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A General Outlook on Methicillin Resistant *Staphylococcus aureus*

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Authors' contributions

This work was carried out in collaboration between all authors. Author BS designed and written the study with authors GI and AC. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Methicillin resistant *Staphylococcus aureus* (MRSA) is a kind of bacteria which is resistant against methicillin and other kind of many antibiotics. *S. aureus* and MRSA can lead to serious problem in human as well as animals. The problem can be simple or sometimes serious such as skin infections, sepsis, pneumonia and bloodstream infections. Firstly, MRSA was largely related to hospital-acquired (HA) infection. However, it is well understood that there is other source of MRSA. Nowadays, MRSA has been divided three group; (1) Hospital-Associated MRSA (HA-MRSA), (2) Community-Acquired MRSA (CA-MRSA) and (3) Livestock-Associated MRSA (LA-MRSA). In addition to the three groups, MRSA has been found variety of animal origin foods (beef, poultry and pig meats and milk like that). Therefore, food of animal origin can contaminate with MRSA bacteria,

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and it can spread to human and animal through food chains. MR (methicillin resistance) in *S. aureus* is primarily mediated by overproduction of the penicillin-binding protein (PBP) 2a, and altered PBP with extremely low affinities for ß-lactam antibiotics. The *mecA* gene encodes a PBP2a form that is absent in susceptible isolates. The importance of MRSA; (i) MRSA can acquire resistance against many antibiotics more easily than other microorganisms, (ii) it acquires resistance to one antibiotics and to go into antibiotic groups, (iii) the Panton-Valentine leucocidin (PVL) toxin is a cytotoxin causing leukocyte destruction and necrosis of tissue. It is very important a virulent factor and produced by *Staphylococcus aureus*. The toxin is very common in especially CA-MRSA strains, and these strains are commonly considered far more likely to carry the gene coding for the toxin than are other MRSA strains, and (iv) MRSA infections require long-term inpatient cure and have a high rate of mortality. For these reasons, today, MRSA is among the most important causes of antimicrobial-resistant health care-related to infections across the world.

Keywords: MRSA; animal origin food; public health.

1. INTRODUCTION

Antimicrobial resistance is an important public health issue around the world based on the persistent circulation of resistant bacterial strains in the environment, and thereafter contamination of foods as well as water. Particularly animal origin foods and their products are important sources of MRSA. In farm animals, antibiotics are used different aims like treatment of disease, to prevent or control diseases (in particularly poultry sectors), increase animal growth. It is estimate that the global average annual antimicrobials consumption for per kilogram of animal produced was 45 $mg \cdot kg^{-1}$ for cattle, 148 $mg \cdot kg^{-1}$ for chicken, and 172 $mg \cdot kg^{-1}$ for pigs [1]. It is alleged that recurring exposure to low antimicrobial agents' doses (for prophylactic or growth-promote in farm animals) creates spread of antimicrobial resistance bacteria in animals [2]. For this reason, the contamination sources of animal origin foods with MRSA may beoccur in the farm or processing steps of food or humans' contact to animal or food processing steps. For instance, in farm animals especially in pigs and poultry, the use of avoparcin as a food additive develops resistant enterococci against vancomycin in their intestinal system. As a result, MRSA and other antibiotic resistance bacteria can pass the consumer's gastro-intestinal system by consumption of these kinds of contaminated foods [3]. An increase in AR bacteria isolated from animals of various origins has also been observed. Besides other microorganisms, especially *S. aureus* and other *Staphylococcus* species have been commonly reported to acquire multi-antimicrobial resistance patterns [4].

S. aureus is a highly important pathogen. It is a major causative agent for infective endocarditis bacteremia, skin and soft tissue infections, osteoarticular, device-related infective disease and pleuropulmonary infections. It leads to considerable human mortality and morbidity around the world. [5]. At the beginning, most staphylococcal infections were susceptible against penicillin. Therefore, staphylococcal infections would be treated with penicillin or pencillin-related antibiotics. In time, in 1950s, *S. aureus* developed resistance against penicillin. After that, semi-synthetic penicillin was developed. The antibiotic was called methicillin. At the beginning, *S. aureus* was sensitive to methicillin. That time, it was called methicillin-sensitive *S. aureus (*MSSA). Nevertheless, in 1962s, MRSA was identified. Nowadays, antibiotic resistant bacteria and MRSA are a widespread global problem [6].

