Methicillin Resistant Staphylococcus aureus (MRSA): A Review

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Abstract | Staphylococcus aureus (S. aureus) is a gram positive organism that serves as an opportunistic pathogen and frequent colonizer of the epithelium causing severe diseases in human and animals. The widespread use of antibiotics both in human and Veterinary medicine resulted in the emergence of resistant strains of S. aureus. Methicillin-resistant Staphylococcus aureus (MRSA) is a common bacterial pathogen responsible for a variety of infections. Resistance to methicillin is determined by the mecA gene, which encodes the low-affinity penicillin-binding protein PBP 2. Lately, new methicillin resistance gene, mecC has been discovered from humans, animals and food products. MRSA infection was first considered hospital-associated (HA-MRSA) and community-associated MRSA (CA-MRSA) infections. However, another group emerged known as livestock-associated MRSA (LA-MRSA). The isolation of MRSA from different species, food products and the environment raised concern on the role of animals particularly livestock and wildlife in the epidemiology of MRSA. The spatial distribution of MRSA indicates interspecies transmission and colonization of different populations. This review summarizes the current knowledge, transmission pattern and the epidemiology of MRSA from hospitals, communities, animals and their products.

Keywords | HA-MRSA, CA-MRSA, LA-MRSA, Epidemiology, Transmission

INTRODUCTION

Staphylococcus aureus is a bacterium of significant importance because of its ability to cause a wide range of diseases and capacity to adapt to diverse environmental forms (Lowy, 1998; Waldvogel, 2000). The organism colonises skin, skin glands and mucous membrane, causing infections both in human and animals such as rashes, inflammations of bones and the meninges as well as septicaemia (Aklilu et al., 2010). In addition, S. aureus causes inflammation of the mammary gland in bovine and the lower part of the foot in poultry (Quinn et al., 2000). Penicillin and its derivatives, including methicillin have been used for the treatments of infections caused by S. aureus (Rayner and Munchhof, 2005). However, certain strains of S. aureus developed resistance known as methicillin resistant Staphylococcus aureus (MRSA). At present, less than 90% of S. aureus strains are resistant to most penicillin derivatives (Freeman-Cook
A gene known as mecA gene is responsible for the resistance to methicillin which codes for penicillin-binding protein PBP 2A (Wielders et al., 2002). Lately, a new methicillin resistance mechanism gene, mecC was described in S. aureus (Porrerio et al., 2014). García-Alvarez et al. (2011), Paterson et al. (2012), Walther et al. (2012) and Paterson et al. (2014) reported MRSA isolates carrying mecC gene from humans and animals. Harrison et al. (2013) suggested the public health hazard of mecC-positive MRSA isolates as it has been isolated in human case and their livestock.

Until recently, MRSA was associated with prior exposure to health care facility, and as such, was considered a nosocomial pathogen (Tiemersma et al., 2004). A number of publications on MRSA infections in populations lacking traditional risk factors (Herold et al., 1998) have been reported. This raised concern for infections originating from the community and veterinary species (Cohn and Middleton, 2010). Reports of MRSA isolation in domestic animals seems to be rising in number (Devriese and Hommez, 1975; Hartmann et al., 1997; Tomlin et al., 1999; Lee, 2003; Goni et al., 2004; Rich and Roberts, 2004). The epidemiology of MRSA isolates from human and animal sources showed that for certain strains, a cross-infection might have happened (Seguin et al., 1999; Strommenger et al., 2006; Weese et al., 2006). Studies conducted by Feirreria et al. (2011) and Verkade and Kluytman (2014) suggested that animals can be a potential source of MRSA infection to humans.

Therefore knowledge on the epidemiology of MRSA will underpin effective prevention and control strategies, including the rational use of antibiotics. This review article wishes to highlight the epidemiology and possible source of MRSA transmission in hospitals, community and livestock settings.

