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Assessment of the Zoonotic Potential of Proteus mirabilis in Humans with Emphasis on Detection Methods, Virulence Mechanisms, and Antibiotic Resistance

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Abstract

Proteus mirabilis bacteria are a major cause of urinary tract infections, particularly in people who use catheters or have urinary tract problems. These bacteria are able to survive and cause disease thanks to their production of several virulence factors. There has been increased concern recently about its presence in animals and their products, which could allow it to be transmitted to humans. These bacteria usually live in the intestines of humans and animals, and have been found in farm animals, pets, wild animals, as well as food products. This review explains how it spreads, how it jumps to humans, and highlights the similarities between strains found in animals and humans, particularly in antibiotic resistance and detection, and in its ability to cause disease. It also shows that it may worsen bowel diseases, not just urinary tract infections. The study highlights the necessity of employing the "One Health" concept to enhance surveillance.

Introduction

The facultative anaerobic Gram-negative bacterium P. mirabilis is a member of the genus Proteus in the family Morganellaceae. It was previously categorized under the Enterobacteriaceae family, but breakthroughs in genomic analysis have led to a reevaluation of its classification, which resulted in its reclassification under the Morganellaceae family (Adeolu et al., 2016). In 2024, P. mirabilis and additional species including Proteus vulgaris, Proteus cibi, and Proteus faecis were classified in the LPSN database as officially recognized members of this family. Ten officially identified species and additional unnamed genomic types (genotypes Four, Five, and Six) make up the genus Proteus (Liu et al., 2025). Morphologically, P.mirabilis bacteria exhibit distinctive characteristics, the range of cell size is 1.0–3.0

micrometers in length and from (0.4 - 0.8) micrometers in width. These bacteria are characterized by their plural forms, manifestation the form of short rods, balls, threads, and lacking both a capsules & a bacterial structure (Liu et al., 2025). These bacteria are characterized by their ability to move thanks to the existence of flagella, and they exhibit a distinctive behavior of spreading across agar surfaces. This powerful movement results in Forming concentric rings and visual dividing stripe , known as Dennis lines, which are utilized to distinguish breeds (Ali et al., 2023). Bacteria also possess hairs that enable them to adhere to the epithelial cells of plants and fungi (Kao, 2014).

in 2024 Gonzalez and other found Proteus mirabilis is a major urinary pathogen, It contributes to more than 40 percent of catheter-associated UTI. (Gonzalez et al., 2024).Yang et al ., Its virulence factors, inclusive of filaments , hemolysins metalloproteases, , flagella, and ureases, are essential to its ability to infiltrate the host, damage tissues, and elude immunological reactions. (Yang et al., 2024). Although P.mirabilis bacteria are usually considered to be commensal organisms in the gut, recent study have connected them to Crohn's disease and other inflammatory bowel conditions (Zhang et al., 2021). Jiang and colleagues (2025) It has been shown to worsen colitis by altering the host's immunological responses and breaking down the intestinal mucus barrier. (Jiang et al., 2025). Even though Proteus mirabilis's toxicity and epidemiology have been thoroughly studied, its significance as a zoonotic pathogen is still not well established. Current research on the spread of Proteus mirabilis in farm animals, pets, and associated ecosystems and products is compiled in this study . By focusing on documented genetic commonalities and shared patterns of antibiotic resistance, we also hope to explain how this zoonotic virus spreads from humans to animals. This review aims to raise awareness of the zoonotic concerns connected to Proteus mirabilis and lay the groundwork for further research into its pathogenic mechanisms and effects on the health of humans and animals.

1- The Probability Pattern Of Proteus Mirabilis Transmission.

