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Review Article

Microbiology for Health Care

An Early Year History of Emergence of Multidrug-Resistant *Staphylococcus aureus* in West Bengal: A Review

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Abstract: *Staphylococcus aureus* has been recognized as a causative agent of human diseases for more than 100 years. *Staphylococcus aureus* can cause numerous fatal diseases including sepsis, soft tissue injury, urinary tract infection. Emergence of multidrug resistance in *Staphylococcus aureus* is a very common problem worldwide. Multidrug resistant (MDR) bacterium can be identified if the strain is non-susceptible against at least one antibiotic agent in three or more antimicrobial categories. Multidrug resistant *Staphylococcus aureus* are becoming resistant against various antibiotics like azithromycin, clarithromycin, clindamycin, gentamicin, amikacin, imipenem and other β-lactam antibiotics. Resistance against methicillin and vancomycin can be said as methicillin resistant *Staphylococcus aureus* (MRSA) and vancomycin resistant *Staphylococcus aureus* (VRSA) respectively. However, 11% to 56% of the available *Staphylococcus aureus* are methicillin resistant in West Bengal. Whereas, the emergence of VRSA was found to be equally high in this geographical region. Vancomycin resistant *Staphylococcus aureus* infections is too hard to treat, as vancomycin is said to be the last resort of antibiotics to treat methicillin resistant Staphylococcus aureus. These emergence of resistance against several antibiotics may include many ways like inhibition of drug entry into the cell, inactivation of β-lactamase enzyme, etc. several genes are also responsible for the drug resistance like mecA, vanH, vanA and vanX. The present review article deals with the research done on the antibiogram of *Staphylococcus aureus* within the last decade in West Bengal. It also puts light on the various methods by which the *Staphylococcus aureus* might become resistant against antibiotics and also tries to deals with the genetics involved in it.