MRSA has been admitted as a significant causative agent of HA-MRSA in humans for many years. After that, until the 1990s, MRSA was identified in patient at the hospital and was occasionally outside the health care environment. However, infections of MRSA were admitted in human living outside of the hospital or in no touch with people in nursing centers in the 1990s. After that time, more often MRSA patient has highly increased in human living in population. During 2006s, more than 50% of patient with skin infections because of MRSA happened in or else well people living in the population. Therefore, MRSA strains have come to be existed, which are involved in CA-infections in humans in plenty of countries [7]. Methicillin resistant *S. aureus* and CA-MRSA are thought on a large scale affect humans and, generally, are not taken in infection of farm animals. Nevertheless, LA-MRS is other way of contamination source for human. A people may be direct contact to farm animals in the farm or pets etc. Other important source of LA-MRSA is

abattoir or slaughter houses. If animals carry the MRSA, people can contaminate with MRSA during touching steps. Workers at the laboratory, may take MRSA during slaughtering [8]. Then, the LA-MRSA isolation from livestock and accompany animals have been informed, too [9,10,11].

2. METHICILLIN RESISTANCE MECHANISIM

2.1 Penicillin-binding Proteins (PBPs)

Peptidoglycan is the basic cell wall component. It comprises of glycan strands N-acetylmuramic acid (NAM) and N-acetyl glucosamine (NAG) disaccharides bond by peptide cross-links between them. Cell wall biosynthesis procedure is generally similar among bacteria including staphylococci. NAM and NAG disaccharides (Fig. 1) are attached via a β-1,4-glycosidic connect to the decreasing end of the growing peptidoglycan chain in a transglycosylation reaction. To add of a new NAM and NAG disaccharides to adjacent peptidoglycan strand, cross-linked is necessary, and transpeptidation reaction is a big role for cross-linking procedure [12]. Both transglycosylation and transpeptidation are conduct by PBPs. Therefore, the PBPs are critical components of the cell wall synthesis in bacteria.

Generally, there are two groups of PBPs a) Low-molecular-mass (LMM) PBPs and b) High-molecular-mass (HMM) PBPs. The HMM PBPs binds penicillin and catalyzes peptidoglycan cross-linking [13]. Without cross-linking of the peptidoglycan (Figs. 1 and 2), the cell wall becomes mechanically weak, and some of the cytoplasmic contents are released out of the cell and the cell dies. The cross-linking or transpeptidation reactions take place on the external surface of the cytoplasmic membrane in a reaction catalyzed by PBPs. In *S. aureus*, there are four types of PBPs. These are PBP1, PBP2, PBP3 and PBP4 [14]. HMM PBPs contain 2 types of proteins. These are (i) transpeptidation (cross-linking) b) (ii) transglycosylation (extending the glycan chain). The β-lactam antibiotics inhibit the transpeptidation domain of PBPs and carboxypeptidase activity of LMM PBPs. Without transpeptidation, cross-linking of the peptidoglycan is not take shape and staphylococcal membrane become weak and other metabolic activity don't form. At the end, the bacteria die [15].