Among their species, Proteus mirabilis bacteria have the highest isolation rate and the largest geographic distribution. They have been found to be a normal component of both human and animal gut flora (Shakur et al., 2024). These bacteria are characterized by their remarkable diversity, because they are found in sewage, soil, and water, where their metabolic activity is aided by the breakdown of organic matter. (Shakur et al., 2024). Its main clinical importance lies in the fact that it is among the most common opportunistic bacteria that cause UTIs. It is a major due to both community-acquired and health care associated urinary tract infections, and is generally ranked as the most second common type of intestinal bacteria after Escherichia coli. It represents (1 to 10%) of all human urinary tract infections (Hassouneh et al., 2025; Shaffer and Pearson, 2017). Following the urethral catheterization, the frequency of CAUTIs (catheter-associated urinary tract infections) results in P.The percentage of mirabilis bacteria can increase to between 20% and 45% (Chakkour et al., 2024; González et al., 2024).

Although catheter-associated urinary tract infections are usually polymicrobial, Proteus mirabilis bacteria are one of the most common pathogens (Armbruster et al ., 2017). It is the leading causative agent (10-44%) in urinary tract infections associated with double J stents (DJUTIs) (Hunt e al ., 2024). The potent urease enzyme found in P. mirabilis bacteria is a major factor in the complications of urinary tract infections. This enzyme breaks down urea into ammonia and carbon dioxide, increasing the acidity of the urine and leading to the precipitation of struvite or apatite crystals (Chakkour et al ., 2024). These crystals clump together to form bladder stone, which work as a persistent bacterial reservoir, making the infection challenging to cure and likely to recur. This procedure may also be lead to deposits accumulating on the

catheter and causing it to become blocked, which may cause hydronephrosis and kidney injury (Armbruster et al ., 2018). Urinary tract stones in the bladder and kidneys, such as Armbruster stones and others, can harm the kidneys irreversibly and frequently necessitate surgery. (Armbruster et al., 2018). Many infections outside of the urinary tract are caused by P. mirabilis, especially in those with weakened immune systems. Ten percent of clinical isolates are related to respiratory ear, encephalitis, tract, osteomyelitis, meningitis, burn, nose, eye, skin, and wound infections, while the remaining ninety percent are connected to UTIs and catheter-associated UTIs (Chen et al., 2023). It encourages tissue colonization and spread by its swarming motility (Chakkour et al., 2024). It has been linked to hospital-acquired epidemics, rheumatoid arthritis, diarrhea, and infectious endocarditis (Drzewiecka, 2016). Furthermore, P. mirabilis has been linked to incidences of food poisoning; between 2016 and 2017, 3.61% of cases were reported in China. Signs include diarrhea, nausea, dizziness, and abdominal discomfort (Gong et al., 2019). In 2018 incident in Beijing, cooked meat balls contaminated with P. mirabilis made customers ill, with the bacteria discover on hands of the chef and and service staff (Wang et al., 2010).

This association has been confirmed by later research, which found a markedly higher quantity of Proteus mirabilis in feces and inflamed colon samples from Crohn's disease patients compared to healthy persons. Experimental findings have also shown signs of colon shortening & enlargement of the spleen and liver, suggesting that P.mirabilis play a crucial role in induce inflammations in Crohn's disease (Zhang et al., 2021). Furthermore, Proton pump inhibitors have been suggested to promote the growth of P. mirabilis and other bacteria in the digestive tract which would cause intestinal inflammation, and that oral inflammation may worsen intestinal inflammation (Kitamoto et al., 2020). P.mirabilis has been identified in a wide range of hosts, including, poultry ,ruminants and domestic animals, illustrating its re-markable diversity in veterinary medicines . Its family range goes well beyond those of household animals., include a wide spectrum of wild animals, underscoring its diverse habitat and ability to move between animals and humans. It has been isolate from wild animals in natural environments, such as fruit bats in Indonesia, migrant bird droppings in China, and Egyptian vulture chicks in the Canary Islands. (Gao et al., 2024). Additionally, an The MDR strain of P.mirabilis was found to be the cause of fatal lobar pneumonia and liver necrosis in the critically endangered Malayan pangolin, indicating that it poses a threat even to rare and protected species. The genomic analysis of this strain revealed a worrying range of antibiotic resistance genes, including those that produce broad-spectrum beta-lactamases, and confirmed the presence of significant virulence indicators (Mohammed & Hamzah . 2021 ; Chen et al., 2025).It should be noted that in zoos, some Proteus species can causes serious systemic infection a fatal state of septicemia in Humboldt penguins has been refer to a simultaneous infection with Proteus vulgaris, Proteus pinnerii, Proteus common, and Proteus sibari, draw attention to the possibility of extreme, multi-species Infections with Proteus in confined wild animals (Gu etal, 2020).

