Travel-associated faecal colonization with ESBL-producing Enterobacteriaceae: incidence and risk factors. J Antimicrob Chemother 68(9):2144–2153 (**Epub 2013/05/16**)
31. Maier J, Melzl H, Reischl U, Drubel I, Witte W, Lehn N et al (2005) Panton-Valentine leukocidin-positive methicillin-resistant *Staphylococcus aureus* in Germany associated with travel or foreign family origin. Eur J Clin Microbiol Infect Dis 24(9):637–639 (**Epub 2005/09/17**)
32. Niniou I, Vourli S, Lebessi E, Foustoukou M, Vatopoulos A, Pasparakis DG et al (2008) Clinical and molecular epidemiology of community-acquired, methicillin-resistant *Staphylococcus aureus* infections in children in central Greece. Eur J Clin Microbiol Infect Dis 27(9):831–837 (**Epub 2008/06/10**)
33. Johansson PJ, Gustafsson EB, Ringberg H (2007) High prevalence of MRSA in household contacts. Scand J Infect Dis 39(9):764–768 (**Epub 2007/08/19**)
34. Mohsin M, Raza S, Schaufler K, Roschanski N, Sarwar F, Semmler T, et al. High Prevalence of CTX-M-15-Type ESBL-Producing *E. coli* from Migratory Avian Species in Pakistan. Front Microbiol 8:2476 (**Epub 2018/01/10**)
35. Köck R, Mellmann A, Schaumburg F, Friedrich AW, Kipp F, Becker K (2011) The epidemiology of methicillin-resistant *Staphylococcus aureus* (MRSA) in Germany. Deutsches Ärzteblatt International 108(45):761–767 (**Epub 2011/12/14**)
36. Cuny C, Kock R, Witte W (2013) Livestock associated MRSA (LA-MRSA) and its relevance for humans in Germany. Int J Med Microbiol 303(6–7):331–337 (**Epub 2013/04/24**)
37. Zamfir M, Adler AC, Kolb S, Dammeyer A, Nasri L, Schomacher L et al (2017) Evaluation of sampling locations in pregnant women and newborns for the detection of colonisation with antibiotic-resistant bacteria. Eur J Clin Microbiol Infect Dis 36(10):1819–1826 (**Epub 2017/05/06**)
38. Adler AC, Zamfir M, Hendrowarsito L, Dammeyer A, Schomacher L, Karlin B et al (2017) Hospitalization cost at childbirth: Health parameters and colonization with antimicrobial resistant bacteria and methicillin susceptible *Staphylococcus aureus*. Eur J Obstet Gynecol Reprod Biol 215:20–27 (**Epub 2017/06/09**)
39. Valenza G, Nickel S, Pfeifer Y, Eller C, Krupa E, Lehner-Reindl V et al (2014) Extended-spectrum-beta-lactamase-producing *Escherichia coli* as intestinal colonizers in the German community. Antimicrob Agents Chemother 58(2):1228–1230 (**Epub 2013/12/04**)
40. RKI. Staphylokokken-Erkrankungen, insbesondere Infektionen durch MRSA. https://www.rki.de/DE/Content/Infekt/EpidBull/Merkblaetter/Ratgeber_Staphylokokken_MRSA.html: RKI; 2016 [cited 2019 13.01.2019].
