The Distribution and Drug Resistance Characteristics of Methicillin Resistant Staphylococcus aureous to be Public and Animal Health Burdon in Ethiopia: Meta-Analysis

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Abstract

**Introduction:** Antimicrobial resistance to specific antibacterial drugs in bacteria have led many drugs of choice ineffective against pathogens. Methicillin resistant *S.aureus* (MRSA) is one of the pathogens, which loses sensitivity to Methicillin. Methicillin has been considered as the drug of choice of choice to treat infections caused by β-lactams and other antibiotics resistant *S. aureus*.

**Objectives:** The objectives of the current study were to analyse the prevalence of MRSA in *S. aureus* isolates from different sources of samples and to assess the risk factors associated with the prevalence. The multidrug resistance pattern of the pathogen was also one of the outcome of interest of the review.

**Methods:** The original research articles were collected from PubMed and PMC databases from 12th to 14th December 2021. The English language articles conducting on MRSA prevalence in Ethiopia were included in the analysis. Relevant data were extracted, coded and displayed on Excel spreadsheet. The pooled prevalence of MRSA was determined per *S. aureus* isolates. The analysis were made by using R statistical software at 95% CI.

**Result:** 79 research eligible articles were selected for the meta-analysis. 26930 samples were collected from different sampled materials. Of these 4219 (15.65%) were *S. aureus* positive of which 1695 were found MRSA strains. The overall pooled prevalence of MRASA in *S. aureus* was found to be 40%. The pooled prevalence of MRSA in human, animal, food and environment was 38%, 15%, 77%, and 54% respectively. The strain was determined significantly highest in food and environment than in animal and human samples (p<0.05). The subgroup analysis based on the health status of the individual in samples of human indicated that MRSA was significantly prevalent in patients than in healthy individuals (p<0.05). The assessment of MDR pattern of MRSA revealed that it was highly resistant to cefuroxime (100%), Tobramycin (100%), Neomycin (99%) and Penicillin (92%), Pipracillin (91%), Erythromycin (88%), Bacitracin(84%) and Amoxicillin-clavulanacid (80%). In contrast Clindamycin, chloramphenicol, Amikacin, vancomycin, Knamycin and Ceftriaxone with pooled resistance rates of 21%, 22%, 27%, 20%, 25% and 30% respectively were antibiotic of relatively better effective.

1. Introduction

*Staphylococcus aureus* (*S.aureus*) is a Gram positive grouped spherical (cocci) bacteria widely distributed in the world. It resides, as microflora in the mucosal cavities and on the skin of the hosts without harming them. Researchers have isolated it from hand, nasal, buccal cavity and urogenital organs. However, in some specific conditions, *S.aureus* can be associated with disease conditions as an opportunistic pathogen. As a result it may cause diseases ranging from simple diseases such as pimples and boils to serious infections such as wound infections, pneumonia, and/or septicaemia, which result in life-threatening illness particularly in immune compromised patients (Torrence & Isaacson, 2008).

The pathogenicity of the *S. aureus* attributes to its antibiotic resistance, enterotoxogenicity, biofilm formation and other virulence factors including adherence factors, nucleases, proteases, lipases, hyaluronidase, and collagenase productions. In addition, *S. aureus* is becoming important in that it has developed resistance to commonly used antibiotics including methicillin. Methicillin has been used to treat β-lactam resistant *S. aureus* infections. Such characteristics of the microbe made it to be near one to one of the most non-treatable pathogenic microbe in the globe. Methicillin resistant *Staphylococcus aureus* (MRSA) has emerged and increased its intensity to be one of the global issues of health concerns (Eshetie et al., 2016).

Furthermore, studies have found that MRSA strains are resistant to all beta-lactam antibiotics (including penicillin G, cefitiofur sodium, Cloxacillin, cephalin, and ampicillin) and other antibacterial agents such as tetracycline and sulphonamides (Torrence & Isaacson, 2008). Despite the fact that Vancomycin is the drug of choice for treatment of MRSA infections, studies revealed MRSA has reduced susceptibility to vancomycin, and vancomycin intermediate susceptible *Staphylococcus aureus* (VISA) strains are increasing. Therefore, MRSA strains are approaching to the pathogen with lack of alternative antibiotics (Arun K. Bhuni, 2008).

Methicillin resistant *Staphylococcus aureus* (MRSA) has been developed by acquisition of genes of chromosomal cassette “mec” elements. This cassette consists gene (mecA) which encodes the novel penicillin binding protein PBP2a. PBP2a confers resistence and renders the entire antibiotic class ineffective (Wielders et al., 2002).