in Farm animals are a considerable reservoir for Proteus mirabilis bacteria, impacting animal health and food safety. The bacteria has been isolated from both healthy and sick cattle, sheep, and poultry in several nations, and reports from flocks of chickens and ducks as well as cattle excrement attest to its widespread existence in agricultural settings throughout various locations (Sun et al ., 2020;Ramatla et al ., 2024). Its significance as a factor influencing livestock product and health is confirmed by its link with clinical disorders such diarrhea in cattle and poultry (Ge et al., 2021). Humans are another bioreservoir and possible source of zoonotic disease transmission because of their frequent interactions with pets. Since Proteus mirabilis has been isolated from both dogs and humans in shared homes, it is widely detected in

pets. Both domestic and stray dogs' feces typically include it (Marques et al., 2019; Liu et al., 2023). According to the study, P. mirabilis' rate of intestinal colonization is notably increases in dogs than in the humans who live with them. Significantly, molecular research has shown that dogs and humans living in similar households have genetically related strains of Proteus mirabilis; some of these shared fecal strains also exhibit genetic affinity with bacteria that cause urinary tract infections. This confirms dogs' possible significance as a human illness reservoir and offers a direct directory of interspecies transmission (Marques et al., 2019 ; Mohammed & Hamzah . 2021). UTI are a major public health concern. Numerous studies conducted on various continents have shown that P. mirabilis is a prominent cause of UTIs in dogs and to a lesser level in cats (Fonseca et al., 2021; Amphaiphan et al., 2021).

2. Identification Of P.Mirabilis In Animals

Proteus mirabilis is the one common bacteria in the digestive system of human and animal , and is widely spread among various animal species, including wild animals, farm animal, and pets. This wide range of families points to possible transmission pathways . Between wild environments and domestic , as well as between animal and human. The P.mirabilis bacteria's extensive dispersion is confirmed by the repeated isolation of the germs from different animal sources. Since these bacteria have been recovered from a variety of species and their habitats, wildlife has been identified as a significant reservoir for them, indicating the possibility of animal-to-human transmission (Mohammed & Hamzah . 2021; Saputra et al., 2021 ; Suárez-Pérez et al., 2023; Gao et al., 2024).

For wild mammals, P.mirabilis bacteria were isolated from two wild boars out of 110 from northern Tunisia's (19) rural and urban areas . This bacterium has also been found in birds of prey in Spain's Catalonia, such as barn owls and Eurasian buzzards (Darwish et al., 2019). Notably, it was taken from a little sea lion in Uruguay (20%) (Eleopulos, 2022), indicated its presences in marine mammals. Besides vertebrates, external parasites may also play role in transmitting the infection. Ergunay et al. found P.mirabilis bacteria in 48.5% of ticks taken from a variety of wild animals in Kenya, including cattle and giraffes, lions, and rhinos (Ergunay et al., 2022). Farm animal are important reservoirs for P.mirabilis bacteria, raising concerns about animals safety and foods health. Chinam et al. reported an isolation rate of 15.95% (26/163) of rectal swabs from pigs in India (Ko et al., 2022). In China, broiler chickens showed an isolation rate of 7.07% (Li et al., 2022). but , the associated of P.mirabilis that causes illness in agricultural animals is of great concern. Similarly, Sun et al. discovered isolation rates in diarrheal cattle and poultry in northeastern China, suggesting that P. mirabilis may exacerbate animal health (Sun et al., 2020). In Egypt, Algammal et al. The bacteria were detected in duck , both healthy and sick, mark their varied impact on animal health (Algammal et al., 2021). Pets are a possible source of zoonotic infections, including the bacterium Proteus mirabilis, due to their frequent interaction with people. The detection of this bacteria in pets has increased, highlighting its epidemiological importance. Marquez and colleagues reported isolating it from humans and dogs in homes, without detecting it in cats (Marquez et al., 2021). Urinary tract infections have been linked to Proteus mirabilis in pets. Fonseca and colleagues found it in dog urine samples, but only In cats in the United Kingdom (Fonseca et al., 2021).

