

# **REVIEW ARTICLE**

# EMERGENCE AND MANAGEMENT OF DISEASE BURDEN OF MRSA; A REVIEW FOR THE GLOBAL CHALLENGES

Prabhurajeshwar C.

Research Scientist-I Department of Microbiology, Gulbarga Institute of Medical Sciences (GIMS), Kalaburagi - 585105, Karnataka, India.

.....

# Manuscript Info

*Manuscript History* Received: 11 September 2018 Final Accepted: 13 October 2018 Published: November 2018

#### Abstract

..... MRSA is a major human pathogen responsible for wide spectrum of diseases, prefers to grown pH environment above 6.5. They can survive down to pH 5 for extended periods of time. However the limits of endurance can be stretched if the organisms are first adapted to moderate acid pH or any antibiotic stress. MRSA is one of the major resistant pathogen found in the much members and skin of around one third of the population. It is extremely adaptable to antibiotic pressure. MRSA is associated with a number of virulence factors. Over half a century; the medical practitioner's gas relied on the antibiotics to treat many pyogenic infections as well as other diseases. Unfortunately the misuse, overdose and overuse of antibiotics have triggered an increasing quality, variety and proliferation of multi-drug resistant (super bug). And consequently particularly virulent strain of MRSA these virulence strain gas developed resistant to all types of antibiotics including the last resort vancomycine. Now this natural ability of bacteria to develop resistant has become alarming health concern. Alternative method of treating of these antibiotic resistant staphylococcus infections are current being explored. This study helps in knowing theoretical problems associated with the resistant organism and leads to the development of new drug or any antibiotic or inhibitors which counteracts MRSA infections. It is possible to use in the human being also as a Therapeutic agents.

Keywords: MRSA, Staphylococcus aureus, Antibiotic Resistance, Methicillin, Pathogenicity, Epidemiology.

Copy Right, IJAR, 2018,. All rights reserved.

**Introduction:-**

Methicillin Resistant *Staphylococcus aureus* (MRSA) grows in large round, opaque colonies at an optimum temperature of 37 °C, though it can grown anywhere between 10°C and 46 °C. The species is a facultative anaerobe, whose growth is enhanced in the presence of  $O_2$  and  $CO_2$ . Its nutrients requirements can be satisfied by routine laboratory media and most strain are metabolically versatile that is they can digest protein and lipids and ferment a variety of sugars. This species is considered the most resistant of all non-spore forming pathogen, with well developed capacities to withstand at high salt (7.5-10%) extremes in  $p^H$  and high temperature (up to 60 °C for

# Corresponding Author:-Prabhurajeshwar.

Address:-Department of Microbiology, Gulbarga Institute of Medical Sciences, Gulbarga, Karnataka

60 minutes). It also Viable after month of air drying and result the effects of many disinfectants and antibiotics. These properties contribute to the reputation of MRSA as a troublesome hospital pathogen.

#### MRSA virulent characters:-

MRSA is associated with a number of virulence factors. The virulence factors include surface proteins that promote colonization of host tissues, invasions that promote bacterial spread in tissues (leukocidin, hyaluronipase), surface factors that inhibit phagocytic engulfment (capsule), biochemical properties that enhance their survival in phagocytes (catalase production), and membrane damaging toxins that lyse eukaryotic cell membrane (heamolysins, leukotoxin) [1].

#### Pathogenesis of MRSA

It is surprising that bacterium with such great potential for virulence as MRSA is a common, inimate human associate. The microbe is present in most environments frequented by human and readily isolated from fomites [2]. The carriage rate for normal healthy adults varies anywhere from 30% to 50% and the pathogen tends to be harbored intermittently rather than chronically. Carriage occurs mostly in the anterior nacres and to lesser extent, in the skin, nasophyrnx and intestine usually this colonization is not associated with symptoms, nor does if ordinarily lead to decrease in carriers of their contacts.

Circumstances that predispose an individual to infection include poor hygiene and nutrition, tissue injury, preexisting primary infections and immunodeficiency states. Staphylococcus infections in the new born nursery and surgical wards are the third most common nosocomial infection. The so called "Hospital strain" can readily spread in an epidemic pattern within and outside the hospital.

# Drug resistant in bacteria

Over half a century, the medical practitioner's gas relied on the antibiotics to treat many pyogenic infections as well as other diseases. Unfortunately the misuse, overdose and overuse of antibiotics have triggered an increasing quality, variety and proliferation of multi-drug resistant (super bug). And consequently particularly virulent strain of MRSA these virulence strain gas developed resistant to all types of antibiotics including the last resort vancomycin. Now this natural ability of bacteria to develop resistant has become alarming health concern. Alternative method of treating of these antibiotic resistant staphylococcus infections are current being explored.