Keywords: *Staphylococcus, MRSA, VRSA, Methicillin, Vancomycin, Multidrug.*

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1. INTRODUCTION

Staphylococcus aureus has been recognized as a cause of human diseases for more than 100 years[1] and is a normal flora of human beings as well as of animals[2]. It has an opportunistic behaviour, and can be found on skin, in nose, throat, mouth, blood, and intestinal tract causing some life-threatening diseases such as sepsis, soft-tissue injury, UTI, endocarditis, respiratory infections, intestinal tract infections, bloodstream infections, Surgical site infections (SSI), Staphylococcal scalded skin syndrome (SSSS), etc[2-6]. Apart from the entire above, *S. aureus* can also cause toxic shock syndrome which belongs to a class of toxin-mediated disease that promotes multisystem disorder in human beings due to the Staphylococcal toxic shock syndrome toxin (TSST-1)[7]. Staphylococcal enterotoxin (SE) can be of six different groups as per serological classification established. The groups are: Staphylococcal Enterotoxin A, Staphylococcal Enterotoxin B, Staphylococcal Enterotoxin C, Staphylococcal Enterotoxin D, Staphylococcal Enterotoxin E and Staphylococcal Enterotoxin H having molecular weight falling between 26,000 to 29,600 Dalton [8,9]. *S. aureus* frequently causes surgical wound infections with a high prevalence rate ranging from 4.6% to 54.4% worldwide [2,10,11]. To control *S. aureus* infection, different kinds of antibiotics are being used by medical practitioners. *S. aureus* was one of the common pathogens causing a nosocomial infection that was eradicated by just penicillin [12,13,14]. But recently, various antibiotics are failing to treat *S. aureus* generated infection in human beings. The journey started from the discovery of penicillin in 1929[15]. Before 1944, Penicillin was treated as a potent agent to treat *S. aureus* infection as in the same year first penicillin-resistant *S. aureus* was isolated and identified[16]. The present scenario for penicillin is really worse, more than 90% *S. aureus* strains are resistant to penicillin. Not only penicillin, but S. aureus has also developed resistance against erythromycin, roxithromycin, cotrimoxazole, ciprofloxacin, chloramphenicol, streptomycin, cefotaxime, kanamycin, oxacillin, norfloxacin, amoxiclav, fucidin, methicillin, vancomycin and many more [17,2,5]. Though the prevalence of resistance against vancomycin, linezolid is very low but will rise in a very short period of time, if any step is not taken by the government or any other authority. Now-a-days, researchers are much interested in methicillin and vancomycin resistant *Staphylococcus aureus* strains i.e., MRSA (methicillin resistant *Staphylococcus aureus*) & VRSA (vancomycin resistant *Staphylococcus aureus*). Researchers found many ways like horizontal transfer of genes from outside sources, chromosomal mutations and also antibiotic selections[18], which allow *Staphylococcus aureus* isolates to grow resistance against methicillin and vancomycin. It is believed that the resistance property can be transferred from one bacterium to another with the transfer of *SCCmec* gene and *PVL* gene for methicillin[19] and for vancomycin it is *vanH, vanA, & vanX* gene [20]. This *van* gene is a part of transposon *Tn1546* found in VRE (vancomycin resistant *Enterococcus*)[21,22]. Definition for multidrug-resistant bacteria varies by country[23] as both the prevalence of specific bacterial strain/species as well as the use of antibacterial agents vary accordingly. However, the globally accepted definition of MDR (Multidrug Resistant) bacteria is, if any strain or species acquires non susceptibility towards at least one of the few most effective antimicrobial agents/antibiotic groups like penicillin, amynoglycoside, etc. In the same way, XDR (Extensive Drug resistant) isolates can be defined as their nonsusceptibility towards at least one of the few specific/common antimicrobial agents, so to say that the bacterial isolates remain susceptible to only one or two of the rare and PDR (Pan drug Resistant) as non-susceptibility to all agents in all available antimicrobial categories[23,24]. Specific strains like MRSA or VRSA are not only resistant to methicillin or vancomycin respectively, but also they show resistance against other potent antibiotics. Hence, MRSA, VRSA are critical MDR isolates present in our environment. In India, prevalence of MRSA has been increased from 29% to 47% between a tenure of 6-7 years (2008-2014). Whereas, the nations who implemented some preventive measures against AMR (antimicrobial resistance) recorded a decrease in prevalence of MRSA[25]. More than 50000 new-born deaths annually in India due to pathogens resistant to first line antibiotics[26]. According to a report by the Centre for Disease Dynamics, Economics & Policy, about 2 million deaths can be projected to occur in India by 2050 due to the increase in AMR[27]. Death rate may be 10 million per year globally by the year 2050 and will cost 100 trillion dollars, if proper actions are not taken to deal with the AMR[28].

1.1. RELEVANCE OF THE STUDY

Staphylococcus aureus flora and its infection in humans are much common all over the world. But when we see the occurrence rate in West Bengal, it is a little bit disappointing that very few research articles can be seen about the prevalence and epidemiology of *S. aureus* infection. After searching for data regarding *Staphylococcus aureus* drug resistance in west Bengal online, almost 250 search results, we could find 65 related articles and 40 were selected for the study, as those articles were enriched with the information on *Staphylococcus aureus*, MDR, MRSA, VRSA, genetic epidemiology and prevalence in West Bengal. After searching with the above said keywords in esteemed journals like Springer, Nature, BMC & Elsevier, 94 results were observed in the recent years (after 2010) and 12 articles were selected for the study, as those articles were relevant to the aim of the present study.
We aim to figure out the following points specified for *Staphylococcus aureus* in West Bengal:

- The current status of the emergence of MDR.
- Genetic characteristics of the MDR *Staphylococcus aureus* isolated and studied.
- Prevalence of different modes of acquiring infections.

The present study will be a little contribution as a review with reference to the active and fruitful works done on drug resistance of *Staphylococcus aureus* in West Bengal.