In staphylococci, resistance to ß-lactam antibiotics is controlled by ß-lactamase enzyme. However, the ß-lactamase has limited only to penicillin. The other way is a fifth PBP called PBP2a (also called PBP2′) in MRSA strains [16,17]. The latter control mechanism resist inhibition by all ß-lactam antibiotics not only penicillin [17]. It is named methicillin resistance. The PBP2a is encoded by the gene *mecA*. While other 4 PBSs are inhibited efficiently by β-lactam antibiotics, PBP2a is a unique transpeptidase,

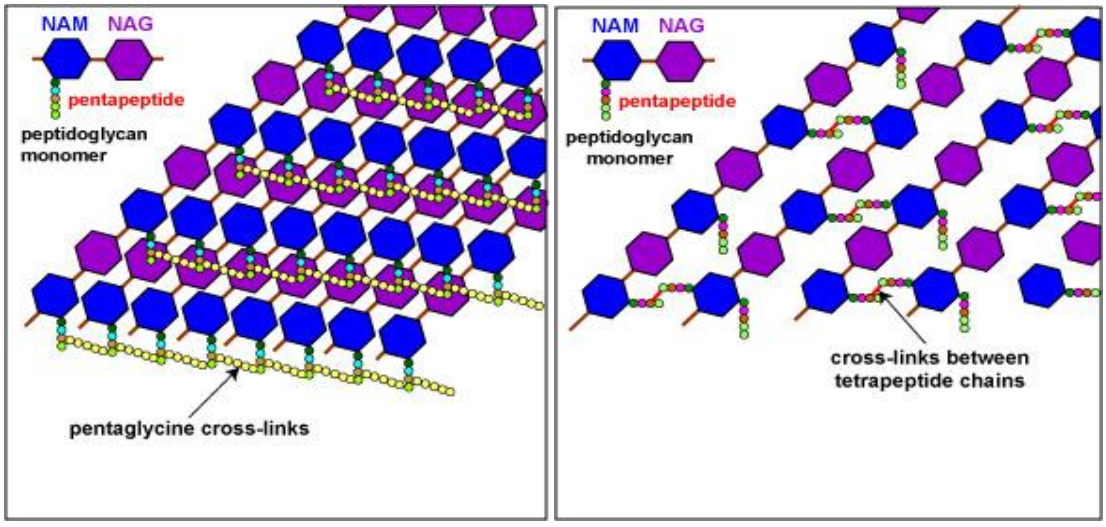

Fig. 1. Cross-linked chains of peptidoglycan monomer. Transglycosylase enzymes join peptidoglycan monomer to shape chains. Then, transpeptidase enzymes cross-link the chains [15].

which is not inhibited by β-lactam antibiotics under challenging conditions because of continue peptidoglycan cross-linking. *S. aureus* PBP2a is a HMM class of PBPs. This type PBP is only found in resistance strains. Therefore, chief MR mechanism of *S. aureus* is expression of PBP2a. Beside *mecA*gene, additional factors such as *fem* (factors essential for expression of methicillin resistance) and *aux* (auxiliary) required for MR have also been identified [18].

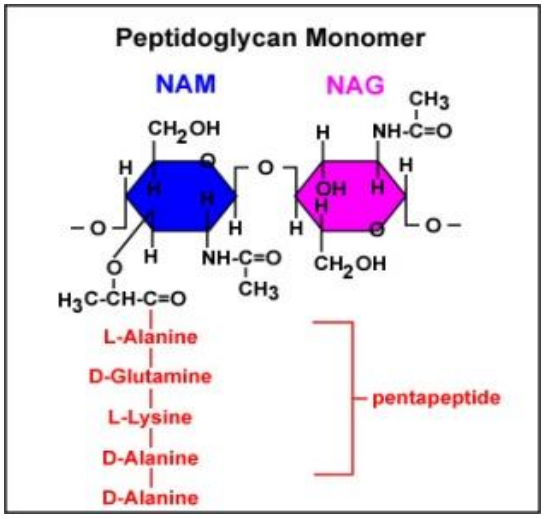

Fig. 2. A peptidoglycan monomer consists of two joined amino sugars (NAG and NAM) with a pentapeptide. In *S. aureus*, the pentapeptide consists of L-alanine, D-glutamine, L-lysine, and two D-alanines amino acids [15].