The mec gene cassette also carries several virulence factors due to the fact that virulence factors and antibiotic resistance are closely linked. A single horizontal gene transfer of the Staphylococcal cassette chromosome (SCC) may contain other several genes coding various virulence factors. This renders methicillin resistant *S. aureus* strains more virulent than other *S. aureus* (Lakhundi & Zhang, 2018).

In Ethiopia, many studies have been conducted to isolate MRSA in public health aspects since a decade. However, few systematic reviews made so far in the country have mostly focused on public health issues and the animal health bourdon, environmental and food contaminations by MRSA has not been given emphasis. The aim of this systematic review is, therefore, to assess the distribution of MRSA in food animals, environment and foods to be bourdon on public and animal health in Ethiopia.

2. Materials And Methods

2.1. Inclusion and Exclusion Criterion

Original research articles, which have reported extractable data on the prevalence of MRSA in Ethiopian, and only in English language, were included in the study. On the other hand, studies which did not report MRSA in Ethiopia and were not original research articles were excluded from the study.

2.2. Study Selection
The search of the literatures was from PubMed and PMC databases. Accordingly, original research articles accessed online between 12th December to 14th December 2021 and potentially relevant to the study were collected and identified. The search was performed by using “MRSA in Ethiopia” and/or “methicillin resistant Staphylococcus aureus in Ethiopia” as keywords. The PDF of the articles accessed in the aforementioned scholars databases during the study period were then retrieved.

After obtaining the articles, first the titles of the articles were checked for whether they full fill the set criterion. Accordingly, only the original research articles were passed to the next step of screening. Next, the abstracts of the selected articles were then reviewed to determine if they have studied the drug resistance pattern of Staphylococcus aureus and/or identified MRSA. Finally, the relevant articles were accessed in full text to obtain detail information included in the meta-analysis.

2.3. Outcome of Interest

The major outcome of interest was to determine the prevalence of MRSA among total sample size and among total S. aureus isolates in the samples. The prevalence was calculated by dividing the numbers of MRSA isolates by the total number of sample size, or S. aureus isolates. The study has also determined the pooled resistance pattern of MRSA isolates to specific antibiotics.

2.4. Data Extraction

Data from eligible studies were extracted and summarized into an excel spreadsheet. For each of the included studies, the following prominent information was extracted.

- Name of the authors
- Years of publication
- Study design
- Period of the study
- Region in which the study was conducted
- Study population
- Sample type
- Sample sizes
- Total numbers of S. aureus isolates
- Total number of S.aureus isolates tested for MRSA
- Types of drug used to test MRSA
- Total number of MRSA isolates
- Drug resistance pattern of MRSA (if any)

The current review has collected data of total sample size, number of S. aureus isolates and total MRSA isolates. However, in studies aimed to identify multiple bacteria and MRSA in due the process, the prevalence of MRSA get smaller. However, in the studies aimed to isolate and identify MRSA, the proportion of MRSA got increasing as the number of the S.aureus isolates were considered as sample size. As the result, in order to report consisten results re, we prefer to conduct the meta-analysis based on the proportion of MRSA per S.aureus isolates. Therefore, it should be noted that the pooled proportions of MRSA in the review were per number of S.aureus isolates.

2.5. Quality Control

The quality of eligible studies was checked using a set of predetermined criteria such as research design, quality of paper, and methods employed to isolate and identify MRSA. As the result, only original research articles performed the research by isolating and identifying MRSA, and of which full article could be downloaded from PubMed and PMC were included in the analysis.

2.6. Data analysis

The random effects size model was accepted to determine pooled prevalence at 95% confidence interval (CI) using momentum estimate (Der Simonian and Laird method) (Der Simonian and Laird, 1986) approach (Harrer et al.,2019). In addition, the analysis needed transformation; because there were reports with zero percent prevalence. As the result, the double arcsine transformation method was preferred to logit transformation or analyzing without transformation (Barendregt et al., 2013). The heterogeneity of study results was assessed by the use of $I^2$, $I^2$ and Q-statistics tests. Significant heterogeneity was considered when p-value < 0.05 and $I^2 > 75\%$ were observed (DerSimonian and Laird, 1986, Rücker et al., 2008). The pooled resistance pattern of MRSA to specific antibiotics was calculated, and presented using table. All the statistical analyses were performed by the use of the R-software (Ri386 4.2.1.lnk)(Andy Bunn, 2008).