1.1.1. HOW DO OUR BODY REACT TO THE Staphylococcus aureus

Our body has professional phagocytes such as neutrophils, macrophages and dendritic cells to engulf the microorganisms[29]. Upon internalization by macrophages it is assumed that *S. aureus* confined within the phagosome following its maturation and fusion with endosomes and lysosomes, which creates an incompatible environment for invading microorganism, boosting acidification, augmentation of ROS, and other charged antimicrobial peptides[30]. Which further reduces the chances of severe infection inside the body.

1.2. HOW BACTERIA DEVELOP RESISTANCE AGAINST ANTIBIOTICS?

There is evidence to explain the development of antibiotic resistance by bacteria by various means like enzymatic degradation of functional groups of antibiotic, cell wall thickening/modification, etc. There are three basic mechanisms which allow a bacterium to grow resistance against any antibiotic agent – [1] Enzymatic degradation of antibacterial drugs, [2] Alteration of bacterial proteins that are antimicrobial targets, [3] Changes in membrane permeability to antibiotic agents[14]. Penicillin and other β-lactam antibiotics inhibit the bacterial growth by inhibiting the cell wall synthesis. PBPs (Penicillin binding proteins) are the bacterial proteins like transpeptidases, which is the final key element for cell wall synthesis by crosslinking peptidoglycan chains by the process transpeptidation [31,32]. And these PBPs are the primary target for β-lactam antibiotics [33,34]. Upon binding of β-lactam with PBPs blocks the transpeptidation leading to failure of cell wall synthesis [31,33]. Cell wall lysis, disruption of cell shape and inhibition of cell division can be the results upon binding of β lactam to PBPs 1, 2 and 3 respectively [35,36]. Other than binding with different PBPs, β lactam can bind with murein hydrolases which is an autolytic enzyme that causes a nick in the cell wall to make a space for new peptidoglycan synthesis so that the cell wall will be enlarged[37]. β lactam induces unsuppressed activity of murein hydrolases resulting lysis of cell wall[33]. Now coming to the resistance against penicillin and β lactam antibiotics, there are three classes of enzymes produced by different gram-positive and gram-negative bacteria [38,39], that can hydrolyse β lactam antibiotics – [1] β lactamases, [2] acylases and [3] esterases[40]. These enzymes are able to degrade the β lactam nucleus of the β lactam antibiotics, facilitating the bacteria to grow resistance against the group of antibacterial. The β lactamases can hydrolyse the β lactam bond to acidic derivatives, which do not have any antibacterial property [41-44]. Alteration of the β lactam antibiotics lead to the production of some newer antibacterial agents like methicillin, oxacillin, etc. Somehow bacteria manage to develop resistance against these newer antibiotics too with the production of an altered PBP2 enzyme i.e., PBP2a or PBP2' [45]. Even after the administration of methicillin (β lactam antibiotic), PBP2a, bacteria exhibit transpeptidation and cell wall synthesis and thus they remain resistant to methicillin[32,46,47]. The expression of PBP2a protein is regulated by the gene *mecA* which is located on the mobile genetic element, *SCCmec* (SCC: Staphylococcal cassette chromosome) elements [46,47]. Then after emergence of MRSA (methicillin-resistant *Staphylococcus aureus*) lead to finding of some other antibiotics. Vancomycin came into action and is a unique glycopeptide, a fermentation product of streptomycetes[48], structurally unrelated to any of the earlier antibiotics [49,50]. Vancomycin inhibits the cell wall synthesis by preventing the polymerization of the phospho disaccharide-pentapeptide lipid complex by binding to the free carboxyl end of the peptides containing D-alanyl-D-alanine during the second stage of its synthesis [51,52,53]. It is postulated that vancomycin causes a steric hindrance for peptidoglycan synthesis and so cell wall synthesis disrupts[54]. It has also been seen that vancomycin also alters the permeability of the cell membrane and inhibits the nucleic acid synthesis[55]. Bacteria can grow resistance against vancomycin due to the presence of *van* gene operon encoding two enzymes, one of which can modify vancomycin-binding target by replacing C-terminal D-Ala by D-Lactate or D-Serine and second enzyme can remove the vancomycin-binding target [56,57]. Thus, it may all lead to the emergence of vancomycin resistant bacteria. Bacteria are capable of preventing drug access to targets by various means – [1] Local inhibition of drug access, [2] Drug specific efflux pumps and [3] Non-specific inhibition of drug access. Which includes the apparent change in ribosomal conformation [58,59], proton motive force dependent outward pumping[60] of drug with the help of specific proteins[61], and mutation in coding sequence of porin may also reduce the permeation of drug[62]. Hence bacteria may grow resistance against the particular antibiotic agent or against the group of antibiotics.

