Acinetobacter Genus: Pathogenic and Non Pathogenic species

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Abstract: -

The genus *Acinetobacter* are ubiquitous, gram-negative bacteria belonging to the wider class of Gammaproteobacteria. *Acinetobacter* species are oxidase negative, catalase-positive, non-fermentative, non-motile and strictly aerobic in nature. Few of the species under *Acinetobacter* contain twitching motility, also called as crawling bacterial motility. The genus *Acinetobacter* comprises38 species which include both pathogenic and non-pathogenic species. It contains clinically significant pathogenic species under the ABC complex (*Acinetobacter baumannii* and *Acinetobacter calcoaceticus* complex). The most important pathogenic species under this genus are *A. baumannii, A. calcoaceticus and A. nosocomialis* etc. The pathogenic species mainly infect immunocompromised patients and are rarely found in healthy individuals. They cause nosocomial infections, meningitis, pneumonia, bacteraemia and urinary tract infection. The mortality rate of the *Acinetobacter* infection found to be 26-55.7% annually. There are few non-pathogenic species present in the environment which have beneficial roles such as detoxification, removal of oil spillage, soil improvement etc. They are also part of the normal flora of skin in the human body. The current review paper provides information about the pathogenicity and various virulence factors of the bacterium, antimicrobial property, treatment used to treat *Acinetobacter* and other non-pathogenic species.

Keywords: - Introduction, pathogenic species, other pathogenic species, the impact caused due to *Acinetobacter*, antimicrobial resistance, treatment, nonpathogenic species.

1. Introduction: -

The history of the genus *Acinetobacter*dates back to the early 20th century, in 1911, when Beijerinckii, a Dutch microbiologist isolated an organism from soil enriched with calcium acetate-containing minimal medium and named it *Micrococcus calcoaceticus*. (Beijerinck MW, 1911). Brisou and Prevot in 1954 proposed the genus name *Acinetobacter*.This was originated from the Greek word akinetos which means non-motile and was given to separate non-motile from motile organisms (Brisou and Pervot, 1954). The name *Acinetobacter* was proposedand then further sub-classification into different species based on phenotypic characteristics was not possible (Baumann *et al*., 1986). In 1971 the subcommittee on Taxonomy of Moraxella and Allied Bacteria made *Acinetobacter* an official bacteria (Lessel, 1971). Later in 1974, the genus *Acinetobacter* was listed in the edition of Bergey's Manual of Systematic Bacteriology (Lautrop, 1971).

Acinetobacter species are ubiquitous, spread in nature and are commonly found in soil and water. They have made the environment as their main reservoir. They can survive in several ecological niches such as moist and dry surfaces. In general, members of the genus *Acinetobacter* are found in wet environments, including moist soil/mud, wetlands, seawater, wastewater, ponds, rivers, sewage, activated sludge, dumpsite etc. They were also found in hydrogen contaminated areas. These are considered asfree-living saprophytes (Ahmad *et al.,* 2016). *Acinetobacter* is also isolated from foodand vegetables purchased from the marketslocated in the United Kingdom. The isolated species were found to be *A. pittii, A. lwoffii and A. calcoaceticus* etc. Different species of *Acinetobacter*were isolated from milk, fish, meat and cheese samples (Berlau*et al*., 1999). Thesespecies were are also isolated from animalssuch as duck, livestock, donkey, horses and arthropods. The *A. johnsonii, A. lwoffii, A. junii*. *Acinetobacter* genome 15UT were isolated from livestock's, horses and pets in Lebanon (Rafei*et al.,* 2015). *Acinetobacter* species are also found in normal human flora. They undergo colonization in the skin, mucous membrane, toe webs, body sites and the outer surface of the nose. The most infecting *Acinetobacter* species are *A. baumannii, A. nosocomialis, A. calcoaceticus, A. pittii and A. junii* etc. They were also found in healthy volunteers (Ahmad *et al.*,2016; Seifert *et al.*,1997). The organism found in the hospitals were surviving in clothing ventilators, patient care items, humidifier, respiratory care equipment, medical equipment, floor,mops, doorknobs, windows, beds and walls etc. They cause infections through nosocomial transmission. These species were also isolated from the faecal sample collected from the patient who was tested positive for *Acinetobacter* infections. The organism was found to be *A. guillouiae* and *A. Junii*etc (Ahmad *et al.,* 2016; Dijkshoorn *et al.,* 2005). Many microorganisms can be transmitted through air, but *Acinetobacter* bacteria are not airborne and can spread only through direct contact with the surface of a contaminated object or through the skin of those people who are infected with the bacteria.*Acinetobacter* species were also found to be surviving in the dry area for a long period. When these microorganisms are subjected to various stress parameters in the environment such as temperature, air humidity, desiccation conditions etc., they may affect the growth and other parameters of the organism.But organism may tolerate these harsh conditions due to the different mechanisms present in them such as efflux pump (Wendt *et al.,* 1997). *Acinetobacter* may be identified to the genus level as gram-negative, catalase-positive, oxidase-negative, motile, non-fermenting, non-fastidious, coccobacilli. They are short, plump, gram-negative rods. *Acinetobacter*is usually rod shape bacteria during the rapid growth later they change into coccobacillary in the stationary phase. Most of the species under these genus are encapsulated. Few of these are opportunistic infection-causingbacteria, which may lead to the death of the patients if not treated properly. It grows well on Macconkey agar, blood agar, chocolate agar and tryptic soy agar at 37°C incubation temperature. These form smooth, mucoid and greyish white colonies with a colony diameter of 1.5 to 3 mm. Unlike the *Enterobacteriaceae*, some *Acinetobacter* species outside the *A. calcoaceticus-A. baumannii* complex may not grow on Macconkey agar. The *Acinetobacter*comprised of G+C content was found to be 39-47%. (Anton *et al.,* 2008). The identification of *Acinetobacter* species can be done by using different techniques such as 16S-rRNA, RNA polymerase subunit B (rpoB), DNA gyrase subunit B (gyrB), gene sequencing,DNA-DNA hybridization and whole-genome sequencing etc. Theyprovide good information about *Acinetobacter* taxonomic studies. The rpoB sequence comprises PCR amplification and gene sequencing. The *Acinetobacter* isolates were also isolatedfrom direct microscopy, pulsed-field gel election, MALDI-TOF MS and susceptibility test etc.(Jiahjeng Wang *et al.,* 2014). They look similar to gram bacteria so they are difficult to distinguish and may be misidentified as either gram-negative or gram-positive cocci. Hence they got their former name as Mimae (Anton *et al.,* 2008).