2.2 SCCmec

There are genetically differences between PBP2a-MRSA and methicillin-sensitive *S. aureus* isolates. In MRSA' chromosome, there has been additional a large strech foreign DNA of 40-60 Kb. This refers to presence of *mecA* gene. In another saying, the *mecA* gene is located on a genomic island. The genomic island is called staphylococcal cassette chromosome *mec* (SCC*mec*) [19]. There are three elementary genetic element; cassette chromosome recombinases (*ccr)* gene complex, the *mec* gene complex and Joining (J) region) [20]. It is integrated into the staphylococcal chromosome at a specific site. Besides *mecA* gene, all SCC*mec* carry *mecR1/mecI* genes [*mecR1*(promoter-encoding the signal transduce protein MecR1) and *mecI* (encoding the repressor protein *Mec*I)]. These genes are mutant or intact *mecA* gene regulators. The role of *mecR1/mecI*genes mediates the site-specific integration and excision of SCC*mec* (*ccr* genes-recombinase genes) [19]. According to sequences of *ccr* and *mec* complexes, SCC*mec* elements commonly classify five group based on the *mec* as SCC*mec* type I,II, III, IV and V [19,21]. However, after that, in the research reported by Ito et al. [22] announced that to date, based on the *mec*, SCC*mec* is classified 11 types. Based on the *ccr*, 8 classes have been reported (Table 1). The differences types and subtypes of *ccr* and *mec* gene complex effect on the multi-drug resistance minimal inhibitory concentration (MIC) of β-lactams [20].

Table 1. SCC types in *S. aureus* [25]

SCC*mec*types	*ccr* gene complexes	*mec* gene complexes
I	1 (A1B1)	B
II	2 (A2B2)	A
III	3(A3B3)	A
IV	2(A2B2)	B
V	5 (C1)	C2
VI	4 (A4B4)	B
VII	5 (C1)	C1
VIII	4 (A)	A
IX	1(C2)	C2
X	7 (A1B6)	C1
XI	8 (A1B3)	E

SCC*mec* is considered to be mobile genetic element because of the integration into or excision from the chromosome. It acts as a carrier to exchange genetic information between *Staphylococcus* strains. These procedures take places between a site on SCC*mec* (*attS*) and one on the chromosome (*attB). attB* gene consists of highly preserved gene called *orfX*. This *orfX* is located close to the *S. aureus* origin replication [23]. If SCC*mec* is inserted, the *attB* sequence will be dublicated at the other end of the element with the site in *orfX (*or called *attR*) and the one connected the non-*orfX* end of SCC*mec* designated *attL*. If the SCC*mec* excises, in the chromosome, the *attB* gene site will be reconstituted. Then, the two ends of the element come together to form *attSS* within a nonreplicating circular version of SCC*mec* [24].

2.2.1 Three elementary genetic element of SCCmec

***1. ccr* gene complex:** The *ccr* gene complex is composed of the *ccr* gene(s), and surrounding ORFs. The gene complex consisted of one or two site-specific recombinase genes. The

complexes are responsible for SCC*mec* mobilization. In *S. aureus*, three types of *ccr* genes have been reported. These are *ccrA*, *ccrB*, and *ccrC.* Based on allelic variations in *ccr*, a series of allotypes has been defined [19]. For instance, *ccrA1* and *ccrB1* (in type-ISCC*mec*), *ccrA2*, and *ccrB2* (in type-II SCC*mec* and type-IV SCC*mec*), *ccrA3*and *ccrB3* (in type-III SCC*mec*), and *ccrA4* and *ccrB4* (in type-VI SCC*mec*). In *S. aureus,* the *ccr* gene complex identified as type 1 (carrying *ccrA1B1*), type 2 (carrying *ccrA2B2*), type 3 (carrying *ccrA3B3*), type 4 (carrying *ccrA4B4*), and type 5 (carrying *ccrC*) [19,25].

***2.mec* gene complex:** The *mec* gene complex is composed of *mecA*, its regulatory genes (*mecI* and *mecR1)*, and associated insertion sequences (IS431 and IS1272). Up to today, there are six classes of *mec* gene complexes. These are class A, B,C (C1 and C2), D and E [19]. It is important to determining SSC*mec* element typing for defining MRSA clones in epidemiological studies, antibiotic susceptibility pattern-SCC*mec* type I, IV-VIII causing only resistance to β-lactam antibiotic. In contrast, types II and III cause resisyance to many antibiotics.