Table 1: Mechanism of becoming AMR[14]

Mode of action of growing resistance against antimicrobial agents	
Antibiotic/Group	Mechanism of resistance
Penicillins and cephalosporins	Enzymatic inactivation of β lactamase and alteration of PBPs.
Monobactams	Enzymatic inactivation of β lactamase.
Carbapenems	Enzymatic inactivation of β lactamase.
Vancomycin	Glycopeptide access inhibition.
Trimethoprim	Production of dihydrofolate reductase.
Sulfonamides	Increased production of *p*-aminobenzoic acid.
Aminoglycosides	Enzymatic modification by acetylation, phosphorylation.
Chloramphenicol	Decreased drug permeability.
Macrolides	Enzymatic modification by esterase.
Lincosamides	Enzymatic modification by nucleotidyl action or phosphorylation.
Tetracyclines	Active efflux preceded by chemical modification.
Quinolones	Alteration of DNA gyrase.

1.3. MDR STAPHYLOCOCCUS AUREUS IN WEST BENGAL

As we have already discussed the introduction and definition of MDR. Very less or no article could be found regarding antibiograms, which could claim that *Staphylococcus aureus* studied were not resistant for each and every antibiotic set they have used in their study. Therefore it can be said that the availability of PDR is very less. Whereas MDR and XDR isolates can be found more often. There are a lot of antibiotics, used as major life saving drugs. But the misuse of antibiotics during therapy is the major cause of generation of resistance in bacteria or drug resistant disease-causing organisms in the environment[63-65]. Study conducted by Balaram et al in 2016 revealed that, out of 20 *Staphylococcus aureus* isolated from 36 pus samples from a tertiary care hospital of West Bengal, 100% were resistant for penicillin G, ampicillin, cefotaxime, oxacillin, and amoxiclav antibiotics.

95%, 75%, 65%, 20% 15% and 10% *S. aureus* were resistant for methicillin, ciprofloxacin, erythromycin, tetracycline & vancomycin, streptomycin & norfloxacin, chloramphenicol and kanamycin, respectively. Whereas 100% isolates were sensitive to gentamicin, amikacin and imipenem[2]. They also found that 100% Staph were MDR. Published in the same year, a study conducted by Nupur et al. within 2011-2012, collected 930 urine samples form tertiary care hospitals of West Bengal and found pure cultures of *Staphylococcus aureus*, but they did not assess the antibiogram of the same[66]. But they have also found MRSA, which is already MDR. Most recently, out of 50 MRSA isolates collected by Sonia Jain et al from a hospital in Kolkata, orthopaedic department in 2019, revealed following resistant pattern: amoxyclav (84%), erythromycin (82%), ciprofloxacin (80%), levofloxacin (72%), cefuroxime (70%), clindamycin and gentamicin (62%), trimethoprim-sulfamethoxazole (40%) and amikacin (20%). The least resistance was observed for doxycycline (12%)[67]. Sumanth et al conducted a study throughout India, including Fortis hospital in West Bengal in 2015 and published later in the year 2019 showed that overall 11% mortality rate was due to MDR *Staphylococcus aureus*. They could not find any significant difference between patients with MRSA infections compared to MSSA (methicillin-sensitive *Staphylococcus aureus*)[68]. Apart from all the above antibiogram results, we found huge interest of microbiologists on MRSA and VRSA isolates and their genetic epidemiology.