41. Huang SS, Platt R (2003) Risk of methicillin-resistant *Staphylococcus aureus* infection after previous infection or colonization. Clin Infect Dis 36(3):281–285 (**Epub 2003/01/23**)
42. Paterson DL, Bonomo RA (2005) Extended-spectrum beta-lactamases: a clinical update. Clin Microbiol Rev 18(4):657–686 (**Epub 2005/10/15**)
43. Popp W, Kundt R, Haamann F (2010) al. e. Personalrisiko durch MRSA—ein unterschätzes Thema [Personnel risk of MRSA—an underestimated topic]. Arbeitsmed Sozialme Umweltmed 45:107–110
44. Safdar N, Bradley EA (2008) The risk of infection after nasal colonization with *Staphylococcus aureus*. Am J Med 121(4):310–315
45. Chen KT, Campbell H, Borrell LN, Huard RC, Saiman L, Della-Latta P (2007) Predictors and outcomes for pregnant women with vaginal-rectal carriage of community-associated methicillin-resistant *Staphylococcus aureus*. Am J Perinatol 24(4):235–240 (**Epub 2007/04/21**)
46. Canton R, Novais A, Valverde A, Machado E, Peixe L, Baquero F et al (2008) Prevalence and spread of extended-spectrum beta-lactamase-producing Enterobacteriaceae in Europe. Clin Microbiol Infect 14(1):144–153 (**Epub 2007/12/25**)
47. Dhillon RH, Clark J (2012) ESBLs: a clear and present danger? Crit Care Res Pract 2012:625170 (**Epub 2011/07/19**)
48. DGU L. Interdisziplinäre S3 Leitlinie: Epidemiologie, Diagnostik, Therapie, Präevention und Management unkomplizierter, bakterieller, ambulant erworbender Harnwegsinfektionen bei erwachsenen Patienten. https://www.awmf.org/uploads/tx_szleitlinien/043-044l_S3_Harnwegsinfektionen_2017-05.pdf: DGU; 2017 [20.01.2019]; Available from: https://www.awmf.org/uploads/tx_szleitlinien/043-044l_S3_Harnwegsinfektionen_2017-05.pdf.
49. Goldenberg RL, Klebanoff MA, Nugent R, Krohn MA, Hillier S, Andrews WW. Bacterial colonization of the vagina during

pregnancy in four ethnic groups. Vaginal Infections and Prematurity Study Group. Am J Obstet Gynecol. 1996;174(5):1618–1621 (**Epub 1996/05/01**)
50. Kurki T, Sivonen A, Renkonen OV, Savia E, Ylikorkala O (1992) Bacterial vaginosis in early pregnancy and pregnancy outcome. Obstet Gynecol 80(2):173–177 (**Epub 1992/08/01**)
51. Lietzau S, Sturmer T, Erb A, Von Baum H, Marre R, Brenner H (2004) Prevalence and determinants of nasal colonization with antibiotic-resistant *Staphylococcus aureus* among unselected patients attending general practitioners in Germany. Epidemiol Infect 132(4):655–662
52. Boccaccio C, Verdaguer Babic V, Botto L, Cervetto MM, Cetani S, Paladino S et al (2014) Methicillin-resistant *Staphylococcus aureus* (MRSA) isolation in breast abscesses in a Public Maternity. Medicina 74(3):210–5 (**Epub 2014/06/12. Aislamiento de *Staphylococcus aureus* meticilino resistente en abscesos de mama en una Maternidad Publica**)
53. Stafford I, Hernandez J, Laibl V, Sheffield J, Roberts S, Wendel G Jr (2008) Community-acquired methicillin-resistant *Staphylococcus aureus* among patients with puerperal mastitis requiring hospitalization. Obstet Gynecol 112(3):533–537
54. Carleton HA, Diep BA, Charlebois ED, Sensabaugh GF, Perdreau-Remington F (2004) Community-adapted methicillin-resistant *Staphylococcus aureus* (MRSA): population dynamics of an expanding community reservoir of MRSA. J Infect Dis 190(10):1730–1738 (**Epub 2004/10/23**)
55. von Wintersdorff CJ, Penders J, Stobberingh EE, Oude Lashof AM, Hoebe CJ, Savelkoul PH et al (2014) High rates of antimicrobial drug resistance gene acquisition after international travel. Neth Emerg Infect Dis 20(4):649–657 (**Epub 2014/03/25**)