The genus *Acinetobacter* contains 33 validly named species. This was possible with the help of molecular methods which was used for the identification of species. The genus currently comprises 18 species which are now assigned with the formal species name. There are further 28 groupsthat have been identified but not yet named. There are at least 21 ungrouped single strains (Towner, 2010). The genus has undergone significant taxonomic modification over the last 30 years. Few of the members *are A. albensis, A. baumannii, A. calcoaceticus, A. dispersus, A. gandensis, A. junii, A. pittii* and *A. nosocomialis* etc. *A. baumannii* is the most potent and well-studied pathogenic member of the genus. There are many similarities between *A. calcoaceticus, A. baumannii,* genomic species 3 and 13UT both genetically and phenotypically. They are also genetically highly related and difficult to distinguish phenotypically which made them grouped together and named as ABC complex (*A. Calcoaceticus and A. Baumannii* complex) (Hsien Chang *et al.,* 2005; Gerber and Tjernberg, 1991; Gerber and Tjernberg, 1993). Since the 1970s, the genus *Acinetobacter* had become a trouble-causing agent by increasing regularly. They are recognised as the most important nosocomial pathogen causing severe disease and infection in immunosuppressive patients.They may also cause an episode of epidemic spread among the hospitalized patients (Hsien Chang *et al*, 2005; Bergogne and Towner, 2002). Few of the species under the *Acinetobacter* genus are resistant to many of the antibiotics. One of the most important pathogen under the genus

Acinetobacter is *A. baumannii.* It is found to be associated with greater resistance to antibiotics and higher mortality among bacteraemia patients compared with other genomic species (Hsien Chang *et al.,* 2005; Husch*et al.,* 2002;VikasManchanda *et al.,* 2010).

2. Pathogenic species: -

Acinetobacter during the past three decades has emerged as an organism that leads to most of the infection causing diseases due to their pathogenicity now became an important organism worldwide especially in hospitals. *Acinetobacter* infection commonly found in tropical countries increasing during wartime and natural disaster and also found to cause multiple hospital outbreaks in the temperate climate (Silvia and Robert, 2008). The genus *Acinetobacter* belongs to the family Moraxellaceae. Most of the organism under *Acinetobacter* belongs to ESKAPE that comprises of six highly virulent and antibiotic resistance pathogenic species are*Enterococcus faecium, Staphylococcus aureus, Klebsiellapneumoniae, Acinetobacter Baumannii, Pseudomonas aeruginosa and Enterobacter species* (Michea*let al.,* 2013; Francesco *et al.,* 2014).