1.4. PREVALENCE OF MRSA IN WEST BENGAL

Methicillin (originally called calbenin) was the first antibiotic in a class (β-lactamase-resistant penicillins) to be used to treat penicillin resistant *Staphylococcus aureus* infection in 1959. But the first MRSA was reported in England [6,69] and became a major worldwide nosocomial pathogen[67]. Multicentre MRSA surveillance data from China and India suggests that MRSA accounts for a substantial burden of diseases in the above mentioned countries [70,71,72,73]. Primarily there are two kind of MRSA strains can be found, first HA MRSA (hospital acquired/healthcare associated methicillin resistant *Staphylococcus aureus*) and the second is CA MRSA (community acquired methicillin resistant *Staphylococcus aureus*)[74]. Another kind of MRSA strain has also emerged due to increased use of antibiotics in animal feed, i.e., LA MRSA (livestock associated MRSA)[75]. At present the potential epidemiology of CA MRSA strain is replacing HA MRSA in hospitals of India [76,77]. The first CA MRSA case began to report in the mid-1990s in Australia, New Zealand, US, UK, France, Finland, Canada and Samoa [78,84] Study conducted on HCW (health care workers) of Medinipur Medical College (West Bengal) in 2014 concluded 21.47% positive nasal carrier for *S. aureus*, among which 30.7% were MRSA[79]. More or less, the same study conducted by Kulshrestha et al in 2019 revealed that 95.3% HCW were positive nasal carriers for *Staphylococcus aureus* and 11% HCW had positive MRSA colonization[80]. Another study performed in RG Kar Medical College and Hospital concludes 124 *S. aureus* colonization out of 136 breast abscess pus samples. Among which 70 (56.5%) strains were MRSA[81]. Study conducted in a dental college of Kolkata, revealed 34 positive *S. aureus* cultures from 66 pus samples. Out of which 14 (41.2%) isolates were identified as MRSA [82]. One more cross-sectional study was conducted on SSI (surgical site infections) for 3.5 years. 15.51% SSI were documented, among which 34.93% (1049) were due to *Staphylococcus aureus*. 25.45% *Staphylococcus aureus* were positive MRSA[5]. Amit et al concluded that 70% MRSA were observed in their study, they have conducted in Midnapur Medical College and Hospital[83]. Another study of RG Kar Medical College and Hospital revealed that 102 positive *S. aureus* colonization was observed among 226 pus samples. Out of 102 *Staphylococcus aureus*, 36 (35.3%) were documented as MRSA[84]. Study on CA MRSA by Prashant et al, showed 90 (22.7%) *Staphylococcus aureus* out of 395 samples studied. And 80 (20.2%) MRSA isolates as well[19].

Table 2: Occurrence of MRSA and antibiotics for which the MRSA isolates were resistant.

Sl. No.	Percentage of Occurrence of MRSA	Resistant for other antibiotics	Reference
1	30.7%	Cefotaxim, Amoxycillin, Ciprofloxacin, Azithromycin, Gentamycin and Levofloxacin.	Satpathi et al, 2015[79]
2	11%	Macrolide and Levofloxacin	Kulshrestha et al, 2019[80]
3	56.5%	Amoxyclav, Cephalexin, Clindamycin, Erythromycin, Gentamicin, Tetracycline.	Kumar et al, 2018[81]
4	41.2%	Meropenem, Tazobactam/Piperacillin, Clindamycin.	Batabyal et al, 2012[82]
5	25.45%	Clindamycin, Cefoxitin, Cotrimoxazole, Clarithromycin, Gentamicin, Levofloxacin.	Bhattacharya et al, 2016[5]
6	70%	Ampicillin, Cefoxitin, Kanamycin, Erythromycin, Streptomycin, Chloramphenicol.	Karmakar et al, 2016[83]
7	35.3%	Amoxycillin, Azithromycin, Clindamycin, Cefuroxime, Cotrimoxazole.	Bhattacharyya et al, 2018[84]
8	20.2%	Penicillin, Erythromycin, Clindamycin, Ciprofloxacin, Cotrimoxazole, Gentamicin.	Jindamwar et al, 2016[19]