3. Results And Discussions

3.1. The Selected Publications

Total of 168 articles were downloaded through search of the electronic PubMed and PMC databases, of which 50(30%) of them were duplicated. Eight (4.8%) were conducted not in Ethiopia, and 18 (10.7%) were not original research articles, 6(3.5%) isolated S.aureus but did not identify MRSA, and 7(4.2%) used unclear methods and/or report unclear results. Therefore, 79(47%) of the articles were eligible for the meta-analysis. Two research articles were replicated in the analysis because they conducted the research on both human and animals (Fig. 1).
The year of the publications were between 2010 and 2021. The highest number of publications was recorded in 2021 (27%) followed by 2020 (16%). This indicates that researches on MRSA have been becoming increasing in the country since recent. Most of the publications we found were related with public health 60(74%) and only few were with environments 10(12.4%), food animal 7(8.6%) and food issues 4(5%). The regions in which the studies conducted and the types of sampled materials were summarized in Tables 1–3 and Fig. 2. One research was conducted by collecting samples from Amhara, Oromia and Addis Ababa, and it was assigned as AmOrAd on the figure. It was determined that highest number of the studies were conducted in Amhara (37%) followed by Oromia (18%) regional state. Seventy four percent of the articles collected samples from human followed by environment (12.3%). Figures (2) summarize the percentage of articles in respect to the regions and sampled categories.
### Table 1
Summary of 81 Studies reporting the prevalence of MRSA in Human, 2010–2021