The genus *Acinetobacter* comprises a different and complex group of bacteria.Most of them are opportunistic bacteria often causing infection in human beings. The most important disease caused due to *Acinetobacter* species iscommunity-acquired infections, which widely spreads through direct contact (Silvia and Robert, 2008). However, *A. baumannii* are important nosocomial pathogens, often associated with epidemic outbreaks of infection, that are rarely found outside of the clinical environment (Paolo *et al.,*2011). *A. baumannii*has become the clinical priority pathogenic species due to their antimicrobial resistance property (Michael *et al.,* 2013). These organisms are frequently drug-resistant and are capable of causing substantial morbidity and mortality in patients with severe underlying disease, both in the hospital and in the community. Several epidemic clonal lineages of *A. baumannii* have disseminated worldwide and seem to have a selective advantage over non-epidemic strains. The *Acinetobacter* infection has been reported among patients residing for long term at the hospital and even in acute care hospital patients (George *et al.,* 2008; Robert, 2000). Due to pathogenicity and multiple drug resistance, the organisms are said to achieve very dynamic reorganization and rapid evolution of their genome (Silvia and Robert, 2008). Few of theextensive pathogenic species are mentioned below.

2.1 *A. baumannii*: - *A. baumannii* has emerged as a highly pathogenic species for many health institutions globally. This is one of the most troublesome pathogens for health care institutions (Anton *et al.,* 2008). *A. baumannii* is a gram-negative bacterium belonging to the wider class of Gamma proteobacteria. These are short and rod-shaped bacterium. These are capsulated bacteria. *A. baumannii* was discovered by M.W Beijerinckii. It is an opportunist pathogen in humans affecting people who have a weak immune system. *A. baumannii* are widely distributed in the hospital environment.Thesespecies are not isolated from the outside of the hospital environment It causes nosocomial infections. They are part the of ACB complex comprising of *A. baumannii* and *A. calcoaceticus*complex. It is also isolated as an ESKAPE pathogen (Baumann *et al.,*1986; Francesco *et al.,* 2014; Chang Ro Lee *et al.,* 2017). It is a clinically significant bacterium, especially over the last 15 years, has been propelled by its remarkable ability to upregulate or acquire resistant determinants. Therefore, it is one of the most threatening organism in the current antibiotic era. *A. baumannii*can grow in a wide range of temperature and pH conditions but they do not contain the fastidious growth (Foster and Daschner, 1998). Italso grows well on different carbon and other energy sources, on the dry and wet surface which makes them easier for transmission (Wendt *et al.,* 1997; Sengstock*et al.,* 2010). The strains resistant to all known antibiotics have now been reported by the international health care community and in most recent times it has been found that *Abaumannii* infections are involving in the central nervous system, skin and soft tissues etc (Silvia and Robert, 2008; Federico *et al.,* 2007). *A. baumannii* causes infection in critically ill patients in the intensive care unit who have a weak immune system. The infection caused due tothese have been increasing gradually. This may lead to pneumonia, bloodstream infections, meningitis etc. (Anton et al., 2008). It is difficult to isolate *A. baumannii* due to their similarity with gram bacteria which forms clusters so they cannot be identified using phenotypic traits and chemical taxonomy methods. Molecular methods are used for the exact identification of the species (Chang Ro Lee *et al.,* 2017; Lee *et al.,* 2007). Different methods are used for the identification of species such as repetitive extragenic palindromic sequence-based polymerase chain reaction, pulsed-field gel electrophoresis, matrix-assisted laser desorption ionisation time of flight (MALDI-TOF), mass spectrometry, multilocus sequencing typing (MLST) and amplified fragments length polymerisation analysis etc (Chang Ro Lee *et al.,* 2017; Chang H C *et al.,* 2005).

2.1.1 Pathogenesis: - Several virulence factors are responsible for its pathogenicity's such as porins, capsular polysaccharide and lipopolysaccharide phospholipase, outer membrane vesicles, metal acquisition system, protein secretion systems, penicillin-binding protein and beta-lactamase and others. Few of them are mentioned in detail.

2.1.1.1 Porins: -

These are the outer membrane proteins associated with modulating cellular permeability. OmpA present in the outer membrane is called asa beta-barrelporin. In *A. baumannii*, OmpA is the virulence factor with a variety of biological properties. Random mutagenesis showed that the *A. baumannii* ompA mutant is defective in inducing apoptosis in human epithelial cells. The apoptosis takes place by the attachment of the purified OmpA to the host epithelial cells, they release proapoptotic molecules such as cytochrome c and apoptotic inducing molecules which targets mitochondria and leads to cell death (Chang Ro Lee *et al.,* 2017; Choic*et al.,* 2005). Another study showed that OmpAtranslocate to the nucleus by a novel monopartite nuclear localization signal and induces cell death (Choic C *et al.,* 2008b). OmpA also plays a major role in adherence and invasion of epithelial cells by interacting with fibronectin (Choic C *et al.*,2008b; Gaddy*et al.,* 2009) and binds to factor H in human serum which may allow *A. baumannii* to avoid complement-mediated killing. Furthermore, OmpA is also involved in the antimicrobial resistance of *A. baumannii* (Sugawara and Nikaido, 2012). This also helps in biofilm formation (Gaddy*et al.,* 2009). OmpA is immunogenic in a healthy person, but the patient affected with *Acinetobacter* species this result as virulence factors and cause infection (Chang Ro Lee *et al.,* 2017; Zan X *et al.,* 2016). Omp22 is a novel conserved and safe antigen which is used for the development of a vaccine against *A. baumannii* infections (Chang Ro Lee *et al.,* 2017; Hung *et al.,* 2016).

