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Review Article

The role of food in the spread of the Methicillin – resistant *Staphylococcus aureus* (MRSA)

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Abstract

Methicillin-resistant *Staphylococcus aureus* (MRSA) are important human pathogen. It is present in a wide range of animal species (pigs, cows, sheep, and chickens) even in healthy animals. Identification of MRSA in foods has led to concerns about the role of livestock in the epidemiology of MRSA infections in human. This review focuses on the spread of MRSA in different types of food and its antimicrobial resistance to the most widely used antimicrobials in human and veterinary medicine. The results of review indicates that livestock is major source of MRSA in humans and mainly transmitted to humans through contaminated food. The actual prevalence of MRSA in animals and food as well as impact to the human health is not well understood. It is clearly that MRSA is an important pathogen to veterinary medicine and human health which requires more and in-depth research to understand the hazard and take effective measures to limit it.

Keywords

methicillin-resistant *Staphylococcus aureus*, pork, beef, antimicrobial resistance

Abbreviations

MRSA – methicillin-resistant *Staphylococcus aureus*; RTE – ready-to-eat

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Introduction

Staphylococcus aureus is the most important human pathogen of staphylococci, causing diseases ranging from mild skin infection to severe life-threatening infections (Lowy 1998). *Staphylococcus aureus* possesses strong pathogenic properties due to the presence of large number of different virulence factors. In addition, *Staphylococcus aureus* can easily develop a resistance to the antimicrobials. The frequent use of β -lactam antibiotics to treat infection may lead to the development resistance in some strains *Staphylococcus aureus*. This resistance is known as methicillin resistance. Most animals are colonised with *Staphylococcus aureus*, but only few of them has methicillin-resistant *Staphylococcus aureus* (MRSA) and most have been isolated from livestock such pigs, cows and chickens (De Neeling et al. 2007).

Staphylococci are spherical, non-spore forming, non-motile bacteria which are placed in double, short chain or grapes under the microscope. Staphylococci are facultative anaerobes, Gram positive and catalase positive microorganisms and divided into two groups depending on their ability to coagulate rabbit plasma: coagulase-negative and coagulase-positive (Archer 1998; Lowy 1998).

Coagulase-negative staphylococci are involved in the fermentation of some dairy and meat products. Therefore, they are used as ingredients in the recipe of certain food products (Archer 1998). The group of coagulase-positive staphylococci includes several main species: *Staphylococcus aureus*, *Staphylococcus intermedius*, *Staphylococcus pseudointermedius*, *Staphylococcus delphini*, *Staphylococcus schleiferi* ssp. coagulance and *Staphylococcus lutre* (Hennekinne et al. 2012). *Staphylococcus aureus* is considered to be the main causative agent of human and animal diseases. It belongs to the healthy skin and mucosal membrane microflora. Important characteristic properties of *Staphylococcus aureus* are its ability to survive in environment for a long time and demonstrate close adaptation to the specific hosts.

The worldwide used of antimicrobials in treatment of banal bacterial infections has led to the development of antimicrobial resistance. Antimicrobials are used in human and veterinary medicine. This allows the transmissions of resistance bacteria from animals to the humans. The

transmission occurs not only through contact with animals, but also through consumption of food of animal origin (Bywater et al. 2004).

Staphylococcus aureus which developing resistances to the β -lactam antibiotics are included in the group of methicillin-resistant *Staphylococcus aureus*. It has been proven that MRSA are resistant to almost all antimicrobials in this group. MRSA was found for the first time in 1961 in American hospitals (Barber 1961). Thereafter it began to be detected more often in hospital isolates around the world. Nearly ten years later, in 1972, MRSA was first isolated from mastitis cows in Belgium (Devriese et al. 1975) and gradually became worldwide pathogens (Goudarzi et al. 2017). MRSA show resistance to the penicillin and other antimicrobials of its group and pose a serious risk to humans' health (Tacconelli 2009; Tiemersa et al. 2004).

Prevalence of MRSA

Prevalence of MRSA in food-producing animals.

Various studies in last decades have been shown the increasing prevalence of MRSA in livestock. By comparing the different literature data, Lakhundi and Zhang (2018) summarized data of relation between farm animals and the spread of MRSA and concluded that is most commonly related with pigs comparing the different literature data. Van Duijkeren et al. (2008) also showed that pigs are main risk factor for the spread of MRSA in Netherland. In 2006, they analysed different type of pig farms and found that 23% of them were positive for MRSA. Furthermore, 5 out of 6 breeding farms, that supply fattening farms with piglets, were also MRSA positive. The presence of MRSA positive workers in all positive farms indicated possibilities of animal to human transmission of MRSA. A study conducted by European Food Safety Authority showed the prevalence of MRSA in 26.9% of breeding pig farms (EFSA 2020). The analysis of the Report on antimicrobial resistance in zoonotic and indicator bacteria in 2017/2018 (EFSA 2020) shows that 91% prevalence of MRSA was found in Estonian pig farms. In 2018, the situation in Denmark was similar.