3. J (junction or Junkyard) regions: There are three J region in the SSC*mec*. The region is nonesential component of SCC*mec*. However, it is consider that the region may be responsible for additional anti drug resistance determinants [19]. In brief, the *mecA* gene forms part of the *mec* gene complex in SCC*mec* elements. There are four classes of the *mec* gene complex. The *ccr* genes form another essential component of SCC*mec* that are involved in site-specific integration and excision of SCC*mec.* To date, five *ccr* gene complexes (*ccrA1B1*, *ccrA2B2*, *ccrA3B3*, *ccrA4B4*, and *ccrC*) are reported [19,25]. The SCC*mec* carries both the *mecA* or *mecC* gene, encoding for a novel specific PBP2a, and site-specific recombinase genes *ccrAB* or/and *ccrC.* All SCC*mec* have 4 common features. These are (i) carrying the *mec* gene complex (composed of *mec* gene, insertion sequences and surrounding ORFs); (ii) carrying the *ccr* gene complex (composed of *ccrAB* or/and *ccrC* and surrounding ORFs); (iii) being flanked by characteristic nucleotide sequences, inverted repeats, and direct repeats, at both ends; (iv) being integrated at the integration site sequence (ISS) for SCC, which is located at the 3′-end of *orfX* or at the extremity of the SCC element [20].

3. MRSA TYPES ACCORDING TO ORIGIN

Numerous MRSA isolates showed multiple resistances against the prevalent used antimicrobial drugs such as oxacillin, penicillin, tetracycline, erythromycin and amikacin [26]. Hence, MRSA is one of the highly important hospital-acquired pathogenic bacteria due to resistant to much kind of antibiotics. The multiple resistance properties against many antibiotics of MRSA create difficulties in treatment of MRSA's patients [27].

Human's MRSA is generally separated into two groups: HA-MRSA and CA-MRSA [28]. In addition to these, there has been a third MRSA group, known as LA-MRSA. Today, LA-MRSA has come to existed and infected to farm animals, wild animals and pets [29]. In addition of these, MRSA has been found variety of animal origin foods (beef, poultry and pig meats and milk like that). So, MRSA, animal origin foods has seen last group of MRSA sources.

3.1 CA-MRSA

Over the past 25 years arising in the MRSA prevalence was recorded around the world. HA-MRSA is distinguished from CA-MRSA in terms of independent risk factors [30]. Although infection of CA-MRSA has been a public health challenge in many countries through of the world like South America and the US, and in the most European countries, they are comparatively rare [31]. CA-MRSA like HA-MRSA have been generally distinguished by their functional and structural genomic properties [32]. The hospital-onset infections monitoring caused by CA-MRSA genotypic [33] and the HA-MRSA establishment in the community [34] cannot clear the epidemiological distinction.

3.1.1 CA-MRSA and PVL

Besides MR properties, another important concern in *Staphylococci* is a PVL toxin. The toxin of PVL is a bicomponent cytotoxin. The toxin is encoded by *luk-S-PV* and *luk-F-PV* genes. The *luk-S-PV* and *luk-F-PV*genes, two contiguous and co-transcribed genes, produce 32 and 38 kDa protein, respectively. The PVL toxin causes the occurrence of pores in the mitochondrial membrane, which subsequently results in leukocyte destruction. *Staphylococci* containing PVL genes are responsible for CA infections such as soft-tissue and skin

abscesses, invasive osteomyelitis and necrotizing pneumonia [35].