#### **Methicillin Antibiotic**

Methicillin is a broad-spectrum antibiotic that is in the penicillin family of medications. A physician may prescribe this particular antibiotic for a variety of bacterial infections throughout the body. It is vital to take antibiotics exactly as prescribed and for the total duration of therapy to prevent relapse infections. Failing to completely cure an infection can lead the infectious bacteria to become resistant to methicillin, as in the case of MRSA. Common side effects of methicillin therapy should be reported to a physician if they become worse in severity or are persistent [3]

# Side Effects of Methicillin

# Hematologic Changes

The body contains several types of white blood cells which all have different jobs within the immune system. Some fight bacterial infections, while others fight viral or fungal infections. Decreases in normal levels of various white blood cells have been reported with methicillin therapy, but the levels return to normal once the medication is stopped.

# Hypersensitivity

Some people may experience symptoms of hypersensitivity to methicillin. These can range from mild to severe in nature. Someone undergoing methicillin therapy may experience itching, skin rash, fever, fatigue, and chills. Hypersensitivity symptoms usually occur after 10 days of use and should be reported to a health care provider right away.

# **Hepatic Changes**

While rare, some people may experience changes within the liver during or after taking methicillin. The liver filters out wastes and poisons from the bloodstream. After a person takes methicillin, the liver may become sluggish and unable to filter out these wastes efficiently, which can result in liver damage. A simple blood test can be performed

at a physician's office to monitor liver enzymes within the bloodstream. When hepatic, or liver, changes do occur, the damage can be permanent but is usually reversible.

# **Renal Changes**

Renal, or kidney, changes are also rare but do occur in some people during or after methicillin therapy. The kidneys also eliminate wastes from the bloodstream in combination with the liver, and these wastes are excreted in the urine. Methicillin is harsh on the kidneys, and the extra workload imposed by methicillin on the kidneys can cause them to cease functioning as effectively as they should. This can result in an increase of wastes and poisons within the bloodstream. Renal function can be monitored via blood or urine tests. A physician may choose to utilize both testing methods. Renal function can also be permanently affected, but in most cases these changes are reversible as well [4].

# Methicillin resistant

Over the last four decades, MRSA has spread throughout the world and became highly endemic in many geographical areas. This pathogen causes several morbidity and mortality in hospitals worldwide [5-6]. All MRSA strains isolated before 1990 were homogenously resistant to methicillin also resistant to increasing number of major classes of antibiotics, including, fluroquinolones and macrolides.

#### Methicillin resistant mechanism

Treatments of MRSA infections before the 1950s involve the administration of benzylpencillin (Penicillin G),  $\beta$ lactam antibiotic, but by the late 1950s MRSA strain resistant to benzyl penicillin were causing increasing concern. Resistant strains typically produced an enzyme, called a  $\beta$ -lactamase. Efforts were made to synthesis penicillin derivatives that were resistant to  $\beta$ -lactamase hydrolysis. This was achieved in 1959 with the synthesis of methicillin, which had the phenol group opf benzyl penicillin disubstituted with methoxy groups. The methoxy group produce steric hindrance around the amibebond reducing its affinity for MRSA strains were isolated [7]. Resistance was not due to  $\beta$ -lactamase production but due to expression of an additional penicillin binding protein (PBP2G), acquired from another species which was resistant to the action of the antibiotic [8]. The use of different types of antibiotics over the years has lead to the emergence of multi resistance MRSA strains [9].

#### Morphological studies in MRSA

The morphology of microorganisms also changes in response to variation of the environment [10]. The effect of antibiotic stress on morphological traits in experimental populations of step wise adopted Methicillin resistant *Staphylococcus aureus* were investigated by electron microscopy. However, microorganisms can adapt to different organic substances and other forms of environmental stress by several adoptive mechanism [11]. Here especially pyogenic pathogens like MRSA have been shown to be the most antibiotic resistant mechanisms [12].Thus, The major adopting responses of microorganism to externally occurring changes in the environment are modifications of the cell envelopes [13], these change in cell envelope are also connected with change in the overall morphology of the cells [14]. In their natural environment, microbial cells have to sense and to cope with different growth restricting condition, like chemical stresses and nutrient deprivation [15]. Therefore, cells develop strategies for survival and resistantce against multiple stresses. As reported in several reviews, this process triggers dramatic changes in cellular physiology and even in morphology [16]. Some bacteria, like Bacillus species, form endospores to survive nutrient-poor conditions. However, little information available about the starvation response in gram positive, Non-spore forming Bacteria such as MRSA resistant clinical isolates have been reported with morphological and physiological changes when compared to susceptible isolates [17].