2.1.1.2 Capsular polysaccharide and lipopolysaccharide

A. baumannii have outer surface capsular made up of polysaccharide and contain a conserved gene cluster called the K locus. This helps in the production of capsular polysaccharide (Chang Ro Lee *et al.,* 2017; Geisinger and Isberg, 2015) The ptk and epsA genes are used for capsular polymerisation and assembly. When ptk and epsA are deficient in capsule production, this results in the decrease of survival in soft tissue infection site. This may lead to the defect of growth in the human serum. Therefore, the capsular polysaccharide is found to be targeting the antibody production site which leads to the infection (Russo *et al.,* 2009).

2.1.1.3 Phospholipase: -

Phospholipase is a lipolytic enzyme essential for phospholipid metabolism and acts as the virulence factor in*A. baumannii*. Three classes of phospholipase are found in these species, such as phospholipase A (PLA), phospholipase C (PLC), and phospholipase D (PLD) have been defined based on the cleavage site. PLA hydrolyses fatty acids from the glycerol backbone, whereas PLC cleaves the phosphorylated head group from the phospholipid. PLD is a transphosphatidylase that only cleaves off the head group. Degradation of phospholipids affects the stability of host cell membranes and the cleaved head group can interfere with cellular signalling, resulting in changes in the host immune responsethat may lead to cell death. These results suggest that phospholipase enzymes are important virulence factors in *A. baumannii* pathogenesis (Chang Ro Lee *et al.,*2017; Songer, 1997).

2.1.1.4 Penicillin-binding protein: -

Although PBPs are commonly involved in resistance to β-lactam antibiotics, PBP7/8 encoded by the *pbpG* gene is a virulence factor in *A. baumannii*. The *pbpG* mutant strain grows well on the Luria-Bertani medium. When both mutant and wild strain is allowed to grow the mutant shows reduced growth in human serum compared to the wild strain. An investigation of bacterial morphology using electron microscopy suggested that loss of PBP7/8 may have affected peptidoglycan structure, which may affect susceptibility to host defence factors. Hence, β-lactamase PER-1 has been suggested to be an *A. baumannii* virulence factor (Russo *et al.,* 2009).

2.2 *A. nosocomialis*: - These are gram-negative and are strictly aerobic in nature. They belong to the *Acinetobacter baumannii-Acinetobacter calcoaceticus* complex. *A. nosocomialis* are usually isolated from the patient who hasa weak immune system. These are commonly isolated from the hospital environment. They were first isolated as *A. nosocomialis* strain M2 in 1996 was first under *A. baumannii* later after the study of whole-genome sequencing resultedin the reclassification of species (Chang Ro Lee *et al.,* 2017; Harding *et al.,* 2013). These are the

most important nosocomial pathogen causing infections in human beings. These are highly resistant to antibiotics due to the presence of a few efflux pump. The efflux pump may also act as an antimicrobial agent, helps in surface motility and biofilm formation. They are causative organisms for bacteraemia, pneumonia, meningitis, urinary tract infection and wound infection. These are opportunistic bacteria and have multiple drug resistance (Philip *et al.,* 2018). They are phenotypically and genetically closely related to *A. baumannii.* They can be isolated using different molecular techniques such as 16S rRNA gene restriction analysis, amplified fragments length polymerisation and rpoB gene etc. This also can form a biofilm, cellular adherence, iron acquisition and cytotoxicity in the host cell (Je Chul Lee *et al.,* 2019). The main disease caused due to *A. nosocomialis i*sbacteraemia, urinary tract infections and wound infections etc (Man Hwan oh *et al.,* 2016).

2.2.1 Pathogenesis: - It is an important nosocomial pathogen causing various diseases in human beings. The specific virulence factors of this organism are not found. The mechanism may be similar to the *A. baumannii* where the outer membrane protein A could be involved in the pathogenesis (Philip *et al.,*2018).

The outer membrane protein also involves in the pathogenesis of *A. nosocomialis*. The OmpA is produced through outer membrane vesicles. OMVs are spherical in shape and composed of periplasmic proteins, LPS, phospholipase, DNA or RNA and the outer membrane acts as a vector for bacterial effectors to host cells. Through localisation, nuclear signals are carried to the nuclei of the host cell. They inhibit the alternative pathway of complement activation by binding to the H factor and they also result in the biofilm formation outside the host cell which results in bacterial survival both inside and out the host cell. They stimulate innate immune response and lead to the death of host cell (Je Chul Lee *et al.,* 2019; Man Hwan oh *et al.,* 2016). The other virulence factors produced by OMVs are protease and phospholipase (Chang Ro Lee *et al.,* 2017).