<table>
<thead>
<tr>
<th>Studies</th>
<th>Study design</th>
<th>Regions</th>
<th>Cultured specimens</th>
<th>Sample size</th>
<th>S. aureus</th>
<th>MRSA</th>
<th>MRSA Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Eshetu et al., 2020)</td>
<td>Cohort</td>
<td>Oro, Am, Ad</td>
<td>blood</td>
<td>690</td>
<td>41</td>
<td>35</td>
<td>86</td>
</tr>
<tr>
<td>(Kejela &amp; Bacha, 2013)</td>
<td>Cro-Sect</td>
<td>Oro</td>
<td>Nasal swab</td>
<td>354</td>
<td>169</td>
<td>39</td>
<td>23</td>
</tr>
<tr>
<td>(Godebo et al., 2013)</td>
<td>Cro-Sect</td>
<td>Oro</td>
<td>Wound swab</td>
<td>322</td>
<td>73</td>
<td>56</td>
<td>77</td>
</tr>
<tr>
<td>(Dagnew et al., 2012)</td>
<td>Cro-Sect</td>
<td>Am</td>
<td>Nasal swab</td>
<td>200</td>
<td>41</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>(Shibabaw et al., 2013)</td>
<td>Cro-Sect</td>
<td>Am</td>
<td>Wound swab</td>
<td>184</td>
<td>73</td>
<td>36</td>
<td>49</td>
</tr>
<tr>
<td>(A. Kahsay et al., 2014)</td>
<td>Cro-Sect</td>
<td>Am</td>
<td>Ocular swab</td>
<td>360</td>
<td>77</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>(Ayehubizu et al., 2021)</td>
<td>Cro-Sect</td>
<td>A. A</td>
<td>Nasal swab, pus, ear discharge, blood, throat swab, eye swab, vaginal discharge, urethral discharge, urine, stool, sputum, CSF and body fluids</td>
<td>1360</td>
<td>194</td>
<td>34</td>
<td>18</td>
</tr>
<tr>
<td>(Teweldemedhin et al., 2017)</td>
<td>Cro-Sect</td>
<td>Tig</td>
<td>ophthalmic surgeon collected specimens</td>
<td>270</td>
<td>40</td>
<td>7</td>
<td>18</td>
</tr>
<tr>
<td>(Getahun et al., 2017)</td>
<td>Cro-Sect</td>
<td>Am</td>
<td>Ocular swab</td>
<td>312</td>
<td>69</td>
<td>23</td>
<td>33</td>
</tr>
<tr>
<td>(B. Tadesse et al., 2019)</td>
<td>Cro-Sect</td>
<td>Sid</td>
<td>Ear swab</td>
<td>152</td>
<td>41</td>
<td>7</td>
<td>17</td>
</tr>
<tr>
<td>(Kasew et al., 2021)</td>
<td>Cro-Sect</td>
<td>Am</td>
<td>Urine sample</td>
<td>300</td>
<td>7</td>
<td>2</td>
<td>29</td>
</tr>
<tr>
<td>(Gorems et al., 2018)</td>
<td>Cro-Sect</td>
<td>Oro</td>
<td>Ear swab</td>
<td>173</td>
<td>55</td>
<td>19</td>
<td>35</td>
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<tr>
<td>(Kalayu et al., 2020)</td>
<td>Cro-Sect</td>
<td>Tig</td>
<td>Nasal Swabs</td>
<td>71</td>
<td>22</td>
<td>0</td>
<td>00</td>
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<tr>
<td>(Ramos et al., 2014)</td>
<td>Cro-Sect</td>
<td>Oro</td>
<td>Pus swab</td>
<td>68</td>
<td>15</td>
<td>3</td>
<td>20</td>
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<tr>
<td>(Biset et al., 2020)</td>
<td>Cro-Sect</td>
<td>Am</td>
<td>Urine sample</td>
<td>384</td>
<td>11</td>
<td>4</td>
<td>36</td>
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<td>(Abie et al., 2020)</td>
<td>Cro-Sect</td>
<td>Am</td>
<td>Nasal swabs</td>
<td>436</td>
<td>101</td>
<td>21</td>
<td>21</td>
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<tr>
<td>(Reta et al., 2017)</td>
<td>Cro-Sect</td>
<td>Am</td>
<td>Nasal swabs</td>
<td>400</td>
<td>52</td>
<td>0</td>
<td>00</td>
</tr>
<tr>
<td>(Legese et al., 2018)</td>
<td>Cro-Sect</td>
<td>Tig</td>
<td>Nasal swab</td>
<td>242</td>
<td>29</td>
<td>14</td>
<td>48</td>
</tr>
<tr>
<td>(A. G. Kahsay et al., 2018)</td>
<td>Cro-Sect</td>
<td>Tig y</td>
<td>Nasal swabs</td>
<td>184</td>
<td>69</td>
<td>45</td>
<td>65</td>
</tr>
<tr>
<td>(Belyhun et al., 2018)</td>
<td>Cro-Sect</td>
<td>Am</td>
<td>Ocular swab</td>
<td>210</td>
<td>35</td>
<td>32</td>
<td>91</td>
</tr>
<tr>
<td>(Feleke et al., 2018)</td>
<td>Cro-Sect</td>
<td>Am</td>
<td>Nasal swab</td>
<td>260</td>
<td>77</td>
<td>52</td>
<td>68</td>
</tr>
<tr>
<td>(Temesgen et al., 2019)</td>
<td>Cro-Sect</td>
<td>Am</td>
<td>Sputum</td>
<td>414</td>
<td>24</td>
<td>18</td>
<td>75</td>
</tr>
<tr>
<td>(Wasihun et al., 2015)</td>
<td>Cro-Sect</td>
<td>Tig</td>
<td>Blood</td>
<td>514</td>
<td>54</td>
<td>38</td>
<td>70</td>
</tr>
<tr>
<td>(Hailu et al., 2016)</td>
<td>Cro-Sect</td>
<td>Am</td>
<td>Pus swabs from discharging ears</td>
<td>368</td>
<td>78</td>
<td>27</td>
<td>35</td>
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</tbody>
</table>