HISTORICAL BACKGROUND OF MRSA

Alexander Fleming conducted a research and reported the bactericidal effects of a fungal contaminant that produced penicillin against S. aureus growing on culture plates (Fleming, 1929). A mass production of the drug from vats of cornsteep liquid growing on the mold was preceded due to the high mortalities during World War II (Neushul, 1993). Subsequently, there was a dramatic drop in death rates from bacterial pneumonia and meningitis in World War II compared to World War I. This led to the development of penicillin as the first major driver in selecting for resistant S. aureus. In 1940, an active β-lactam enzyme was described in Escherichia coli that are capable of hydrolyzing the penicillin. This enzyme was later named “penicillinase” (Abraham and Chain, 1940) while in 1944; penicillinase production was also discovered in S. aureus (Kirby, 1944). In 1948, it was observed that over 50% of staphylococcal isolates recovered from patients in a United Kingdom hospital were resistant to penicillin (Barber and Rozwadowska-Dowzenko, 1948). Since then to date, 90 to 95% of S. aureus strains worldwide are penicillin resistant, with the plasmid encoded penicillinase readily transferable via transduction or conjugation. A penicillinase-resistant penicillin known as methicillin was introduced in 1959 to combat penicillin-resistant S. aureus, but within a year, late Professor Patricia Je-vons reported the first human S. aureus strain to be methicillin resistant in UK hospital (Kim, 2009). In 1962, an epidemic occurred at a hospital called Queen Mary’s Children’s Hospital, Carshalton. These strains became widespread in hospitals and into communities by the 1960’s (Spink, 1978). In 1968, United States recorded the first outbreak of MRSA (Palavecino, 2004) while in the 1970s, S. aureus strains have become resistant to most penicillinase-stable penicillins. It was first assumed to be a disease of human origin until when MRSA was first isolated in 1972 in a mastitic cow (Deveriese et al., 1972). Thereafter, reports of MRSA infection became established in domestic and wild animals (Rich and Roberts, 2004; Wardyn et al., 2012).

EPIDEMIOLOGY OF MRSA

Epidemiological typing of MRSA strains resulted in the recognition of different lineages that are zoonotic, humanosis and/or host specific. Seventeen epidemic strains of human MRSA have been described in the United Kingdom (Aucken et al., 2002) but the most dormant are EMRSA-15 and EMRSA-16 (Hardy et al., 2004.). The EMRSA-16 clone represents ma-
The most common lineage in this case was USA300 (CC8-ST8) in the USA. These strains are mostly responsible to skin and soft tissue infections. In comparison, the most dominant lineage causing infection in Europe is CC80 (ST80). However, the strain USA300 has also been reported in Europe (Tietz et al., 2005). Transboundary transmission of MRSA strain is reported between countries like North America and Middle East, Asia and South America (Stefani et al., 2012). The spread of CA-MRSA has extended to healthcare centres in USA and France (Donnio et al., 2004). Outbreaks of CA-MRSA is mostly seen from populations such as sports teams (Collins and O’connell, 2012), prisons (Palavecino, 2004), day care centers (Simmonds et al., 2008), military quarters (Marchese et al., 2000), homeless people (Yano et al., 2000), and intravenous drug users (Torres-Tortosa et al., 1994). Risk factors include international travel (Mikael et al., 2010), overcrowding, compromised skin, poor hygiene and sharing of items such as towels, sporting equipment and unsterilized first aid instruments (Kazakova et al., 2005).

LIVESTOCK-ASSOCIATED MRSA (LA-MRSA)

The scope of MRSA infection is not limited to human medicine only but also in Veterinary Medicine (Lee, 2003; Baptise et al. 2005; Voss et al., 2005; Khanna et al., 2008; Smith et al., 2008). MRSA was first considered a human infection until when it was isolated in a dairy cow with mastitis (Devriese et al, 1972) and in pigs (Stefani et al., 2012). The most pre
Table 1: Prevalence of MRSA carriage in some countries across the world