A cattle farming is an agriculture sector with often spread of MRSA. It was reported a high MRSA prevalence in dairy cows herds in Belgium (14%) and low prevalence in herds of meat production animals (EFSA 2020). In contrast, a low MRSA

prevalence in dairy cows was reported in Denmark – only 6.1%. Reported cases in Germany and Switzerland showed prevalence in slaughter calves (under 1 year of age) of 39.7% and 8.1% respectively. According to the report poultry are less important in the spread of MRSA. Considering the surveillance of poultry flocks, Belgium and Denmark report low MRSA prevalence in broiler and laying flocks. In Germany a moderate prevalence of MRSA was reported in fattening turkey flocks (17.2%), but none of the broiler turkeys flocks were positive for MRSA in Denmark.

The general opinion of researchers is that the source of *Staphylococcus aureus* are animals. However, some literature data reported that mostly people (30-55%) are carriers and a source of infection of domestic animals. In some cases, isolates carried by slaughterhouse workers have even been found to be more resistant to antibiotics than community controls (Neira et al. 2014). These data on the prevalence of MRSA in food-producing animals suggest a risk of MRSA in food.

Prevalence of MRSA in food. A number of studies have frequently shown presence of MRSA in raw pork and beef. In recent years, special attention has been paid to the meat in retail. A higher prevalence of MRSA in raw pork was reported by Tanomsridachchai et al (2021) who analysed 116 sample of pork meat from slaughters and found MRSA in 56 of them. In a relative survey of nasal swabs of healthy pigs, they do not found any positive results. It has already been shown that colonized healthy animals can be a source of food contamination.

In Netherland, a parallel study of raw pork and beef meat in retail was made (van Loo et al. 2007). The authors showed a very low prevalence of MRSA in pork (only 2.5%) and none in beef. Wu et al. (2018) reported similar data for raw and frozen meat, sold in China. A preliminary study in USA reported that MRSA was detected in 5.6 % pork samples and 0.33% of beef samples (Pu et al. 2009). Another team from USA has analysed the prevalence of MRSA in retail pork (O'Brien et al. 2012). They isolated *Staphylococcus aureus* in 64.8% of the samples, but only 6.6% of them were methicillin-resistant.

Jackson et al. (2013) reported MRSA in 3% of tested pork samples in Georgia, while the

Staphylococcus aureus was found in 45% of the samples.

The tendency of more frequent detection of MRSA in pork compared to beef has been maintained in other similar studies (Weese et al. 2010; Kim et al. 2020). The significant spread of MRSA in pork and beef was reported by Wells and Juett (2012) who examined samples from different storages in Kentucky and detected MRSA up to 27.7%.

A number of studies have shown a significant prevalence of MRSA in beef. Farahmand et al. (2020) tested 42 beef samples from various groceries in Tabriz and found contamination of 25% of the samples with *Staphylococcus aureus*. Most of the identified isolates were associated with human infections with high level of antimicrobial resistance, 15 of which were methicillin resistance. A study of 40 beef samples in Pakistan showed the presence of *Staphylococcus aureus* in 75% of the samples and 63% identified resistance to cefoxitin, a marker of MRSA (Sadi et al. 2020). Similar data on the prevalence of *Staphylococcus aureus* in 14.6% beef samples in Turkey were reported by Özdemir and Keyvan (2016). Cefoxitin resistance was found in 22.8% of them.

The milk also has been played important role in spread of *Staphylococcus aureus*. A large of studies has reported the risk of *Staphylococcus aureus* in milk sales in different countries. In Southern Bulgaria 44 raw milk samples were studied and were found that 52.3% to be contaminated with *S. aureus*. The authors did not analyse the presence methicillin resistance, but concluded that poor hygiene practices throughout the food chain and large number of *Staphylococcus aureus* (3.4×10^4 cfu/g) could be a risk to human health (Bangieva and Rusev 2019). The artisanal cheese sold in informal markets in Kosovo also showed a high prevalence of coagulase positive *Staphylococcus aureus* (Studenica et al. 2022). The authors reported 46 positive samples from a total of 116 samples, (39.7%) with the highest coagulase-positive staphylococci count of 7.1×10^6 cfu.g⁻¹. Their analyses showed a significant difference between summer and winter seasons, with higher contamination levels observed in summer. Wu et al. (2018) studied pasteurized milk marketed in China and found *Staphylococcus aureus* in 13 of 258 samples. They did not detect MRSA in any of the