After the mid-1990s, in the United States, in many epidemiological studies results have shown that PVL carriage genes has been mainly related to infections brought about by CA-MRSA. The genes of PVL have been found in CA-MRSA isolates (by various definitions) at some 60-100% ratios. For instance, it was reported from Minnesota reported by the CDC definition case that PVL gene determined in 77% MRSA's patients given rise to by CA-MRSA strains, in 2000, whereas PVL genes detected just only 4% ratio in HA-MRSA isolates [36]. In 2003, in Texas, among 812 military with recruit's nasal infection, 45 MRSA isolates were obtained, and PVL genes detected in 66% out of 45 MRSA isolates [37].

3.2 LA-MRSA

Transmission of MRSA from animals to humans is of big worry because of the inference of the health care system and human health. Both MRSA and MSSA have been related to companion and an animal growing for food. In 1972, first LA-MRSA was seen in Belgium. It was detected in bovine mastitis milk. After that, MRSA cases in different food and accompanying animals, like pigs, cats, chickens, dogs, cattle and horses, have arisen [10]. LA-MRSA is initially related to livestock [38]. It is distinguished from genotypic of HA and CA-MRSA in its genomic properties. In 2005, in the France and Netherlands, it was seen a new kind of MRSA type which described firstly. The new kind of MRSA variant related to CC398 (clonal complex 398) [39,40]. Later, MRSA CC398 is also found in other farm animals-veal calves and poultry like that [41,42]. For this reason, it was done a new definition called LA-MRSA. LA-MRSA CC398 is distinguished from other two group of MRSA mentioned above. Since, mostly, it is not contain *scn*, *sea*, *sak* and *chpd* genes as well as PVL. These genes found in the human CC398 MRSA lineage, and the genes refer to the human-associated immune evasive gene cluster. LA-MRSA has also seen in Germany, Italy and Denmark, [10], Northern America [43], Asia [8] and Northern Africa [44]. According to many studies results, among people who works in the livestock industry, there have been growing risk for infected or colonized with LA-MRSA [45,46,47], but LA-MRSA infection rates are growing among the population, too [48,49]. In Germany, Cunny et al. [50] found that at least 10% of these sporadic infections are because of LA-MRSA, which is originally related to livestock. The most MRSA cases are associated with CC398 clonal complex (CC). In about 50% traditional farms of pigs, LA-MRSA CC398 colonizes the animals asymptomatically. It was reported that for about 77%-86% of humans with contact to pigs because of the job, it was detected in their nasal carriage. When they cut or interrupted touch to farm animals, it can be lost. At the same farms, only 4–5% is colonized among family members living.

3.3 MRSA in Foods

In different countries, staphylococcal food poisoning (SFP) is a foodborne diseases, and its prevalence is highly common [51]. A different kind of foods can support the growth of *Staphylococcus* species. Some *Staphylococci* isolated from food poisoning cases are also multi drug resistance and vancomycin resistance, and because of lack of alternative antibiotics, infection caused by these resistant strains may be fatal. The first outbreak of foodborne MRSA was reported in 1995 by Kluytmans et al. [52]. This outbreak resulted in five deaths out of 21 reported cases. Since 1994, consumption of animal origin foods containing MRSA has been recognized as a health hazard and a lot of studies have highlighted the public health threat associated with the MRSA presence in foods [53,54,55,56,57]. In several studies, a high MRSA prevalence has been detected in various retail foods across the world, including milk, beef and fish [53,56,57].

Many researches on MRSA in beef have been conducted in different countries. In these studies, the contamination rate has been reported as high as 10.6% [3,47,53,57,58,59,60]. *S. aureus* is present high prevalence in different kind of retail meat products. For instance, DFSA (A Dutch Food Safety Agency) analyzed 2217 different kinds of meats samples in retail stores according to the bacteria, and MRSA had been found 1.9% of them. The MRSA distribution within different meat types was reported as 10.7% of pork, 10.6% of beef, and 15.2% of veal; 6.2% of mutton and lamb, 3.4% of fowl, 16.0% of chicken, 3.3% of turkey, and 2.2% of game. Whole of the MRSA isolates, 85% out of the isolates belonged to ST398; possibly the other STs were belong to human origin [58]. According to another research reported from Nederland that *S. aureus* was detected in 46% of retail meat samples. In the study, MRSA was determined in