<table>
<thead>
<tr>
<th>Country</th>
<th>Sample size</th>
<th>Prevalence %</th>
<th>Source</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argentina</td>
<td>591</td>
<td>16</td>
<td>Hospital</td>
<td>Egea et al., 2014</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>49</td>
<td>53.1</td>
<td>Hospital specimens</td>
<td>Afroz et al., 2008</td>
</tr>
<tr>
<td>Bolivia</td>
<td>585</td>
<td>0.5</td>
<td>community</td>
<td>Batoloni et al 2013</td>
</tr>
<tr>
<td>Cameroon</td>
<td>295</td>
<td>34.6</td>
<td>Hospital staff/patients</td>
<td>Gonsu et al., 2013</td>
</tr>
<tr>
<td>Chile</td>
<td>246</td>
<td>80</td>
<td>Hospital</td>
<td>Guzman-Blanco, 2009</td>
</tr>
<tr>
<td>Columbia</td>
<td>538</td>
<td>92.4,65.1,43.6</td>
<td>Hospital record</td>
<td>Jiménez et al., 2012</td>
</tr>
<tr>
<td>Congo</td>
<td>60</td>
<td>60</td>
<td>Hospital patients</td>
<td>Iyamba et al., 2014</td>
</tr>
<tr>
<td>Costa Rica</td>
<td>674</td>
<td>58</td>
<td>Hospital</td>
<td>Guzman-Blanco, 2009</td>
</tr>
<tr>
<td>Cuba</td>
<td>80</td>
<td>6</td>
<td>Hospital</td>
<td>Guzman-Blanco, 2009</td>
</tr>
<tr>
<td>Equator</td>
<td>1363</td>
<td>25</td>
<td>Hospital</td>
<td>Guzman-Blanco, 2009</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>118</td>
<td>44.1</td>
<td>Hospital</td>
<td>Shibabaw et al., 2013</td>
</tr>
<tr>
<td>Guatemala</td>
<td>1483</td>
<td>64</td>
<td>Hospital</td>
<td>Guzman-Blanco, 2009</td>
</tr>
<tr>
<td>Hongkong</td>
<td>NK</td>
<td>75</td>
<td>NK</td>
<td>Diekema et al., 2000</td>
</tr>
<tr>
<td>Hounduras</td>
<td>393</td>
<td>12</td>
<td>Hospital</td>
<td>Guzman-Blanco, 2009</td>
</tr>
<tr>
<td>Indonesia</td>
<td>1502</td>
<td>4.3</td>
<td>Hospital</td>
<td>Santosaningsih et al., 2014</td>
</tr>
<tr>
<td>Japan</td>
<td>90</td>
<td>44.4</td>
<td>Environmental surfaces</td>
<td>Asoh et al., 2005</td>
</tr>
<tr>
<td>Kenya</td>
<td>950</td>
<td>7.0</td>
<td>Hospital</td>
<td>Aiken et al., 2014</td>
</tr>
<tr>
<td>Malaysia</td>
<td>26</td>
<td>26</td>
<td>Hospital</td>
<td>Norazah, 2008</td>
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<tr>
<td>Mexico</td>
<td>497</td>
<td>52</td>
<td>Hospital</td>
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<tr>
<td>Nepal</td>
<td>750</td>
<td>26.14</td>
<td>Hospital</td>
<td>Kumari et al., 2008</td>
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<tr>
<td>Netherland</td>
<td>9859</td>
<td>0.03</td>
<td>Hospital</td>
<td>Wertheim et al., 2004</td>
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<tr>
<td>Nicaragua</td>
<td>296</td>
<td>20</td>
<td>Hospital</td>
<td>Guzman-Blanco, 2009</td>
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<tr>
<td>Nigeria</td>
<td>208</td>
<td>19.2</td>
<td>Hospital</td>
<td>Olowe et al., 2013</td>
</tr>
<tr>
<td>North India</td>
<td>6743</td>
<td>46</td>
<td>Hospital</td>
<td>Arora et al., 2010</td>
</tr>
<tr>
<td>Paraguay</td>
<td>980</td>
<td>44</td>
<td>Hospital</td>
<td>Guzman-Blanco, 2009</td>
</tr>
<tr>
<td>Peru</td>
<td>1431</td>
<td>80</td>
<td>Hospital</td>
<td>Guzman-Blanco, 2009</td>
</tr>
<tr>
<td>Singapore</td>
<td>35</td>
<td></td>
<td>Hospital</td>
<td>Hsu et al., 2007</td>
</tr>
<tr>
<td>Sudan</td>
<td>426</td>
<td>69.4</td>
<td>Hospital</td>
<td>Elimam et al., 2014</td>
</tr>
<tr>
<td>Thailand</td>
<td>415</td>
<td>41.5</td>
<td>Hospital</td>
<td>Trakulsomboon and Thamlikitkul, 2008</td>
</tr>
<tr>
<td>Uganda</td>
<td>188</td>
<td>31.5</td>
<td>Hospital</td>
<td>Ojulong et al., 2008</td>
</tr>
<tr>
<td>Uruguay</td>
<td>2114</td>
<td>59</td>
<td>Hospital</td>
<td>Guzman-Blanco, 2009</td>
</tr>
</tbody>
</table>