Above isolated and studied MRSA samples were found to be resistant for many potent antibiotic agents such as penicillin, levofloxacin, erythromycin, gentamicin. Though, some of them showed sensitivity towards a few antibiotics like vancomycin, linezolid, cotrimoxazole, etc (as per the references provided in the table).

1.5. GENETICS FOR MRSA

The emergence of MRSA was attributed to the expression of a protein that binds penicillin with low affinity (PBP2a)[85]. This protein is encoded by the genes, *mec A* (2007bp), *mecB*, *mecC*[86] carried on a genomic island called Staphylococcal Cassette Chromosome *mec* (*SCCmec*), 52kb[87]. As per the International Working Group on classification of SCC elements (IWG-SCC), eleven (I-XI) genotypes of MRSA have been identified by Liu et al, till 2016[88,89]. Some researchers suggest that the *SCCmec* element in MRSA has been differentiated into 12 different genetic types (I-XII)[90-92]. HA

MRSA is traditionally associated with *SCCmec* type I-III, while CA MRSA is associated with type IV, V& VII[89,92]. Skin and soft-tissue infections are predominantly caused by Panton Valentine Leukocidin (PVL) producing *Staphylococcus aureus* isolates, as the leucocidal activity of these strains increases their pathogenicity and also provides survival advantage to the organisms [93,94]. PVL is one of the important cytotoxins produced by *S. aureus* and is encoded by two genes, *LukS-PV* and *LukF-PV*[95]. PVL gene can also be used for *S. aureus* identification. Literature reveals that epidemiology CA-MRSA is PVL positive, but PVL negative MRSA and PVL positive MSSA (methicillin-sensitive *Staphylococcus aureus*) can also be seen[92]. Other than *SCCmec* & *PVL*, *nuc* & *hlb* genes can also be used for *S. aureus* identification[83].

1.6. PREVALENCE OF VRSA IN WEST BENGAL

Emergence and spread of MRSA isolates lead to failure of treatment for *Staphylococcus aureus* infection in human beings, causing increased mortality and morbidity. Then vancomycin (a glycopeptide) became the only antibiotic agent to treat MRSA infection, as MRSA are not only resistant to methicillin but also for a handful number of antibacterial agents [96,97]. The very first *S. aureus emerged* in 1997, with reduced susceptibility against vancomycin [98,99] in Japan. And in 2002, first VRSA (vancomycin resistant *Staphylococcus aureus*) emerged in the US[100], whereas in India (Kolkata, West Bengal) it was first observed in 2008[20]. Various studies also suggest the incidence of VISA (vancomycin intermediate *Staphylococcus aureus*) throughout the world[101]. Though the prevalence of VISA & VRSA is very less in India[102], researchers can find some VISA and VRSA, while testing in their laboratories. Susmita et al. showed the emergence of 4 VISA isolates with MIC value between 4-6mg/L in West Bengal. The strains were found to be resistant against penicillin, cefotaxime, co-trimoxazole, cefoxitin, ciprofloxacin, oxacillin, gentamicin, netilmicin, ofloxacin, piperacillin-tazobactam[103]. In 2011, researchers from Vidyasagar University, West Bengal found 8 VRSA isolates among 30 *Staphylococcus aureus* they have studied[104] and those isolates were also resistant against erythromycin, cefotaxime, gentamicin, streptomycin, tetracycline, chloramphenicol, norfloxacin, methicillin. Another study from the same university revealed 38 VRSA isolates among 70 MRSA studied with MIC value ranging from 16-32mg/L[83] and those strains were also specifically resistant against methicillin and other antibiotic agents. Prevalence of VRSA and VISA bacteria is not only restricted to human beings of West Bengal, nowadays, researchers detected VRSA isolates in bovine and caprine milk also. Debraj et al found 7 VISA and VRSA isolates ranging MIC value from 8 to 256 mg/L in West Bengal in 2016[105]. All the isolates were also resistant to methicillin and carried the *mecA* gene.