# Methicillin resistance scenario in India

Methicillin resistant among *S. aureus* isolates have reached phenomenal proportion in Indian hospital, with some cities reporting that up to 70% of strain are resistant to methicillin [1]. About 40-50% of MRSA isolated from burn and trauma ward in hospital in and around Bangalore, India are resistant [18]. For the presence studies, clinical isolates have been collected from major hospitals in the city of Gulbarga, many of these MRSA strains are multi drug resistant.

# Acknowledgment:-

We thank to the Prof. Chandrakanth kelmani R, Department of Biotechnology, Gulbarga University, Kalaburagi, Karnataka for their constant support in writing this article.

# **Conflict of Interest**

The author declares no conflict of interest





Figure 2: The Mechansim of Resistan



# **References:**

- 1. Anupurbha S, Sen G, Nath BM, Sharma AK, Gulati and Mohapatra M. 2003. Prevalence of MRSA in a tertiary referral hospital in Eastern Uttar Pradesh. *Indian. J. Med. Microbiology* 21: 49-51.
- 2. Ananthanarayan R and Jayaram CK. 1996. Text book of microbiology. 5<sup>th</sup> edition. Orient Longman.
- 3. Boyce JM, CXausly WA. 1982. Increasing occurrence of MRSA in United States, J.inf. Control 3: 377-383.
- 4. Chambers HF. 1997. Methicillin resistant *S.aureus*; Molecular and Biochemical basis and clinical implications. Clin. Microbial Rev.10: 781-791
- 5. Boyce TM. 1990. Increasing prevalence of MRSA in the united state. *Infected control of hosp. Epidemoit* 11: 639-642.
- 6. Voss C, Eyol E, Frank M, Von der Lieth CW, Berger MR. 2006. FASEB J. 20: 1194-11.
- 7. Chamber HF. 2001. The changing epidemiology of S.aureus. Emergence Infections. Dis.7: 178-182.
- 8. Chambers HF.1997. Methicillin resistant *S.aureus;* Molecular and Biochemical basis and clinical implications. Clin. Microbial Rev. 10: 781-791.

- 9. Livemore DM. 2000. Antibiotic resistant in staphylococci. Intl. j. Antimicrob. Agent 16: S3-S4.
- 10. Ritz M, Tholozan JL, Fedirighi M, Pilet MF. 2001. Morphological; and physiological characterization of *Listeria monocytogenes* subjected to high hydrostatic pressure. *Appl. Environ. Microbiol.* 67: 2240-2247.
- 11. Lewis K. 1994. Multidrug resistant pumps in bacteria: Variations on a theme Trends Biochem. Sci. 19:119-123.
- 12. Conrad RS, Howard MJ, Garrison RC, winters S, Henderson D. 1998. The effect of daptomycin on chemical composition and morphology of *Staphylococcus aureus*. *Proc. Okla. Acad Sci*.78: 15-22.
- 13. Heipieper HJ, Weber FJ, Sikkim J. Keweloah H, de Bont JA. 1994. Mechanism behind resistance of whole cells to toxic organic solvents. *Trends Biotechnol*. 12: 409-415.
- Paul F, Cleark, Ruehl WH. 1919. Morphological changes during the growth of bacteria, medical school, university of wiscon, maldiso. An electron microscopic study of glycopeptides antibiotic-resistant strain of staphylococcus epidermis. J. Med. Micro. 39: 204-210.
- 15. Aldsworth TG, Sharman RL, Dodd CE. 1999. Bacterial suicide through stress. Cell Mol. Life. Sci. 56: 378-383.
- Desousa MA, Sanches IS, Ferro ML, Vaz MJ, Saraiva Z, Tendeiro T, Serra J and de Lancaster H. 1998. Intercontinental spread of multidrug resistant Methicillin resistant *Staphylococcus aureus* clone. *J. clin. Microbial.* 36: 2590-2596.
- 17. Lanzarini F. 1990. Effect of teicoplanin and vancomycin on *staphylococcus aureus*. *Ultra structure*. *Microbiol*. 13: 231-237.
- 18. Krishnan PU, Miles M and Shetty N. 2002. Detection of Methicillin and mypirocin resistant in *Staphylococcus aureus* isolates using conventional and molecular method a descriptive study from a burn unit with a high prevalence of MRSA, *J. Clin. Pathol.* 55: 745-748.
- 19. Sulakvelidze A. 2001. Bacteriophage therapy, Minireview. Antimicrob. Agents Chemother. 45: 649-659
- 20. Kutter EB. 2001. Bacteriophage as natural, self replicating and self limiting antibiotics. Astrazeneca research foundation India.
- 21. Escribano I. 2006. Relation between induction of the mar operon and cyclohexane tolerance and reduction in fluoroquinolone susceptibility in *Salmonella spp. J. Infect*. Chemother. 12: 177-180