NK: Not known

Dominant lineage in livestock is CC398 which has been reported in Europe, USA and Asia (Monecke et al., 2011). However, the prevalence of LA-MRSA CC398 in these countries is still very low (Stefani et al., 2012). But in countries like Denmark, Netherland and Belgium, the report of MRSA CC398 in livestock is high (Köck et al., 2009a; Köck et al., 2009b). Epidemiological studies in the UK indicate the spread of LA-MRSA into hospitals particularly in individuals with frequent animal contact (Paterson et al., 2012). Recently, there is evidence of MRSA transmission between human-to-animals and animals-to-humans (Umaru et al., 2011). Voss et al. (2005) reported 23% of pig farmers colonized MRSA from a pig farm in the Netherlands with while VanRijen et al., 2008 found 32% of farm workers colonized with MRSA.
<table>
<thead>
<tr>
<th>Year</th>
<th>Country</th>
<th>Species</th>
<th>Sample Type</th>
<th>Detection Methods</th>
<th>MRSA Characterization</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>Germany</td>
<td>Pigs</td>
<td>Healthy swabs</td>
<td>PCR</td>
<td>ST398, CC398</td>
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<tr>
<td>2000</td>
<td>Belgium</td>
<td>Horses</td>
<td>Nasal, cloaca</td>
<td>PCR, MLST</td>
<td>CC5, CC398</td>
</tr>
<tr>
<td>2007</td>
<td>Belgium</td>
<td>Cows</td>
<td>Nasal, cloaca</td>
<td>PCR, MLST</td>
<td>CC599, CC130</td>
</tr>
<tr>
<td>2007</td>
<td>Canada</td>
<td>Dolphins</td>
<td>Necropsy, swab</td>
<td>PCR, MLST</td>
<td>CC398, CC130</td>
</tr>
<tr>
<td>2006</td>
<td>Czech Republic</td>
<td>Goat Farm</td>
<td>Milk</td>
<td>PCR</td>
<td>Spa type t064</td>
</tr>
<tr>
<td>2006</td>
<td>Malaysia</td>
<td>Tilapia</td>
<td>Brain, eyes, kidney</td>
<td>PCR</td>
<td>CC398, CC130</td>
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<tr>
<td>2005</td>
<td>Egypt</td>
<td>Tilapia</td>
<td>Brain, eyes, kidney</td>
<td>PCR</td>
<td>CC398, CC130</td>
</tr>
<tr>
<td>2004</td>
<td>Germany</td>
<td>Cows</td>
<td>Nasal, cloaca</td>
<td>PCR, MLST</td>
<td>CC599, CC130</td>
</tr>
<tr>
<td>2003</td>
<td>Germany</td>
<td>Calves</td>
<td>Nasal samples</td>
<td>PCR, MLST</td>
<td>CC5, CC398</td>
</tr>
<tr>
<td>2002</td>
<td>Germany</td>
<td>Calves</td>
<td>Nasal samples</td>
<td>PCR, MLST</td>
<td>CC5, CC398</td>
</tr>
</tbody>
</table>