two (2%) of which: while one of them was CC39, the other one was USA300 [47]. From Japan and Switzerland, there have been studies in these countries, and according to the study results, the prevalence of *S. aureus* in meat products was to be 65% and 23%, respectively [61]. MRSA has been detected in beef samples; for this reason, the threat to humans from this kind of food is a concern. Beef can become contaminated with MRSA in different ways. Mainly, the use of antibiotics to promote animal growth can select for resistant bacteria and can result in antibiotic residues in animal tissue and meat products. Another contamination source is the slaughterhouse. Hence, cross contamination can occur in various parts of the slaughter and abattoir environments that have become contaminated with MRSA. The contamination sources could be either the animals moving into the abattoir for slaughter or the workers involved in processing the end products [62].

In the early 1970s, in Belgium, the first MRSA report in farm animals (dairy cows' milk of with mastitis) was published, and the clustered CC398 group was identified [29]. In Korea, MRSA has been found in cows or cows' milk samples [63]. From Brazil, the USA, Pakistan, Nigeria, Turkey and Italy, there have been many MRSA reports from cows or their milk [64].

In commonly, according to detection of prevalence in bovine mastitis, it was found that the quite low MRSA prevalence in the bovine mastitis isolates [65]. Following the initial MRSA isolation from mastitic cow's reports [66], MRSA were isolated from the cow's milk at 0.18% ratio. According to one report from Belgium, a high (15%) MRSA prevalence was determined in the animals of dairy farms in which there had been lactating cows which had a previous MRSA history [65]. Take into account of the years since the first MRSA cattle determination between the humans closely touch and udders of the dairy cattle, the prevalence of low MRSA mastitis in long-term has been fairly surprising. In Germany, at slaughter, the nasal swaps obtained from veal calves was found the highest MRSA prevalence (4.1% out of 45%), whereas bulk tank milk had the lowest MRSA rate [67]. The most isolates, not depended on sources, were the clonal complex CC398 (from spa type's t011 and t034). In Germany, the LA-MRSA CC398 finding in tank' milk claimed that the reason was related to udder colonization and quite likely cases of subclinical mastitis in dairy cattle [67]. Near contact between dairy cattle and humans could give rise to a strains move from human to dairy cattle or versus. From Hungary, there has been one report, and in this reports, MRSA isolates obtained from a worker and mastitic cows were determined as a same by genotypic and phenotypic analysis results. The findings indicated that there was a transfer between cows and human [68].

Numerous studies have also addressed MRSA in milk. Some of them have revealed a relationship of MRSA with mastitistic cows' milk [54,55]. In other studies, MRSA has been found in bulk tank milk samples [56]. There have been several contamination ways of milk with milk with MRSA. Contaminated milk from mastitic cows contaminates milk of bulk and in turn contaminates raw milk products. Dairy workers' hand swabs and food handlers' unveiling a high percentage of CPS (coagulase positive staphylococci) on their skin, and these workers and handlers may compose of another source CPS contamination source in dairy products [56].

There have been several studies around the world. For instance, Cho et al. (57) obtained from 74 *S. aureus* from 209 fish and raw meat samples. They found that 7 (35.4%) out of 74 isolates were evaluated as MRSA because of the resistance against oxacillin. For this, they searched present of *mecA* gene in the isolates. The gene was present in the 7 isolates with oxacillin resistance.