The pump has been divided into five different groups based on the sequence similarity. The resistance modulation cell division RND, the major facilitator, small multidrug resistance, multidrug and toxic compound extrusion and ATP binding cassette. The Multidrug efflux systems also constitute the antimicrobial resistance and pathogenicity in bacteria. RND is the most common efflux pump found in bacteria (Man Hwan oh *et al.,* 2018; Putman *et al.,* 2000). The *A. nosocomialis* contain an RND efflux pump. In this, we study the identification and characterization of RND that is a resistance nodule division efflux pump. It is a transcriptional regulator controlling and the yet uncharacterized multidrug AcrAB in *A. nosocomialis*. In silico analysis revealed that the homologues of AcrR and AcrAB are reported in the genomes of many other bacterial species. The genes encoding the AcrAB efflux pump are acrA and acrBwhich forms a polycistronic operon that is under the control of the acrR gene upstream of acrA. Bioinformatics analysis indicated the presence of AcrR binding motif in the promoter region of acrAB operon and the specific binding of AcrR was confirmed by electrophoretic mobility shift assay (EMSA). The EMSA data showed that AcrR binds to -214 and -217 bp upstream of the start codon of acrA. The mRNA expression analysis depicted that the expression of acrA and acrB genes are elevated in the deletion mutant compared to that in the wild type confirming that AcrR acts as a repressor of acrAB operon in *A. nosocomialis*. This was shown by the quorum-sensing regulator. The AcrR functions as an important regulator of the AcrAB efflux pump and are associated with several phenotypes such as motility, biofilm/pellicle formation and pathogenesis in *A. nosocomialis*. The antimicrobial property can be enhanced by the deletion of the acrA and acrB genes because they lead to the formation of biofilm or pellicle formation. (Kyunghoet *al.,* 2020). acrR mutant gene act as a virulence factor in mouse leading to its death. The intracellular survival of the acrR mutant gene is more compared to the wild strain this regulates the AcrAB pump while may lead to motility. Theseare the factors thatlead to the pathogenesis of the *A. nosocomialis* (Man Hwan oh *et al.,* 2018).

2.3 *A. pittii*: - These are gram-negative bacteria. They show negative for oxidase nitrate and indole biochemical test and positive for catalase test. These are strictly aerobic and non-motile and belong to the ACB complex. They found in both dry and wet environment etc. They are normally found in the human skin and capable of causing transitory colonization in the upper tract (Silvia and Robert, 2008; Rivera *et al.,*2014*)*. They even cause disease to fish and zebra. The case was reported in China where *A. pittii*was responsible for blunt snout bream disease in fish (Ning*et al.,* 2017). These are nosocomial pathogen causing community-acquired infections such as pneumonia, bacteraemia, meningitis etc. It is also found that *A. pittii* is responsible for causing cavitarycommunity-acquiredpneumonia. This is caused due to low immunity or smoking (Philippe *et al.,* 2017).*A. pittii* is an emerging fish pathogen to cause severe mortality in label Catla and hypophthalmichthysmolitrix in a fresh wetland (Ramesh *et al.,* 2020). They have a low mortality rate compared to the other species in the genome. These are resistant to the many antibiotics hence they are multidrug-resistant bacteria. This can be identified based on morphology, biochemical test, 16S rRNA segment, rpoB sequence analysis, tRNA spacer fingerprinting and ribotyping (Ning*et al.,* 2017).

2.3.1 Pathogenesis: - *A. pittii* require the cell to cell adhesion to produce infection in the human being. They have low pathogenicity compared to the other channels of the bacteria. *A.pittii* have low adhesion capacity but they get attached to the epithelial cells and mucosal cells. The low adhesion leads to fewer virulence factors of the organism. The pathogenies take place through biofilm formation. The virulence factors are not known and they have an unsatisfactory response to first-line antimicrobial therapy (Philppe*et al.*, 2017).

3. Other pathogenic species: -

Most of the other *Acinetobacter* species are pathogenicand cause disease to human beings. The species of *Acinetobacter* causes nosocomial infection, pneumonia, catheter-associated bacteraemia, soft tissue damage and urinary tract infection. According to the National nosocomial infections surveillance system, *Acinetobacter* infection has been increasing every year by 77.4% throughout the hospital environment (Anton *et* al., 2008;Souhail*et al.*, 2016*). A.soil* is a gram-negative bacterium strictly aerobic rod shape can cause bloodstream infection in neonates. Theseare non-motile and rod shape they are called B1T strain. The DNA G+C content was 44.1 mol% (Suk Kim *et al.*, 2008). *A. colistiniresistens* are usually isolated from the hospital environment which leads to the infection in human beings. *A. junii* contain a strain that is ATCC 17908 this is pathogenic and causes nosocomial infection includingcatheter-relatedbloodstream infection and cellulitis. They also cause rare disease in human-associated mainly with bacteremia in preterm infants and pediatric oncologic patients called septicemia (Udoreischi*et al.*, 2002). *A. rudis* is a gram-negative bacterium under the genus *Acinetobacter* these are isolated from raw milk and wastewater which may lead to cause infection to human beings. They have two strains G30 and A1PC16 which causes respiratory problems. The G+C content is 38-47 mol% (Ivone*et al.*, 2011). *A. schindler*i is the potential Pathogenic species. The strain LUH 5832 causes urinary tract infection.