**References:**

- Vincze et al., 2014
- Walther et al., 2008
- Van den Ende et al., 2001
- Graveland et al., 2010
- Stastkova et al., 2009
- Vandendriessche et al., 2013
- Atal et al., 2011
- Soliman et al., 2014
- Leggiero 2009
- NE US Academic Publishers

**Table 2:** Prevalence of MRSA infection and carriage rates in different animals.
Likewise, Stein (2009) conducted a study among pig farmers in North America and found colonization rates of 20%. These results backup other findings that revealed the chances of animals becoming reservoirs of human MRSA infections regardless of location (Feingold et al 2012). In addition, human-to-human transmission can occur following one’s exposure to colonized or infected animals due to isolation of MRSA strains from people with no animal contact (Huijsdens et al., 2006). High risk groups are the veterinary clinic personnel and the animals care givers (O’Mahony et al., 2005; Moodley et al., 2005; Wulf et al., 2006; Hanselman et al., 2006).

### MRSA in Companion Animals

Animals such as dogs, cats and horses have become an important part of most families particularly in developed countries like USA and UK (Chomel and Sun 2011). Therefore, there are high chances of human colonization or infection with MRSA from these animals (Mustapha et al., 2014). In the UK, 1.5% of MRSA were recovered from samples of infected companion animals (Rich and Roberts, 2004) and dogs are more infected/colonized with MRSA in comparison to cats (Morgan, 2008). Skin and soft tissue infections are the main form of disease manifestation. MRSA strains isolated in most UK hospitals are identified as EMRSA-15 (ST22) and EMRSA-16 (ST36) (Ellington et al., 2010) while the strains isolated in USA pets are the USA100 (ST5) which has been documented in HA-MRSA infections in humans (Ellington et al., 2010). In addition, a study in UK recovered MRSA clone (ST398) in dogs and horses that were characteristic of livestock animals (Loeffler et al., 2009).

Reports of MRSA colonization in horses with a percentage rate of 0 to 11% has been published (Loeffler et al., 2011). Most cases and outbreak of MRSA infections were reported in large stables and post-operative complications (Weese et al., 2005; Morgan, 2008). In horses, MRSA lineages isolated were distinct from the strains isolated in humans (Loeffler and Lloyd, 2010).

### MRSA in Wildlife

Although the role of wildlife as reservoir for MRSA colonisation and/or infection has not yet been established, there are several studies that revealed the isolation of MRSA in many captive wildlife animals (Loncaric et al., 2014). A study by Wardyn et al. (2012) revealed the isolation of MRSA from cottontail rabbit and a lesser yellow migratory shore bird. Other studies include isolation of MRSA from Wild rat, (Himsworth et al., 2014), wood mice (Gómez et al., 2014) red deer, Iberian ibex, vulture, wild boar (Porreiro et al., 2012). In some of the studies, the homologue of mecA gene known as mecC strain (ST398 and ST1) were isolated and suspected to be of livestock and human origin (Porreiro et al., 2012). Although the mecC homologue is currently uncommon in human infections globally, it has been identified recently in human and animal infections in the UK, Denmark and Ireland (Paterson et al., 2014b). The most common animal lineage that causes disease in wild life is CC130 and ST425 (Paterson et al., 2014a).
into the wild life, control of the disease in human and domesticated animals will become a new challenge. This is due to the fact that wild animals can serve as source of animal and human colonization (particularly park rangers and zoo keepers) as well as contamination of the environment (Guideline for management of zoonoses, 2011; Chethan Kumar et al., 2013).

Summary of MRSA prevalence in animals (both wild and domesticated) is presented in Table 2 according to some reports published.

**MRSA IN ABATTOIRS, FOOD PROCESSING UNITS AND ANIMAL PRODUCTS**

The environment of abattoirs and food production units are contaminated with MRSA (EFSA, 2009). The sources of contamination can either be the animals moving into the abattoir for slaughter or the workers involved in processing the end product (Gilbert et al., 2012). Contaminated skin, feces, infected organs and water used in processing are the vital sources of contamination in abattoirs and food processing units (Soonthornchaikul et al., 2006). Some studies suggest that *S. aureus* from food handlers can be part of normal body flora that subsequently contaminates carcasses. Broens et al. (2011) conducted a study and found 12 out of 117 pigs tested MRSA positive in a slaughterhouse after being tested negative during and after transportation.