56. van Cleef BA, Graveland H, Haenen AP, van de Giessen AW, Heederik D, Wagenaar JA et al (2011) Persistence of livestock-associated methicillin-resistant *Staphylococcus aureus* in field workers after short-term occupational exposure to pigs and veal calves. J Clin Microbiol 49(3):1030–1033 (**Epub 2011/01/14**)
57. Schofer H, Bruns R, Effendy I, Hartmann M, Jappe U, Plettenberg A et al (2011) Diagnosis and treatment of *Staphylococcus aureus* infections of the skin and mucous membranes. J German Soc Dermatol 9(11):953–967 (**Epub 2011/10/27**)
58. Borde JP, Kern WV (2012) Treatment of MRSA infections. Dtsch Med Wochenschr 137(49):2553–2557 (**Epub 2012/11/13. Therapie von MRSA-Infektionen**)
59. Le Page S, Dubourg G, Baron SA, Rolain JM, Raoult D (2019) No global increase in resistance to antibiotics: a snapshot of resistance from 2001 to 2016 in Marseille, France. Eur J Clin Microbiol Infect Dis 38(2):395–407 (**Epub 2018/12/06**)
60. Brinkmann A, Rohr AC, Frey OR, Kruger WA, Brenner T, Richter DC, et al. [S2k guidelines of the PEG on calculated parenteral initial treatment of bacterial diseases in adults : Focussed summary and supplementary information on antibiotic treatment of critically ill patients]. Der Anaesthesist. 2018;67(12):936–49. Epub 2018/12/05. S2k-Leitlinie der PEG zur kalkulierten parenteralen Initialtherapie bakterieller Erkrankungen bei Erwachsenen : Fokussierte Zusammenfassung und erganzende Informationen zur Antibiotikatherapie kritisch kranker Patienten.
61. Baldwin NS, Gilpin DF, Hughes CM, Kearney MP, Gardiner DA, Cardwell C et al (2009) Prevalence of methicillin-resistant *Staphylococcus aureus* colonization in residents and staff in nursing homes in Northern Ireland. J Am Geriatr Soc 57(4):620–626 (**Epub 2009/04/28**)
62. Kallen MC, Natsch S, Opmeer BC, Hulscher M, Schouten JA, Prins JM et al (2019) How to measure quantitative antibiotic use in order to support antimicrobial stewardship in acute care hospitals: a retrospective observational study. Eur J Clin Microbiol Infect Dis 38(2):347–355 (**Epub 2018/11/28**)
63. [Hygiene measures for infection or colonization with multidrug-resistant gram-negative bacilli. Commission recommendation for hospital hygiene and infection prevention (KRINKO) at the Robert Koch Institute (RKI)]. Bundesgesundheitsblatt, Gesundheitsforschung, Gesundheitsschutz. 2012;55(10):1311–54. Epub 2012/09/27. Hygienemassnahmen bei Infektionen oder Besiedlung mit multiresistenten gramnegativen Stabchen. Empfehlung der Kommission fur Kranken-haushygiene und Infektionspravention (KRINKO) beim Robert Koch-Institut (RKI).
64. Beigi RH, Bunge K, Song Y, Lee BY (2009) Epidemiologic and economic effect of methicillin-resistant *Staphylococcus aureus* in obstetrics. Obstet Gynecol 113(5):983–991 (**Epub 2009/04/23**)
65. Patel RI, Kaufman HK (2011) Nasopharyngeal carriage of methicillin-resistant *Staphylococcus aureus*: incidence and outcomes in pregnant women. J Am Osteopat Assoc 111(6):389–395 (**Epub 2011/07/21**)
66. Coates T, Bax R, Coates A (2009) Nasal decolonization of *Staphylococcus aureus* with mupirocin: strengths, weaknesses and future prospects. J Antimicrob Chemother 64(1):9–15
67. Milstone AM, Song X, Coffin S, Elward A (2010) Identification and eradication of methicillin-resistant *Staphylococcus aureus* colonization in the Neonatal Intensive Care Unit: results of a National Survey. Infect Control Hosp Epidemiol 31(7):766–768
68. Mollema FPN, Severin JA, Nouwen JL, Ott A, Verbrugh HA, Vos MC (2010) Successful treatment for carriage of methicillin-resistant *Staphylococcus aureus* and importance of follow-up. Antimicrob Agents Chemother 54(9):4020–4025

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.