4. The impact caused due to *Acinetobacter*: -

Healthcare-associated Nosocomial infections: - During the early days the infection caused due to *Acinetobacter* was post-surgical urinary tract infections and they were isolated from patients, in surgical or medical wards. Inthe past 30 years, the *Acinetobacter*has undergone many changes and started causing different types of infection such as cellulitis and meningitis etc. (Joly Guillou, 2005). The genus *Acinetobacter* is also called Gram-negative MRSA. These bacteria are always compared to methicillin-resistant*Staphylococcus aureus (*MRSA) because their epidemiology behaviour is similar to MRSA and their impact in terms of morbidity and mortality is similar to coagulase-negative staphylococcus. Comparing both *Acinetobacter* and *staphylococcus, Acinetobacter* cause bloodstream infection less than *staphylococcus aureus* (Rello, 2003). Bacteraemia is one of the most important nosocomial bloodstream infections caused due to *Acinetobacter*. The *A. baumannii* was generally isolated from patients suffering from bacteraemia. A survey by the health protection Agency in England found that patients suffering from bacteraemia was aged below 50 years and the majority of them were males (Pouteanen*et al.*, 1997).

Community-acquired infection: - The most frequent community-acquired infection caused due to *Acinetobacter* was acute pneumonia. The patients general has productive sputum and haemoptysis. Pneumonia caused due to *Acinetobacter*is off two types hospital-acquiredpneumonia or ventilator-associated pneumonia and community-acquired pneumonia (Roy *et al.*, 2012). Pneumonia occurs more in ICU patients who require mechanical ventilation because due to the colonization it becomes easy for the growth of bacteria and *Acinetobacter* growth increase gradually (Silvia and Robert, 2008). The infection was generally found in warm and humid months, even in temperate regions. The vectors which can transmit the community-acquired infection from one individual to another was found to be body lice, fleas and ticks (Joly Guillou, 2005).

Atypical infection: - *Helicobacter pylori* cause chronic gastric and they may also cause inflammation. The *A. lowffii*causes the same infection in mice that is hypergastrinemia and stimulation of cytokine release (Rathinavelu*et al.*, 2003). The fimbriae of *Acinetobacter* help to get attached to human gastric cells and may lead to the inflammation of the cells (Joly Guillou, 2005). Meningitis is the post neurosurgical disease that is caused due to *A. nosocomialis.* It is a nosocomial disease that can affect the brain (Roy *et al.*, 2007).

Disasters: - *Acinetobacter* are the most important organisms causing infection and disease in an unusual and emergency situation. During the Marmara earthquake in the north-west of Turkey in 1999, a total of 220 were hospitalised in which 18.6% of people developed nosocomial infections caused due to *Acinetobacter* (Joly Guillou, 2005). During the southeast Asia tsunami on December 24, 2004, 17 people were in

critical condition in ICU suffering from soft tissue injury and fractures. 20% of *Acinetobacter* was isolated from all the individual from blood and respiratory secretions (Silvia and Robert, 2008).

Seasonal variation: - The *Acinetobacter* infections are more in summer compared to other seasons. The growth of bacteria increases in the warm, humid, ambient air and good ventilation environment. It has been reported that more than 50% of *Acinetobacter* infections have been found from July to October in the hospitals (Silvia and Robert, 2008).

Military personnel: - Not only in the hospital environment but these species were also isolated during wartime. During the Korean war, 1955 Military recruits were suffering from bloodstream infection that was caused due to *Acinetobacter* (Strawitz*et al.,* 1995). The infection caused during the Vietnam war lead 63 soldiers to suffer from soft tissue *Acinetobacter* infections (Tong, 1972). The genus *Acinetobacter* was also isolated from the soldiers who had been injured during Operation enduring Freedom in Afghanistan and Operation Iraqi Freedom in the Iraqi and Kuwait regions. After the terrorist bomb blast in Bali in 2002, the patients were suffering from burn injuries and they had bloodstream infections caused due to *Acinetobacter* (Silvia and Robert, 2008). The contamination of wound in war filed, local food, cross-infection and contaminated environments may lead to the growth of *Acinetobacter* and cause several infections and disease during wartime. The proper treatment and prevention lead to the decrease of infection during wartime (Tong, 1972).