Continues from Table 1
<table>
<thead>
<tr>
<th>Studies</th>
<th>Study design</th>
<th>Regions</th>
<th>Cultured specimens</th>
<th>Sample size</th>
<th>S. aureus</th>
<th>MRSA Prevalence (%)</th>
<th>Per S. aureus</th>
<th>Per Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Gebremedhin et al., 2016)</td>
<td>Cro-Sect</td>
<td>Tig</td>
<td>Nasal and throat swabs</td>
<td>249</td>
<td>81</td>
<td>6</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>(Deyno, Toma, et al., 2017)</td>
<td>Cro-Sect</td>
<td>Sid</td>
<td>Ear swab</td>
<td>117</td>
<td>33</td>
<td>30</td>
<td>91</td>
<td>26</td>
</tr>
<tr>
<td>(S. Tadesse et al., 2018)</td>
<td>Cro-Sect</td>
<td>A.A</td>
<td>Wound and corresponding nasal swabs</td>
<td>188</td>
<td>79</td>
<td>77</td>
<td>97</td>
<td>41</td>
</tr>
<tr>
<td>(Birru, Woldemariam, et al., 2021)</td>
<td>Cro-Sect</td>
<td>SNNP</td>
<td>blood</td>
<td>225</td>
<td>7</td>
<td>4</td>
<td>57</td>
<td>2</td>
</tr>
<tr>
<td>(Tolera et al., 2018)</td>
<td>Cro-Sect</td>
<td>Oro</td>
<td>urine, blood, wound swab, throat swab, nasal swab, and other body fluids w</td>
<td>394</td>
<td>10</td>
<td>9</td>
<td>90</td>
<td>2</td>
</tr>
<tr>
<td>(Endris et al., 2014)</td>
<td>Cro-Sect</td>
<td>Am</td>
<td>Blood samples</td>
<td>83</td>
<td>11</td>
<td>2</td>
<td>18</td>
<td>2</td>
</tr>
<tr>
<td>(G. Alebachew et al., 2016)</td>
<td>Cro-Sect</td>
<td>Am</td>
<td>Blood</td>
<td>100</td>
<td>13</td>
<td>5</td>
<td>38</td>
<td>5</td>
</tr>
<tr>
<td>(Semret et al., 2020)</td>
<td>Cohort</td>
<td>A.A</td>
<td>Blood</td>
<td>777</td>
<td>82</td>
<td>62</td>
<td>76</td>
<td>8</td>
</tr>
<tr>
<td>(T. Alebachew et al., 2012)</td>
<td>Cro-Sect</td>
<td>A.A</td>
<td>pus</td>
<td>114</td>
<td>66</td>
<td>51</td>
<td>77</td>
<td>45</td>
</tr>
<tr>
<td>(Sewunet et al., 2013)</td>
<td>Cro-Sect</td>
<td>A.A</td>
<td>Blood and burn wound swab</td>
<td>100</td>
<td>24</td>
<td>5</td>
<td>21</td>
<td>5</td>
</tr>
<tr>
<td>(Beyene et al., 2019)</td>
<td>Cro-Sect</td>
<td>Oro</td>
<td>Nasal and hand swabs</td>
<td>300</td>
<td>86</td>
<td>6</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>(Abosse et al., 2021)</td>
<td>Cro-Sect</td>
<td>Am</td>
<td>wound secretion/pus swab</td>
<td>165</td>
<td>24</td>
<td>10</td>
<td>42</td>
<td>6</td>
</tr>
</tbody>
</table>

Continues from Table 1

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**Table 2**

Summary of 81 Studies reporting the prevalence of MRSA in Food Animals, 2010–2021

<table>
<thead>
<tr>
<th>Studies</th>
<th>Study design</th>
<th>Regions</th>
<th>Cultured specimens</th>
<th>Sample size</th>
<th>S. aureus</th>
<th>MRSA Prevalence (%)</th>
<th>Per S. aureus</th>
<th>Per Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Tesfaye et al., 2021)</td>
<td>Cro-Sect</td>
<td>Oro</td>
<td>milk</td>
<td>121</td>
<td>37</td>
<td>12</td>
<td>0.32</td>
<td>0.099</td>
</tr>
<tr>
<td>(Daka et al., 2012)</td>
<td>Cro-Sect</td>
<td>Sid</td>
<td>milk</td>
<td>160</td>
<td>78</td>
<td>47</td>
<td>0.60</td>
<td>0.29</td>
</tr>
<tr>
<td>(Kalayu et al., 2020)</td>
<td>Cro-Sect</td>
<td>Tig</td>
<td>Milk</td>
<td>385</td>
<td>48</td>
<td>1</td>
<td>0.02</td>
<td>0.003</td>
</tr>
<tr>
<td>(Girmay et al., 2020)</td>
<td>Cro-Sect</td>
<td>Tig</td>
<td>Milk</td>
<td>64</td>
<td>21</td>
<td>7</td>
<td>0.33</td>
<td>0.109</td>
</tr>
<tr>
<td>(Dabele et al., 2021)</td>
<td>Cro-Sect</td>
<td>Oro</td>
<td>Milk samples</td>
<td>1528</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>(Tibebu et al., 2021)</td>
<td>Cro-Sect</td>
<td>Oro</td>
<td>Milk and Udder swab</td>
<td>181</td>
<td>40</td>
<td>2</td>
<td>0.05</td>
<td>0.01</td>
</tr>
<tr>
<td>(Grima et al., 2021)</td>
<td>Cro-Sect</td>
<td>Oro</td>
<td>Milk</td>
<td>116</td>
<td>18</td>
<td>1</td>
<td>0.06</td>
<td>0.01</td>
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</table>

Oro = Oromia, Tig = Tigray, Sid = Sidama, Cro-Sect = cross Sectional,
3.2. Prevalence of MRSA in *S. aureus* Isolates