samples. It is interesting to note that the same authors have researched the prevalence of MRSA in a number of food products. They reported a higher prevalence of MRSA in raw meat (4.8%) followed by seafood (3%) and quick frozen food (2.7%). They detected MRSA in only 1.1% of ready-to-eat foods. A similar survey was carried out in Bulgaria and *Staphylococcus aureus* was detected in ready-to-eat roasted chicken legs related to the foodborne outbreak in amount of over 8.4×10^6 cfu.g⁻¹ (Ivanova et al. 2017). In contrast to the previous authors not resistance to any antimicrobials including cefoxitin was found. However in the study carried out by Wu et al. (2018) reported prevalence of MRSA in 8.1% of the examined ready-to-eat foods. A study of foods, associated with foodborne outbreaks carried out in Bulgaria showed the highest prevalence of MRSA at 45.7%. MRSA was detected in only 36.4% of foods not related to foodborne outbreaks (Gogov 2011). A high percent of MRSA was reported in China, in 24.1% of tested food samples (Wu et al. 2019). In a study of ready-to-eat beef burger in Egypt 5 strains of *Staphylococcus aureus* are isolated and all were resistance to methicillin (El-Razika et al. 2017). The authors concluded that the risk of antibiotic resistance genes transmission between *Staphylococcus aureus* isolates from different sources might be increase. Similar data were

reported by Mahros et al. (2021). They confirmed MRSA in 22.6% of the tested hot dog sandwiches.

The poultry play an outstanding role in the spread of MRSA in Pakistan (Sadi et al. 2020). The authors detected MRSA in 63% of analysed poultry samples. Iran, Korea, Turkey and Canada were reported different data (Farahmand et al. 2020; Kim et al. 2020; Özdemir and Keyvan 2016; Wells and Juet 2010). They found MRSA in only 2 samples in Iran, 0.9% in Korea and 1.2% in Canada. In Turkey they did not detected MRSA in any of the poultry samples. A study of retail meat samples carried out in Denmark at 2014-2015 showed some differences between different meat types. MRSA were isolated from 13 % of the tested meat samples. Interestingly, in this study the authors reported the highest prevalence of MRSA in turkey samples (52%) compared to pork (15%) and chicken (4%) (Tang et al. 2017).

Based on the above data we can summarize that MRSA is widespread in various food sources such as pork, beef, poultry, milk, vegetables and some ready-to-eat foods (RTE) (Table 1). This leads us to believe that food can be a dangerous source of MRSA.

Table 1. Methicillin-resistance *Staphylococcus aureus* in food

Food type	Country	Prevalence of <i>Staphylococcus aureus</i> , %	Prevalence of MRSA, %	Reference
Raw pork meat	Netherland	39	4	van Loo et al. 2007
	Korea	18.2	1.3	Kim et al. 2020
	USA	64.8	6.6	O'Brien et al. 2012
Pork products	Georgia	45	3	Jackson et al. 2013
	Canada	Not tested	9.6	Weese et al. 2010
	Thailand	Not tested	44.8	Tanomsridachchai et al., 2021
Raw beef meat	Netherland	33	Not detected	van Loo et al. 2007
	Iran	23.8	13	Farahmand et al. 2020
	Korea	13.4	0.3	Kim et al. 2020
	Pakistan	75	63	Sadi et al. 2020
	Turkey	14.6	Not tested	Özdemir et al. 2016
Beef products	Canada	Not tested	5.6	Weese et al. 2010

Antimicrobial resistance of MRSA in food

MRSA resistance to antimicrobials can be transmitted through food. A review of the literature suggests that food is a good route to transmit antimicrobial resistance to the humans. Most authors found high resistance to penicillin and ampicillin (up to 100%). The data by erythromycin and tetracycline resistance are similar (Jackson et al. 2013; Kim et al. 2020; Mahros et al. 2021; Özdemir and Keyvan 2016; Wu et al. 2018; Wu et al. 2019). Antibiotic susceptibility testing showed that most of MRSA isolates from meat samples in Denmark were resistant to erythromycin (95%), tetracycline (84%), and clindamycin (79%), and some were resistant to ciprofloxacin (32%). No MRSA isolates were resistant to chloramphenicol, trimethoprim, sulphamethoxazole, rifampin, linezolid or gentamicin (Tang et al. 2017). Chloramphenicol is an antimicrobial agent that has not been used in humans and productive animals for many years. This is precisely the reason for lack of resistance in this day and age. All of this was expected since these antibiotics have a wide spectrum of action and are commonly used to treat infection in humans and animals. However, at this moment, there are still antibiotics to which MRSA are fully susceptible. Some data shows 100% susceptibility to erythromycin, ciprofloxacin, vancomycin and gentamycin (Jackson et al. 2013; Kalupahana et al. 2019; O'Brien et al. 2012; Özdemir and Keyvan 2016). This is inconsistent with the results reported by Sadi et al. (2020) which reported 80% resistance to vancomycin and 100 % resistance to ciprofloxacin (Table 2).