5. Antimicrobial resistance of *Acinetobacter* species: -

Acinetobacter has become one of the most successful pathogens in modern healthcare because of its amazing ability to acquire antimicrobial resistance. Several strains of *A. baumannii* are highly resistant to most clinically available antibiotics. *Acinetobacter* has several resistance mechanisms, including β-lactamases, aminoglycoside-modifying, efflux pumps, permeability defects, and modifications of target sites (Chang Ro Lee *et al.,* 2017). The accumulation of several resistance mechanisms in *Acinetobacter* has gradually decreased the number of antibiotic classes available to treat *Acinetobacter* infections in clinical practice (Vikas *et al.,* 2010). A few of the antimicrobial resistance pathways are mentioned below: -

Beta-lactamasehasthe ability to inactivity beta-lactams. They are grouped into four different the molecular class that is class A, class B, class C and class D beta-lactamase. They are chromosomally encoded and become resistant to broad-spectrumcephalosporin's such as penicillin, cephalosporin and carbapenems. They also lead to loss of proteins which is transferred through porin channels from the outer membrane and become resistant to lactam agents. The main function of beta-lactamase is to alter the cell wall channels and efflux pump (George *et al.*2008; Thomson and Bonomo, 2005).

The bacteria may undergo point mutations that alter the bacterial target site function and make them resistant to the antibiotics (Turnidge*et al.,* 2005).

Permeability changes may also lead to antibiotic resistance. The porins form channels and help in transportation sometimes they may affect membrane permeability and lead to antibiotic resistance. The outer membrane protein, envelope components such as LPS and peptidoglycans also involved in antibiotic resistance. The loss or modification of LPS causesa decrease in membrane integrity and increases resistance (Seemann*et al.,* 2010).

Aminoglycoside modifying enzyme is the important antimicrobial resistance agents in *A. baumannii.* They are resistant to aminoglycosides. They undergo modification and alterations of the site and lead to antibiotic resistance of the bacteria (Chang Ro Lee *et al.,* 2017).

Alterations of target site such as penicillin-binding protein site PBP make the antibiotic not bind to the specific site and become resistant (Chang Ro Lee *et al.,* 2017).

*Acinetobacter*isresistant to many antibiotics, Antimicrobial Therapy, Colistin, Tigecycline, AmpC enzymes, and carbapenemases in various combinations. This makes them multidrug-resistant MDR, Extensively Drug-Resistant (XDR), and Pan Drug-Resistant (PDR) bacteria (Vikas *et al.,* 2010).

6. Treatment: -

As above mentioned, *Acinetobacter*ismultidrug-resistant and pan drug-resistant. There are antibiotics to treat *Acinetobacter* Infection as carbapenem, colistin, tigecycline, sublactam and trimethoprim etc. These are used to treat infection caused by antibiotics susceptibility *Acinetobacter*. There are only a few antibiotics are available to treat multidrug resistant *Acinetobacter* infections (Silvia and Robert, 2008; Yohei*et al.,* 2015). To treat MDR and PDR *Acinetobacter*, a combination of antibiotics and therapies are used such as colistin/imipenem,colistin/meropenem, colistin/rifampicin, colistin/tigecycline, colistin/sulbactam, colistin/teicoplanin, and imipenem/sulbactam, have been extensively used to treat *Acinetobacter* (Chang Ro Lee *et al.,* 2017; Lee C *et al.,* 2013).

Sublactam along with ampicillin are used to treat bloodstream infections and soft tissue infection caused due to multidrug-resistant*Acinetobacter*. Thesearebeta-lactamase inhibitors and also have an affinity for penicillin-binding proteins (Yohei*et al.,* 2015). Colistin and daptomycin are used to treat pneumonia. Minocycline is the most used antibiotic to treat *Acinetobacter* infection. They are broad range spectrum hence it is easy to treat the infection. Trimethoprim-sulfamethoxazole is the combination of two antibiotics effectively killing all carbapenem resistance strain. They are combined with colistin to kill all strains of *Acinetobacter* for up to 24 hours (Velerie*et al.,* 2006).

Non-antibiotics therapy such as bacteriophage therapy is also available to treat the *Acinetobacter* (Chang Ro Lee *et al.,* 2017). AB1, vB_Ab-M-G7 and Bo62 bacteriophage are very effective against the *Acinetobacter*. The bacteriophage produce endolysin this are lytic enzyme they degrade the cell wall and cause cell death (Roy *et al.,* 2012; Joly Guillou, 2005). Bactericidal gene transfer is done into attuned donor cell through conjunction may help to treat *Acinetobacter* infections. Other treatments such as Radio immunotherapy, photodynamic therapy, Nanoparticle technology and cathelicidins are used to treat *Acinetobacter* infections (Roy *et al.,* 2012). Bulgecin is a natural product that acts as lytic transglycosylase inhibitors and suppresses the growth of organisms. Cyanide 3 chlorophenylhydrazone (CCCP) is an efflux pump inhibitor that decreases the MIC of *Acinetobacter*. Gallium is a semi-metallic element that disrupts essential redox driven biological processes and used to treat MDR *A. baumannii.* Probiotics are living organisms that are consumed for healthy befits. Few researchers believe and stated that probiotics are also responsible to protect against the infection caused due to *Acinetobacter* (Joly Guillou, 2005).