The total of 26930 samples were collected by the researches of which, 20943 (77.78%) were from human, 2555 (9.5%) from food animals, 2010 (7.5%) from environment and 1422 (5.3%) from foods and related materials. All the articles included in this review have identified MRSA based on the resistibility of the *S. aureus* to meticillin or other alternative antibiotic discs by using disc diffusion method. Accordingly, 59.76%, 25.61%, 13.41% and 1.22% of the articles have used Cefoxitin, Oxacillin, Methicillin and Cloxacillin respectively. Of 4219 (15.65%) *S. aureus* positive samples, 1695(40.2%) were found MRSA strains. Of the total MRSA isolates, 1254 (74%) were from human samples, 68 (4%) were from food animals, 192(11.3% ) were from environmental and 180 (10.6%)were from food samples.

The overall pooled proportion of MRSA in *S. aureus* was found to be 40% (95% CI: 32–48%) (Fig. 3). However, its proportion was highly diversified. The between-study heterogeneity was $I^2 = 0.1085$ (95% CI: 0.07–0.15), $I^2 = 23.60$ (95% CI:16.54–31.34), $I^2 = 95.76%$ (95%CI:93.95–96.81%), and $Q = 1887.8927$, $p < 0.0001$ all of which suggests significant heterogeneity in the effect sizes of the study. As it is observed visually from the forest plot, the proportion of MRSA in the articles were highly diversed that they are deviated from the center, which is the estimate of the pooled proportion.

The sources of the heterogeneity were determined by assessment of outliers and/or moderators (factors). The outliers were tested to estimate the potential impact of the outliers on the overall pooled proportion . The first screening test for outliers was made by using rstudent function to assess the presence of studentized residual. Accordingly, two articles were found having the z values above 2. However, since the number of studies in the current review was large enough, our cutting point was expected to be at 3. Hence there was no outlier, which potentially affects the summary effect size, and the heterogeneity observed in the above assessment might be due to moderators.

3.3. Subgroup Analysis

3.3.1. Sampled Materials

The subgroup analysis was conducted to determine the factors associated with the prevalence of MRSA in the isolates of *S. aureus*. The comparison was made based on the types of sampled materials as human, food animal, environmental and food related. The human samples were collected from either patients or apparently normal individuals. The articles studied food animals have collected samples from food animals and their products for the purpose of animal health assessments. The samples collected from the environment include, inanimate surfaces swabs, water and air in health settings and other public services to investigate the distribution of MRSA in the environment.

The subgroup analysis based on the sampled materials was displayed on forest plot (Fig. 3). In the subgroup analysis based on sampled materials, the pooled prevalence of MRSA was 0.38 (95% CI: 0.31–0.46) in human isolates, 0.15(95%CI:0.01–0.38) in food animals isolates, 0.54 (95%CI: 0.34–0.73) in environmental samples, and 0.25 (95% CI: 0.10–0.39) in food samples.
environmental isolates and 0.77 (95% CI: 0.29 1.00) in food isolates Fig. (3). Moreover, the result of the $\tau^2$ and $Q$ tests were $\tau^2 = 0.0847$ & $Q = 1167.065$ in human, $\tau^2 = 0.1095$ & $Q = 106.3283$ in animals, $\tau^2 = 0.0890$ & $Q = 128.3886$ in environmental and $\tau^2 = 0.2379$ & $Q = 123.1971$ in food isolates. The heterogeneity level of the proportion in human, animals, environmental and food isolates were 95%, 94%, 93% and 98% respectively. In all of the categories of the types of sampled materials at 95% confidence the $p$-values were less than 0.05. Therefore, the types of the sampled materials were found associated with the prevalence of MRSA in *S. aureus* isolates. The result of the subgroup analysis revealed that significantly high rate of the strain was identified in *Staphylococcus aureus* isolates from food followed by environmental samples than from human and food animals ($p < 0.05$).

### 3.3.2. Human Health Status

The human related articles were in turn further sub-grouped according to the health status of the individual from which the samples were collected and the subgroup analysis was conducted. As the result the pooled prevalence of MRSA strain in the *S. aureus* identified from samples of apparently health individuals was 0.15 (0.01–0.38) whereas it was 0.38 (0.31–0.46) in *S. aureus* isolated from patient samples. In the overall subgroup analysis result, there was significant difference in the prevalence of MRSA between the two groups that *S. aureus* in isolated from the patients were more resistant to methicillin than those isolated from the health individuals. ($p > 0.05$). However, the proportion of the strain was highly heterogeneous between the articles that the $\tau^2$ was 0.0859 with $I^2 = 95\%$ in patients and 0.0597 with $I^2 = 93\%$.