Animal food products such as meat, meat products and milk may become contaminated with MRSA through slaughter or milking of colonized/infected animal, thus, contaminating the product and environment. MRSA strains have been discovered from foods such as bovine milk and cheese, pork and beef as well as raw chicken meat (Kwon et al., 2006; Normanno et al., 2007; Van Loo et al., 2007; O’Brien et al., 2012). The strains of MRSA isolated in most food samples include ST398, ST125 and ST217 (Faccioli-Martins and de Souza da Cunha, 2012) while the recent mecC homologue of mecA gene has been isolated in bovine milk in England (Paterson et al., 2014b). The presence of these strains on food products could suggest possible human or animal contamination. An important link in food borne infections connecting humans and food producing animals is the meat and milk or their products (Mayrhofer et al., 2004). Although food products may serve as vehicle for MRSA transmission, consumption of such meat carry only small risk as *S. aureus* found on meat surfaces and can be killed by high temperature. However, there is high risk of transmission from live animal or raw meat to people working directly with animals or their products. The prevalence of MRSA isolation from food/meat products is presented in table 3.

**MRSA TRANSMISSION IN HOSPITAL SETTINGS**

For hospital infection, the hands and nostrils of colonized individuals are the major sources of MRSA transmission. MRSA is released into the hospital environment either through aerosol, skin cells or stools of infected patient (Klotz et al., 2005). Areas contaminated in the hospital include medical instrument, beddings, clothing, furnitures, toiletries and the atmosphere (Dancer, 2008). Gehanno et al. (2009) found similar strain of MRSA in patients of a hospital and the room atmosphere. While Loeffler et al. (2005) and Weese et al. (2004) reported MRSA in environmental samples collected from small animal veterinary hospital and equine veterinary hospital, respectively. Although, hospital cleaning reduces MRSA contamination of the environment, in some cases it does not eliminate it.

**MRSA IN THE COMMUNITY**

Some studies investigated environmental contamination of MRSA outside hospital settings (EFSA, 2007). Reports include continuous colonization of a medical staff which was related to contamination of home environment (Allen et al., 1997; de Boer et al., 2006). Again, contamination of animal housing revealed the possibility of human and animal colonization. Van Den Broek et al. (2008) isolated MRSA from pig house dust and humans working in MRSA positive pig farms.

Airborne MRSA in livestock settings are mostly seen in dust particles that are derived from the animals. MRSA was isolated in dust from infected herds which may be subsequently inhaled by workers in the farm (EFSA, 2007; Schulz et al., 2012). Transmission of disease through water may occur in aquatic animals such as fish. Transmission from fish to humans could be through injury from cleaning aquarium with bare hands (Alinovi et al., 1993) and exposure to fish tank water (Kern et al., 1989).

**MRSA DETECTION IN HUMANS AND ANIMALS**

In an effort to control MRSA in major settings (hospital, community, animals) colonized and infected
humans, animals and environmental surfaces must be identified. The menace of MRSA colonization and infection has extended from human, companion and food animals into wildlife animals. The screening of human carriers in hospitals and communities is necessary for the successful diagnosis and control of MRSA. In addition, companion animals with skin and soft tissue infections should be screened for MRSA. Sites for screening of MRSA colonized animals include nose, skin, perineum and rectal or cloacal swabs (de Neeling et al., 2007; Khanna et al., 2008) and nostril for humans (Peacock et al., 2001). Nasal screening alone identifies 80% of carriers, and addition of sampling from throat, may increase this to 92% (Grundmann et al., 2006). For environmental samples, swabs are taken from dust samples (EFSA, 2007; Broens et al., 2008), tables, containers, feed material or feces and bedding material (Lee, 2003). Other samples like milk and meat from animals and cloacal swab from poultry should be cultured for detection of MRSA.