7. Non-pathogenic species: -

Most of the *Acinetobacter* species are pathogenic few of them are non-Pathogenic. Few of these species such as *A. baylyi*is used in genetic engineering because they being natural competent. They can take up exogenous DNA from its surrounding and incorporate the DNA into its own chromosomal DNA (Spyros *et al.,* 2016). *A. venetianus* are used in the production of bio emulsifier. These are called emulsan. *A. venetianus*is also notable for the degradation of n alkanes. *A. pakistanensis* are isolated from the textile dyeing in Pakistan which shows tolerance towards the heavy metal (Toshiya *et al.,* 2014). *A.radioresistens* exhibit a strong potential characteristic as a candidate for the bioremediation of hexavalent chromium in the environment (Vincent *et al.,* 2008).

7.1 *A. radioresistens*

They are radiation-resistant bacteria. These are gram-negative oxidase negative and spore-forming, non-motile and non-fermentation bacteria. These are aerobic in nature (Vincent *et al.,* 1995; Venezia*et al.,* 1995). *A. radioresistens* KA53 isolated by the enrichment culture was found to produce an extracellular non-dialyzable emulsifying agent when it is grown on an ethanol medium in a batch fed fermenter. This emulsifying agent is referred as Alasan (Veneziaet *al.,* 1995). *A. radioresistens* exhibit a strong potential characteristic as a candidate for the bioremediation of hexavalent chromium in the environment. (Vincent *et al.,* 2008). Methyl parathion is widely used as an organophosphorus pesticide. *A. radioresistens* USTB 04 can totally biodegrade methyl parathion (Yan *et al.,* 2007).

7.2 *A. pakistanensis*

These are gram-negative cocci or short rod in shape they are non-motile, strictly aerobic, a heavy metal tolerant and psychrotolerant bacterium. They occur in pairs sometimes in triplet form. The strain NCCP 644 was isolated from a textile dyeing wastewater treatment pond in Pakistan. They grow well in tryptic soy agar medium. To determine the tolerance of the novel strain to a toxic concentration of heavy metals the isolated strain was grown on the TSA supplement with different heavy metals concentration. After incubation, there was the

growth of *A. pakistanensis* which shows that they are tolerant towards heavy metal. The g + c content of genomic DNA of strain NCCP 644 was found to be 40.6 mol% as determined by HPLC (Toshiya *et al.*, 2014).

7.3 *A. venetianus*

They are notable for degrading n alkanes. It contains plasmids carrying sequences similar to the pseudomonas oleovorans alkane that hydrolysis gene alkBFGH. Thesecan grow with n alkanes that contain C10, C14, C20 and their respective oxidation products as the sole carbon source. *A. venetianus* VE-C3 was isolated from Venice Lagoon this is also n alkanes degrading strain (Zutic*et al.*, 1999).

Acinetobacter strain RAG-1 is theindustrially important strain that has been extensively characterized concerning its growth on hydrocarbons and its production of high molecular mass bio emulsifier emulsan. This helps in oil degradation (Tjernberg*et al.*, 1999). *A. venetianus* has potential for future application in remediating diesel contaminants also helps in the biodegradation of tetradecane (Zuliang*et al.*, 2015).

8. Conclusion: -

The current review briefly describes the Pathogenic and non-Pathogenic species of Genus *Acinetobacter* followed by the individual description of the members focusing on their key attributes and virulence mechanism of pathogenic, antimicrobial resistance and treatment used for *Acinetobacter*. To overcome the problem caused due to the genus *Acinetobacter*, knowledge of pathogenic and antibiotic resistance is important. *Acinetobacter*is considered as the low category pathogen and easily isolated from the hospital environment. These had become the most troublesome pathogen in the hospital. They are well recognised due to their multidrug-resistant property. They have a broad range of spectrum and survive in all environmental condition. The whole-genome study was possible from molecular techniques and this leads to a better understanding of the genome. They cause disease such as pneumonia, septicemia, bloodstream infection, meningitis etc. They can spread only through direct contact. The mortality rate caused due to *Acinetobacter* is less compared to other bacteria. Different types of drugs are used to treat *Acinetobacter* such as carbapenem, sublactam, colistin etc. The combination of treatment is used to treat multidrug-resistant*Acinetobacter*. Few non-antibiotic therapies are used to treat MDR *Acinetobacter* and PDR *Acinetobacter*. Few of the non-pathogenic species are used for several purposes in genetic engineering and a few of the strains help in oil degradation acts as bio emulsifier.

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