### 3.4. Publication Bias

As determined from funnel plot (Fig. 4) most of the publications were placed at the top of the plot. Only one study was found at the right bottom of the funnel and two were at the middle. As the result there was no evidence to decide the presence of publication bias in the current review and the variation in effect sizes might be due to sampling error.

### 3.5. Antibiotic Resistance Patterns of MRSA

Furthermore, of the selected articles, twenty two studies had extractable data on the antibiotic resistance profile of MRSA isolates. In this review, the pooled proportion of MRSA to 32 antibiotics has been determined. Accordingly, the pooled resistance rates of MRSA for each tested antibiotics was presented in Table 4. The result indicated that more than 90% pooled resistance rates were observed to penicillin, Neomycin, cefuroxime, Pipracilin and Tobramycin. In addition, MRSA was found highly resistant to amoxacilin-clavulanicacid (80%), Bacitracin(84%) and Erythromycin (88%). In contrast, relatively less pooled resistance rate was observed to clindamycin (21%), chloramphenicol (22%), Amikacin (27%), vancomycin (20%), Knamycin (25%) and Ceftriaxone (30).
4. Discussion

MRSA, which was previously considered as health care associated pathogen is seen highly distributed in the surroundings. Of the total 26,930 samples collected 4219 (15.7%) were S. aureus positive. According to the publications when these S. aureus isolates were tested for Methicillin resistance, 1695 (40%) were found to be MRSA. The pooled prevalence of MRSA was 6.45% in the total samples and 41% among the S. aureus isolates. The review also determined
that the prevalence of the strain in samples collected from human was 6.5% per total sample size and 38% in S.aureus isolates. The result was less than the report of Eshetie et al.(Eshetie et al., 2016) and Sarrafzadeh et al.(Sarrafzadeh et al., 2021) who reported the pooled prevalence of MRSA in total sample size collected from human to be 32.5% in Ethiopia and 42% in Iran respectively. Our result is also less than the analysis of Deyno et al.(Deyno, Fekadu, et al., 2017) which reported the pooled prevalence of MRSA among S.aureus in Ethiopia as 47%. However, it is coincided with the report of Khanal et al. (Khanal et al., 2021) who reported the pooled prevalence of MRSA among S.aureus as (38.2%). According to the assessment of WHO (Morrison & Zembower, 2020), the resistance rate of S.aureus to methicillin exceeds 50% in the community and hospitals in WHO regions and ranged between. The document of WHO also indicated that the prevalence of MRSA in Ethiopia was reported as 31.6%. A meta-analysis with aim of determining the prevalence of MRSA among the S. aureus in Africa reported that the overall pooled prevalence of the strain in Ethiopia was estimated to be 55% (Falagas et al., 2013).

The review found that the health status of the individual was found as factor associate with the prevalence of MRSA that the strain is significantly prevalent in the patients than in apparently health individuals. The pooled prevalence of MRSA in the apparently normal person was estimated to be 15% whereas; it was 38% in isolates from patients. With similar pace, Hassoun et al. (Hassoun et al., 2017) determined that the pooled prevalence of MRSA in S.aureus isolated from patients (1.8%),was higher than that of apparently health individuals(0.76%).

In the current review 15% (95%CI:1–38%) of S. aureus isolates from food animals were MRSA. MRSA in food animals isolates was less prevalent than in environmental samples and human. In agreement with the findings of Samutela et al. (Samutela et al., 2021) which reported MRSA pooled prevalence among the S.aureus isolates from African pigs as ranged from 10 to 100%, the current finding lied in the range. However, it is higher than the previous report by Lozano et al. (Lozano et al., 2016) who reported the prevalence of animal associated MRSA among S. aureus in different African countries including Ethiopia as ranged between 0 and 3%. It is expected that the Livestock Associated Methicillin-resistant S. aureus (LA-MRSA) is highly associated with usage of antibiotics in animal feed as growth promoter and as prophylaxis. The clonal complex 398 (LA-MRSA CC 398) has been considered to be zoonotically important because of its capacity to colonize a wide range of hosts and can jump between hosts. These species may act as carriers of MRSA originating from humans (so called “humanosis”). Moreover, bovine and human MRSA strains are indistinguishable by phenotyping and genotyping methods providing evidence for MRSA transmission between human and cattle(Hata et al., 2010). However, in most of the cases the LA-MRSA remained non pathogenic in human and even when occur they cause less sever infections than HA- and CA-MRSA (Crespo-Piazzuelo & Lawlor, 2021).