3. Determining P. Mirabilis In Human

Due to the possibility of Proteus mirabilis bacterial contamination, foods derived from animals have emerged as a significant public health problem. The prevalence of this bacteria in animal products varies significantly between nations and areas due to variations in environmental factors and hygienic measures. Beef samples in the Indian state of Andhra Pradesh showed the greatest levels of contamination, but entire

chicken tests showed very low amounts (Chinnam et al., 2021). At 100%, chicken meat has the highest contamination rate in the Londrina-Parana region , while the contamination rate in beef was much lower at 27.8% (Sanchez et al., 2021). In the Qalyubia Governorate of Egypt, the contamination rates in chicken and milk samples reached 1.51% and 3.45% respectively (Idris et al., 2023). Although P. mirabilis can be found in many different settings, such as soil, water sources, and sewage, it is mostly a commensal organism in the human and animal digestive tracts (Armbruster & Mobley. 2012). Although this bacteria can result in a range of illnesses in humans, including wound, eye, gastrointestinal, and urinary tract infections, it is particularly notorious for catheter-associated urinary tract infections, also known as catheter-associated urinary tract infection (CAUTI) (Armbruster et al., 2017; Warren et al., 1982). This infection is common among patients who use catheters for long periods, such as inhabitants of long-term care centers and nursing homes, and may be especially dangerous for people who have had spinal cord injuries (Hunget et al., 2007). P. mirabilis-related urinary tract infections (UTIs) and CAUTIs are typically made worse by the development of kidney and bladder stones (urolithiasis), irreversible kidney damage, and the potential for bacteremia and sepsis(Foxman et al., 2003; Griffith et al., 1976; Kim et al., 2003; Watanakunakorn et al., 1994). The most frequent cause of bacteremia in nursing homes is really CAUTI , and bacteremia caused by Proteus mirabilis (P. mirabilis) occurs more often after a urinary tract infection or catheter-associated urinary tract infection than other sources of infection, and bacteremia & sepsis caused by this bacterium carry a high mortality rate (Hooton et al., 2010; Kim et al., 2003; Watanakunakorn et al., 1994).

For many years, researchers have examined and investigated the amazing capacity of Proteus virulentus bacteria to infiltrate host cells, which has been demonstrated to play a role in the development of infection and the severity of disease in animal models. The degree of host cell invasion and cytotoxicity attained by Proteus mirabilis bacteria in vitro varies substantially based on the studied strain, growth stage, and bacterial shape (e.g., logarithmic growth versus stationary phase, vegetative versus proliferating cells), the host cell type, the number of infections, the medium's pH, and the experiment's duration. Similar to this, the pathological alterations in the kidneys and bladder of infected animals differ slightly depending on the bacterial strain, the amount of inoculation, and the infection pattern. However, it has been demonstrated that Proteus mirabilis is more invasive than Salmonella enterica typhimurium (Mobley et al., 1996). Although Proteus mirabilis bacteria clearly have the ability to invade host tissues during infection, they do not create a large-scale internal environment as is the case with Escherichia coli bacteria that cause urinary tract infections (Schaffer et al., 2016). Numerous virulence factors have been linked to pathological histological alterations in vivo as well as cell invasion and cytotoxicity in vitro. For instance, bacterial cells can approach host cells thanks to flagella, while mutants without flagella can only penetrate cells when they are centrifuged straight onto a monolayer of host cells (Allison et al., 1992; Mobley et al., 1996).