From Turkey, according to Can and Çelik [69]'s study results, a total 200 cheese samples were analysed for determination of *S. aureus* and MRSA, and *S. aureus* was detected in 122 (6%), and 2 out of 122 was MRSA. The other study from Turkey, Siriken et al. [59] found that, *S. aureus* was determined in 62 (35.4%) isolates (44 from beef, 9 from milk, and 9 from fish) among 175 coagulase positive *Staphylococcus*. 15 of 62 *S. aureus* isolates was found MRSA [(24.2%; 9 (60%) from fish), 4 (26.7%) from beef and 2 (13.3%) from milk]. A study again was published by Siriken et al. [60] from Turkey. In their study, 100 salted anchovy samples were analyzed for determination prevalence of *S. aureus* as well as other kind of CPS species, and detection of methicillin resistance properties of the isolates. According to analyze findings, they were detected in 41 isolates. However, 16 (39.02%) isolates were resistance to methicillin. Igbinosa et al. [70] also reported that fifty isolates of MR-*Staphylococcus* species were detected in

14 (28%) beef, 26 (52%) pork and 10 (20%) chicken samples from 126 meat samples analyzed. For MRSA determination, *mecA* gene was detected in whole beef and chicken origin isolates. In addition this, the researchers also detected in PVL gene in 100% of the MRSA isolates.

From Iranian, Arefi et al. [71] reported that 100 Iranian white and feta cheese samples were collected from different suppliers. Then, the samples were initially evaluated for the occurrence of *S. aureus* and MRSA. According to findings, *S. aureus* was detected in 25 (25%) isolates, and 8 (34.78%) of 25 *S. aureus* isolates were MRSA based on genotypic confirmation using PCR.

From Belgium, there has been a study reported by Bardiau et al. [55]. The researchers evaluated the presence of MRSA in 430 *S. aureus* collected from cows milk with mastitis. They obtained 19 MRSA isolates. Although seven SCC*mec* types (IV and V) were determined, PVL not detected in the isolates. The isolates of MRSA were obtained from 4(11%) cows with mastitis (n=36). In addition to these properties of the isolates, the researchers also studied for other characterization of the isolates. For this aim, they choice done MRSA per sample, and then they searched four MRSA isolates in term of typing by used two different pulsed field gel electrophoresis. Finally, they found that the four isolates belonged to t011-ST398-agr1 (accessory gene regulator)–SCC*mec*V and ApaI (restriction enzyme) patterns. There has been another study reported by Siva et al. [72] from Brazil. In the study, MRSA was detected in 4 (11%) out of 36cows with mastitis.

From China, Wang et al. [73] carry out a study according to MRSA determination in retail food samples (n=1979). MRSA was detected in 0.6% (n=3), 1.4% (n=4), 0.6% (n=1), 2.3% (n=6), 2.5% (n=3) in ready-to-eat food, raw milk, pork sample, chicken meat and dumpling samples, respectively. However, MRSA isolates were not detected in infant foods. According to finding, from 17 MRSA detected samples, total 23 MRSA isolates were obtained. They also carried out antimicrobial susceptibility tests in the isolates. According to analyzed findings, they found that these MRSA isolates were higher resistance ratio against clindamycin, erythromycin, and clarithromycin at ratio of 100%, 95.7% and 87.0%, respectively, than cefoxitin, penicillin, oxacillin and ampicillin. They reported also that the *pvl*, *seg*, *seb*, *sed*, followed by *see*, *sec*, and *sei*toxin genes were detected very frequently in the isolates. They also found that as *SCCmec* types, II, IV_b and V were detected. In addition to these findings, t189, t377, t5762, t437, t10793, t899 and a new type were determined as a *spa* typing. As a result, the first range spa type was ST9 (52.2% of the isolates), and it was followed up by ST88, ST188, ST59, ST630 and ST72.

4. CONCLUSION

According to mentioned results, besides HA-MRSA, there are other sources of MRSA-CA-MRSA, LA-MRSA and MRSA in animal origin foods. Among these groups, MRSA in foods could be other MRSA sources for human. There are MRSA transition in the environment between human and animal. In addition, in the MRSA spread, animal origin foods can also play an important role. Hence, MRSA goes into the human intestinal system after the food consumption. After that, the resistance gene (*mecA*) can transmit other bacteria in the tract. At last, after defecation, it can spread into the environment. Therefore, for controlling MRSA, one health concept may be remembered. Food of animal origin could be checked for antibiotic resistant bacteria including MRSA especially risk group hospitalized people before prepare consumption.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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