1.7. GENETICS FOR VRSA

Though the genetic mechanism of VRSA emergence is not well known[106], researchers found a dramatic role of VRE (vancomycin resistant *Enterococcus*) for the birth of VRSA. Transposon *Tn1546* has been identified as the main precursor of the birth of vancomycin resistance in *Staphylococcus* through VRE[21,22]. The evidence was supported and elaborated by Panthee et al, and they also said that the gene conferring resistance to vancomycin and methicillin were common in VRSA isolates[107]. The marker genes for VRSA viz., *VanH*, *VanA*, *VanX* are said to be responsible for the development of resistance against vancomycin[20].

1.8 HOW TO COMBAT WITH THESE MDR BACTERIA

Basic rule to prevent the emergence of MDR bacteria may include the proper use of antibiotics, as improper use of antibacterial agents is the primary cause of emergence of AMR strains[108]. There are lot other ways may be involved to prevent the emergence of MDR. Biosynthesized nanoparticles may be a better way to combat or to overcome the situation. A review from our laboratory revealed that biogenically prepared silver nanoparticles are potent antibacterial agent against various bacteria including *Staphylococcus aureus, Escherichia coli, Bacillus sp, K. pneumoniae*, etc. more research is required in case of the antibacterial effect of biologically prepared nanoparticles on MDR bacteria[109].

2. CONCLUSION

After reviewing more than 50 articles pertaining to the antibiogram of *Staphylococcus aureus* in West Bengal, it may be concluded that the prevalence of multidrug resistant *Staphylococcus aureus* is a real threat in this geographical area. *Staphylococcus aureus* here found to be resistant against various important antibiotics, such as amoxycillin, erythromycin, gentamicin, clindamycin, chloramphenicol, levofloxacin, methicillin; among which resistance against methicillin and vancomycin are an attractive field of research, to find out a stronger way to combat the situation arising out of these MDR *Staphylococcus aureus.* The data showed that the percentage of the available MRSA isolates in this sector varies between 11% to 56%, however regarding VRSA the study showed that though the emergence of VRSA in India is comparatively less, but in West Bengal it was found in a higher range. In one study it has been shown that out of 70 MRSA, 38 isolates were found to be VRSA. In another laboratory 8 VRSA were identified out of 30 MRSA. Causes of emergence of drug resistance in *Staphylococcus aureus* may include inactivation of β-lactamase, glycopeptide access inhibition, reduced drug permeability into the bacterial cell, alteration of DNA gyrase, Cell wall thickening, etc. Moreover the gene responsible for drug resistance, according to the study, may be transferred horizontally from one bacterium to another. Biosynthesized nanoparticles may act as potent antibacterial agent to combat with these kinds of antimicrobial resistant *Staphylococcus aureus* especially silver and gold nanoparticles. The upcoming researches in different laboratory worldwide indicates that a brighter future in this sector is bound to come.

3. AUTHORS CONTRIBUTION STATEMENT

Mr. Kartik Shaw has gathered the data and articles for this review. Dr. Sahana Mazumder conceptualized and provided necessary inputs towards designing the manuscript. Both the authors have equal contribution for writing the manuscript.

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4. CONFLICT OF INTEREST

Conflict of interest declared none.

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