4- Pathogenicity Of Proteus Mirabilis In Human And Animal

The bacterium P.mirabilis has been convey to cause disease in different tissues and organ in both human and animal, and severe cases can lead to decease. One of the most notable associations of this bacterium is that it is a main cause of urinary tract infections in both humans and pets (Moyaert et al., 2017; Costa et al., 2018). Studies indicate that this bacterium is responsible for 1-10% of all cases of urinary tract infection in humans (Schaffer et al., 2017). The prevalence of UTI cause by this bacterium is significantly higher among the elderly and women (Chakkour et al., 2024; Hafiz et al., 2024). According to Liu et al.,

this bacterium has been connected to recurrent urinary tract stones in dogs with urinary tract issues (Liu et al., 2025). inclusive of (Gong et al., 2019). In 2018, Wang et al. documented a case of food poisoning in Beijing, in which cooked meatballs contaminated with Proteus mirabilis bacteria made customers ill. The bacteria were discover on the hands of the chef and service staff (Wang et al., 2010). Additionally, between August and December of 2018, Fan and associates recovered Proteus mirabilis bacteria from a sample of pediatric diarrhea (49–486), noting that 10.1% of them (Liu et al., 2025).

They discovered a notable increase in the abundance of P.mirabilis bacteria in Crohn's disease patients by comparing feces and inflammatory colon samples from both healthy people and Crohn's disease patients. According to experimental studies, there are indications of colon shortening and an increase in the size of the liver and spleen, indicating that the bacteria Proteus mirabilis is a major cause of the inflammation associated with Crohn's disease (Zhang et al., 2021). According to Kitamoto et al.'s addition, Proton pump inhibitors may promote the development of bacteria such as P. mirabilis in the gut, resulting in enteric inflammation, and oral inflammation may worsen intestinal inflammation. (Kitamoto et al., 2020). In animals, the bacterium Proteus mirabilis has been linked to different intestinal diseases. A bamboo rat farm in Guangdong province, China, reported 400 bamboo rat deaths in 2018. The reason of the deaths was confirmed to be vomiting and diarrhea, with P. mirabilis identified as the culprit (Mohammed & Hamzah . 2021 ; Zhai et al., 2021). Diarrhea and bloody feces were among the close symptoms observed in 74 rhesus monkeys infected with Proteus mirabilis bacteria (Yu et al., 2015). A P.mirabilis bacterial infection caused yellow watery diarrhea, lethargy, and mass death in a rabbit farm in Henan, China, along with damage to several organ tissues (Wang et al., 2024). A P.mirabilis bacterial infection caused rabbits on a farm near Lhasa, China, to die after exhibiting diarrheal symptoms. (Liu et al., 2025). Furthermore, Dong et al. reported that Proteus mirabilis bacteria (strain 17f) was recognized as the main due to diarrheal in lambs in China (Dong et al., 2022). These report confirm the important role of P.mirabilis bacteria as the cause of intestinal diseases this affects both human and animal, affect animal welfare, food safety, and public health. In addition to its effects on the gastrointestinal and urinary systems, P.mirabilis has been linked to a variety of illnesses that impact multiple organs in both humans and animals. Proteus mirabilis, the second Staphylococcus after MSSA (24.3%), was isolated from skin abscesses at a rate of 21.6% in human medicine, (Mestre et al., 2010).

In pig , Chen et al. have conducted similar studies. Proteus mirabilis bacteria have been identified as reason of respiratory signs, such as fever and difficulty breathing. It has also, been observed that these bacteria are able to cross the placenta, leading to fetal death (Chen et al., 2023; Liu et al., 2025). Similarly, Li et al. found. Pigs infected with Proteus mirabilis bacteria develop lesions in several organs and systems, inflammation, septicemia, and ultimately death (Li et al., 2021). Sanchez and associates isolated strains of Proteus mirabilis bacterium from broiler chickens in northern Parana, Brazil, when the bacteria caused caseous exudate and bleeding in subcutaneous tissue. Histopathological examination reveals cellulitis, infiltration of inflammatory cells, and necrosis, edema, and congestion of the pectoral muscles (Sanchez et al., 2020). Furthermore, Proteus mirabilis bacteria have been report to cause serious infection in other species of animal. were the first to report purulent pericarditis and purulent dermatitis in sheep brought on by the Proteus mirabilis bacteria (Abdullah et al., 2022; Najd Qahramani et al., 2023). P.mirabilis bacteria have been identified as a major cause of neck abscesses and bacteremia in sea lions (Sacristan et al., 2021). Found that the bacterium caused local necrosis, bleeding in the glomeruli, and mononuclear cell infiltration in the kidneys of infected Indian carp. Miraculous Proteus (Chinnam et al., 2021).