Various methods are applied for the detection of MRSA through phenotypic and genotypic characterization of samples from infected sites such as skin lesions, abscesses or blood. Both has advantages and disadvantages such as speed, reliability and accessibility. Phenotypic methods involves standard microbiological technique of S. aureus detection which include Gram staining, colonial morphology, catalase and coagulase tests, pigment production and anaerobic growth (Karthi et al., 2009). Additional methods include Minimum Inhibitory Concentrations, methods that detect meca gene or PBP2 protein and media containing oxacillin (Louie et al., 2001). Selective enrichment media have been developed to achieve isolation and identification of MRSA in a single step, thus by-passing the conventional procedures (Stoakes et al., 2006). Ideal enrichment media contains indicators, inhibitory agents and antibiotics usually oxacillin or cefoxitin. Examples are Oxacillin Resistant Screening Agar Base (ORSAB) which result in intense blue colonies (Becker et al., 2002), CHROM agar which give rise to a rose to mauve color and MRSA ID which forms distinctive green colonies.

In addition to culture media, antimicrobial susceptibility tests (AST) such as agar disc diffusion technique or minimum inhibitory concentration are used in diagnostic laboratories to isolate MRSA (Aklilu et al., 2010). Detection of the meca gene is considered as the reference method for determining methicillin resistance (Chambers, 1997). Resistance of S. aureus to oxacillin and/or cefoxitin provides a clue for MRSA suspicion (van Eng and Thompson, 1992). Oxacillin and cefoxitin test are the preferred method for testing meca resistant gene of S. aureus (CLSI, 2006). In order to report isolates as resistant or susceptible should be based on the result obtained on the cefoxitin test. Cefoxitin disc diffusion is the most sensitive methods for detecting MRSA isolates showing negative and positive predictive values of 100% and 98%, respectively (Valesco et al., 2005).

A more advanced technique usually accompanies the phenotypic methods in order to enhance specificity and time. Molecular methods such as PCR are used to detect S. aureus specific DNA sequences encoding for protein synthesis and the meca genes. Other molecular typing methods include pulsed-field gel electrophoresis (PGFE) and multilocus sequence typing (MLST), Staphylococcal Protein A Gene (spa) locus typing and Staphylococcal Cassette Chromosome (SCCmec) typing. The strength and weaknesses of the above genotypic methods are presented in table 4.