Apart from its ability to resist antibiotics, the concern of S.aureus to be burden in public, and animal health arise from its adaptation to diversity of environmental conditions (Pournajaf et al., 2014). The environmental isolates of S.aureus were found highly resistant to Methicillin than human and food animals isolates that about 54% (95%CI: 34–73%) of the isolates were MRSA. The isolates were recovered from samples collected from different materials in and around health settings including floor, stethoscope, surface of drug ruminants, air and west waters from hospitals, and other public services such as buses. This might be from the reason that major of the samples were collected from health care settings which might have exposed to the drug.

Staphylococcus aureus has long been mentioned as food-born pathogen as enterotoxin producer and is one of the public health problematics worldwide. The extraordinarily use of antibiotics in food animals might result in the spread of the resistant microorganisms in foods(Abebe et al., 2020). The spread of MRSA strains in food, therefore, adds other difficulty in control of the diseases in food industry particularly from the view point of enterotoxigenicity nature of the bacterium. In the current review, the researches collected samples from raw milk and processed milk, meat and cockroach contacting with the food materials. MRSA isolates from food samples (77% (95% CI: 29–100%)) were the most prevalent of all other sample categories. The presence of S. aureus in food materials for human consumption is indicative for the spoilage of the food and the suspicious of food intoxication.

More over 22 of the studies have determined the multidrug resistance ability of MRSA to different antimicrobial agents. Accordingly, the isolates were found highly resistant (more than 80% pooled resistance proportion) to cefuroxime (100%), Tobramycin (100%), Neomycin (99%) and Penicillin (92%), Pipracillin (91%), Erythromycin (88%), Bacitracin(84%) and Amoxicillin-clavulanicacid (80%). According to the review, the drug of relatively better effective against MRSA were Clindamycin, chloramphenicol, Amikacin, vancomycin, Knamycin and Ceftriaxone with resistance rates of 21%, 22%, 27%, 20%, 25% and 30% respectively.

Similarly, the previous systematic reviews conducted by Eshetie et al.(Eshetie et al., 2016) and Gebremariam et al. (Gebremariam & Zelelow, 2014) have also documented that MRSA strains were found to be too highly resistant to most of the above mentioned antibiotics. It is obvious that MRSA strains are able to express beta-lactam hydrolyzing enzymes so called beta lactamases or capable of modifying penicillin binding proteins (Tenover, 2006) so that MRSA strains are capable of inactivating the beta-lactam agents such as penicillin, ampicillin, cephaplosporins, and carbapenems. Even more, MRSA has a tendency to resist non-beta-lactam antibiotics due largely to co-existence of other resistance gene along with mecA or mecC gen. Most importantly, vancomycin is considerably the most effective and considered as the last resort treatment for resistant infections of MRSA. The emergence of vancomycin resistant MRSA has, therefore, disadvantaged the usefulness of this drug (Enright et al., 2002). In this meta-analysis 14.31% (95% CI:4.87–35.29) of MRSA was found vancomycin resistant indicating huge blow, especially for the future.

5. Conclusion

The studies concerning MRSA has been increasing in Ethiopia specially since a decade. However, majority of the studies are giving more attention to public pathogens. The distribution of the pathogen in the environments apart from health settings have remain mysterious yet. In addition, MRSA in the livestock and pets have not been dug well in the country. The studies so far conducted covered few part of the country. The status of the pathogen in the remote areas far from the capital Addid Ababa seemed to remain unstudied. Despite that all the MRSA studying articles in the country might not be obtained, the current review showed us that MRSA is spreading in the country. The prevalence rate of MRSA was highest in S.aureus isolates from food than other ones. Moreover, the pathogen was prevalent in patients than in health individuals.
The reviewer, therefore, provide advise that care should be given to food preparation and handling in the country. Awareness on the antibiotic utilization should be given to all level of the community. Furthermore, the environments in the health settings need to be clean and disinfected regularly. Lastly, conventional and molecular based identification of MRSA is very important to identify the types of MRSA spreading in the area.

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**References**


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**Figures**
Figure 1

Flow chart shows selected articles for meta-analysis
Figure 2

The Number of the Articles according to Study Area and Sampled Materials

OrAmAd=Oromia, Amhara, and Addis Ababa
Figure 3

Forest Plot of the total pooled prevalence and Subgroup Analysis Based on Sampled Materials
Figure 4

Funnel Plot of the Publication Bias of the Meta Analysis