5. Identifying antibiotic resistance genes in Proteus mirabilis bacteria .

Antibiotic resistance genes have been identified in numerous sources and have significantly contributed to the resistance patterns in isolated P. mirabilis bacteria. The beta-lactam antibiotic resistance genes blaOXA-1, blaPSE, blaTEM, blaCTX-M, blaSHV, blaIMP, and blaNDM were detected in isolates obtained from the wild. In isolates from wild mammals, the resistance genes blaOXA-48, blaTEM, blaTEM-1, blaSHV-28, blaSHV-12, blaCTX-M-G1, blaCMY-1, and blaCMY-2 were discovered (Saputra et al., 2021; Selmi et al ., 2022; Mbehang Nguema et al., 2021; Darwich et al., 2019; Eliopulos et al .,2022; Lv et al .,2022). A wide range of resistance genes have been discovered in farm animals likes ducks, pigs and chickens, including blaDHA, acrB, blaCTX-M, blaTEM, blaNDM, blaOXA, norA, and blaKPC (Chinnam et al., 2021; Qu et al., 2022; Ge et al., 2021; Li et al., 2022; Ramatla et al., 2024; Al-Jamal et al., 2021). BlaDHA, blaCTX-M, blaTEM, and blaOXA-1 were found in the isolates from related cats and dogs (Liu et al., 2023; Marques et al., 2019; El-Tarabili et al., 2022). While the foodborne isolate carried blaCTX-M, blaOXA, blaDHA, blaCMY-2, blaNDM, blaTEM, blaSHV, blaFOX, blaCIT, blaEBC and bleMBL (Li et al., 2023). In isolates of wild animals raised on farms, the resistance genes qnrA and qnrC were found (Lv et al., 2022). The most popular vector for transferring resistance genes in humans is a plasmid. These are circular, double-stranded DNA molecules that are free of chromosomes and have the ability to replicate themselves and occasionally move (oriT). Plasmids can be invasive on a wide scale or host-specific. Plasmids typically lack the genes required for the host to survive in "non-stressful" conditions, and the replication origin (ori) regulates the quantity of copies. Since two plasmids with the same replication origin cannot coexist in the same bacteria and are thus incompatible, the diversity of ori genes is frequently used to classify them (Carattoli, 2009). To differentiate between different plasmid families that circulate among enteric bacteria, including IncHI2, HI1, I1-γ, X, L/M, N, FIA, FIB, FIC, W, Y, P, A/C, T, K, and B/O, they created a molecular classification scheme using polymerase chain reaction (PCR) amplification. While some of these plasmid families have a limited range of hosts, others, including IncA/C, IncP, and IncQ, are broad-spectrum hosts that can be sustained steadily in both Gram-positive and Gram-negative bacteria (Carattoli, 2009).

The majority of the genetic factors causing aminoglycoside resistance in the bacterium Proteus mirabilis are found on integrons in the form of gene cassettes. These genes usually include aadA1 and aadA2, which code for aminoglycoside adenyltransferase enzymes; aadB, which codes for aminoglycoside (2″)-transferase enzyme; aac(6′)-Ib which codes for aminoglycoside acetyltransferase enzymes; and SAT2, which codes for streptothrycin acetyltransferase enzymes. (Mokracka et al., 2012). The initial description of the plasmid containing the 16S rRNA RmtA methylase enzyme came from a clinical isolation of Pseudomonas aeruginosa bacterium (Yokoyama et al., 2003). It was then discovered that gut bacteria, such as Proteus mirabilis, have many variants (RmtA, B, C, D, and ArmA) (Galani et al., 2012; Leulmi et al., 2019). Co-selection is a danger when these determinants are present on acquired genetic constructs that also carry additional resistance genes, such the blaNDM gene on the plasmid from Klebsiella pneumoniae Saitama. Gram negative bacteria's increasing resistance to aminoglycosides due to plasmid-transmitted 16S RNA methylation enzymes could pose a serious therapeutic risk in the near future when the bacteria develop resistance to all aminoglycosides (Gerlich et al., 2020). Genes encoding the chromosomal DNA enzyme gyrase (gyrA and gyrB) or topoisomerase IV (parC and parE) frequently exhibit mutations resistant to fluoroquinolones (Cambau et al., 2006). In a study by Ogbol et al. (2011), resistance associated with chromosomal mutations in fluoroquinolone targets reached approximately 70%