**TREATMENT AND CONTROL OF MRSA**

The indiscriminate exposure of humans and animals to antibiotics created problem through acquisition and dissemination of MRSA which limit the choice of treatment. Most antibiotics used for treatment of MRSA infection has been reported to have developed resistance (Ayliffe, 1997). In order to manage the risk of antibiotic resistance in humans and animals, decolonization of carriers and monitoring of resistant strains through susceptibility test will surely help. The use of antibiotic to treat infection should depend on the result of antimicrobial susceptibility testing, although most strains appear ineffective during treatment even when sensitive in routine susceptibility test. Antibiotics such as trimethoprim-sulphamethoxazole, clindamycin and doxycycline are reported to be effective in the treatment of CA-MRSA infection (Ernst, 2012). Newer drugs such as oritavancin, telavancin omadacycline, tedizolid and dalbavancin have a promising impact on the treatment of MRSA. Other existing agents such as fosfomycin and fusidic acid are under investigation for potential used in the treatment of MRSA infection (Burke and Warren, 2014).
<table>
<thead>
<tr>
<th>Methods</th>
<th>Principle</th>
<th>Strengths</th>
<th>Weaknesses</th>
<th>References</th>
</tr>
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<tr>
<td>Pulsed-field gel electrophoresis (PFGE)</td>
<td>S. aureus DNA fragments are move down the gel, creating unique band patterns that are then compared with those of other isolates to identify related strains</td>
<td>High discriminatory power</td>
<td>Technically demanding, slow</td>
<td>Tenover et al., 1995</td>
</tr>
<tr>
<td>Multilocus sequence typing (MLST)</td>
<td>Uses sequence analysis of ~500-bp internal fragments of seven housekeeping genes: arcC, aroE, glpF, gmk, pta, tpi, and yqiL. The DNA sequences are compared to those of previously identified alleles at each locus on the MLST online database</td>
<td>Phylogenetic structure of core genome, inter laboratory portability</td>
<td>Limited discriminatory power, low throughput, expensive</td>
<td>Enright et al., 2000</td>
</tr>
<tr>
<td>S. aureus protein A (spa) typing</td>
<td>Typing of a single locus zone in the polymorphic region X of S. aureus A which involves duplication and mutation in the variable repeats of 24bp</td>
<td>Rapid, high throughput, inter laboratory portability</td>
<td>Attribution of MLST STs by BURP algorithm, moderate discriminatory power, misclassification of particular STs due to recombination/homoplasy</td>
<td>Szabó (2014)</td>
</tr>
<tr>
<td>SCC mec typing</td>
<td>Used to define the 7 major SCC-mec and ccr gene of 7 major SCC-mec types and subtypes ranging from 20 to 67kb</td>
<td>High discriminatory power</td>
<td>No universally used assay, no nomenclature used but a combination of SCC mec typing and MLST has been proposed</td>
<td>Chongtrakool et al., 2006</td>
</tr>
<tr>
<td>Rep-PCR typing</td>
<td>Polymorphism in chromosomal VNTRs</td>
<td>High discriminatory power</td>
<td>Inter-Repetitive Element Spacers, high throughput</td>
<td>Struelens et al., 2009</td>
</tr>
<tr>
<td>Multilocus VNTR analysis (MLVA)</td>
<td>Polymorphism in number of chromosomal VNTR elements</td>
<td>High discriminatory power</td>
<td>Inter-Repetitive Element Spacers, high throughput</td>
<td>Struelens et al., 2009</td>
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</tbody>
</table>
As the MRSA epidemic becomes life threatening and beyond antibiotic therapy, development of vaccine to combat the disease became important (Ci-{}molai, 2006). The first attempt to develop $S$. aureus vaccine was by the use of Streptococcus pneumonia and hemophilus influenza vaccine model. The formula was called Staphvax developed by biopharmaceuticals in 1990s though unsuccessful (Mckenna, 2014). Continuous attempts were made by different institutions like University of Chicago and the Absynth biologics which uses clotting factors to produce abscess and membrane protein, respectively (Cheng et al., 2010). However, trial on mice did not produce the desired result of abscess development and antibody production (Hu et al., 2013). Recently, Russell (2012) suggested the role of polyvalent pneumococcal vaccine to develop vaccine for staphylococcal infections. Therefore based on published data, researches are still conducted on MRSA vaccine development but no established vaccine is available. In the absence of preventive measures such as vaccination, basic control options that will reduce MRSA colonisation or infection in humans and animals are necessary.

Basic hygiene, good husbandry and biosecurity measures on farms, abattoirs and food processing units have a tendency to reduce the spread of MRSA in animal population. Individuals with frequent animal contact should be educated on the risk of MRSA transmission in animals or their environment. In hospitals, hygienic measures particularly hand washing before and after contact with contaminated surfaces and the avoidance of close contact with discharges from nose, mouth and wounds of infected human and animals will surely reduce the chances of transmission. Decolonization of MRSA positive carriers’ either through the use of antibiotic therapy (chlorhexidine or murocidi) or culling of affected animals or product will reduce the spread in the environment. Medical practitioners should be encouraged to choose antibiotic based on susceptibility test and to wear protective equipment during surgery and handling of patients to reduce contamination and spread.

CONCLUSION

In conclusion, the prevalence of MRSA isolation from hospitals, community, animals and their products has increased in different geographical locations. The continous vigilance of MRSA through monitoring of newer strains, their characteristic, host specificity and transmission routes in each of the settings (HA-MRSA, CA-MRSA, LA-MRSA) will help in effective control of MRSA. MRSA is no longer infection acquired in the hospital alone, but rather in communities through contact with domesticated and wild animals as well as food products and the environment. Therefore, there is need for effective control of MRSA in all the settings and the avoidance of indiscriminate use of antibiotics to prevent further selection of resistance by microorganisms.

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