It is essential to report resistance to more than 3 antibiotics (multidrug resistance) when antimicrobial resistance is reported. In their study, Wu et al. (2019) investigated the sensitivity of MRSA isolates to 26 clinical importance antibiotics.

They found resistance from 4 to 10 antibiotics in 33.3% of the isolates and 46.3% of the isolates were resistance up to 10 antimicrobials. High percent of multidrug resistance were also reported by Kim et al. (2020) – 93.1% of MRSA isolated from retail meat in Korea. Pronounced multidrug resistance was found by Wu et al. (2018). Most of the analysed isolates showed resistance to more than 10 antibiotics (77.4%) and only 1.26% were sensitive to all 24 tested antimicrobials.

Abdel-Moein and Zaher (2019) indicated the circulation of MRSA with multidrug resistance in apparently healthy farm animals. They reported multi drug resistance properties of MRSA in 3.6% of tested isolates with marked resistance to penicillin and ceftiofur in all isolates. The available data lead us to conclude that food and livestock should be considered as a reservoir for multidrug resistance MRSA that can be easily transmitted to humans by direct contact or consumption of contaminated food.

Conclusions

In the context of the risk of diseases caused by MRSA, as well as its widespread prevalence in different types of food products and combined with the increasing evidence of multi drug resistance in these strains, pose a threat to human health. Finding ways to desensitise MRSA to commonly used antimicrobials should be a priority for future research. Reducing the use of antibiotics in livestock production could help reduce resistance to these antibiotics. Appropriate controls on antibiotics used in animals should therefore be implemented and good hygiene practice in food process should be ensured at every stage of production. All this would be help to prevent the emergency and spread of drug-resistant bacteria.

Table 2. Antimicrobial resistance of MRSA in food

Source of MRSA	Antimicrobial resistance, %															References
	Ampicilli	Cefoxitin	Penicillin	Amoxicillin	Ceftazidime	Gentamycin	Kanamycin	Streptomycin	Chloramphenicol	Clindamycin	Erythromycin	Ciprofloxacin	Tetracycline	Vancomycin	Fusidic acid	
Raw meat, aquatic products, quick frozen food, RTE food	1	100	1	87	97.2	27.8	75.9	67.6	38	79.6	83.3	27.8	65.7	0	27.8	Wu et al. 2019
Retail food	-	36.1	94.4	-	-	11.1	61.1	51.4	27.8	63.9	83.4	5.5	47.2	-	27.8	Wu et al. 2019a
Raw meat	1	13.3	-	-	0	-	-	-	-	-	-	-	-	-	-	Farahmand et al. 2020
Beef	-	6.7	64.9	-	-	1.9	5.8	-	4.3	2.4	16.3	1.9	9.1	0	14.4	Kim et al. 2020
Pork	-	10.9	65.8	-	-	6	11.6	-	13.2	19.5	12.8	12.4	39.8	0	13.2	
RTE food	-	-	4	-	-	-	-	-	-	-	-	-	100	-	-	El-Razika et al. 2017
Retail food	85.4	7.14	84.6	11	7.8	19.4	45.3	21.2	13.1	29.6	52.7	16.9	49.3	-	18.4	Wu et al, 2018
Pigs	--	-	-	-	-	0	16	-	0	0	50	-	0	-	0	Kalupahana et al. 2019
Beef, sheep, chicken	70.1	22.8	-	-	-	12.2	-	-	5.2	-	33.3	-	47.3	0	-	Özdemir et al. 2016
Retail beef	1	-	1	-	-	0	-	-	-	25	100	100	25	-	-	Jackson et al. 2013
Retail pork	1	-	1	-	-	33.3	-	-	-	33.3	66.7	66.7	0	-	-	
Beef, pork and turkey MRSA isolates	-	-	-	-	-	0	-	-	0	79	95	32	84			Tang et al. 2017

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