in Gram-negative enteric isolates (Ogbol et al. 2011).Three plasmid resistance mechanisms have also been identified for quinolone resistance: specific (QepA) or non-specific (OqxAB) quinolone ejection pumps; acetylation of ciprofloxacin and norfloxacin by AAC(6′)-Ib-cr; and protection of the quinolone target (DNA gyrase and topoisomerase IV) by protein encoded by qnr genes (Zhang et al., 2013). The most common type of quinolone resistance was caused by the aac(6′)-Ib-cr and qnr genes, which were found in 17.2% and 8.2% of bacterial strains that were resistant to quinolones, respectively (Ogbol et al., 2011), whereas just 3.2% of these strains have the qepA gene. This rate was significantly greater in Nigeria in 2017, where 36.7% and 5%, respectively, of 108 samples of multidrug-resistant P. mirabilis bacteria were found to have the qnrA and aac(6′)-Ib-cr genes. These genes were frequently found on class 1 and class 2 integrons that were linked to beta lactamase genes (blaTEM or blaCTX-M) (Allabi et al., 2017).

The qnrB10 and aac(6′)-Ib-cr genes have been found to be tightly associated with ESBL genes, however the qnrB19 and qnrD genes are not (Albornoz et al., 2014). Given that the majority of isolates with the qnrD gene belong to the Proteus or Providencia genera (Giard et al., 2014), The qnrD gene may have started in the Morganellaceae family and then expanded to other Enterobacteriaceae species, according to research. The qnrD gene is found on short, unpaired plasmids that are 2.7 kb in size in these two sexes, as well as other plasmids that are transposable via moving input cassette (mic) elements (Giard et al., 2014). Two inverted repeat (IR) sequences without a transposable gene and a target repeat site, which are markers of gene transfer events, are what define the mic elements (Giard et al., 2014). plasmids carrying qnrD genes are widely distributed throughout the world, as in China (Zhang et al., 2013), Argentina (Albornoz et al., 2014), Nigeria (Ogbulo et al., 2011), Italy (Mazzariol et al., 2012), and France (Giard et al., 2014). The qnrC gene was described in 2009 in China in a strain of Proteus mirabilis bacteria, and it only causes a decrease in sensitivity to ciprofloxacin and levofloxacin. This gene is included on a 120-kb plasmid that also contains resistance determinants for trimethoprim, ampicillin, and sulfamethoxazole (Wang et al., 2009). The genes qnrA (Ogbolo et al .,2011) and qnrS (Mokraka et al.,2012) have rarely been described in Proteus bacterial isolates. The qnrA gene is located on a plasmid that ranges in size from 20 to 100 kilobytes, above ampR (which codes for the repressor of the ampC gene) and qacEΔ1 (a partially deleted gene believed to contribute to resistance to quaternary ammonium compounds), and below ISCR1. The qnrA gene and the blaVEB-6 (SGI1-V) gene were discovered on the same genomic island in a different strain of Proteus mirabilis that was isolated in France in 2009 (Sebur and Neuwirth, 2011).

In an environmental Proteus mirabilis strain, the qnrA gene was shown to be chromosomally expressed and surrounded by two copies of ISCR1 and an IS10 element (Gayol et AL.,2016). Among the most potent antibiotics against these bacteria are meropenem, piperacillin-tazobactam, and ceftazidime, which stopped the growth of over 98% of clinical strains collected from US hospitals between 2011 and 2013. (Castaneira et al., 2015). Although the first reported broad-spectrum beta-lactamase (ESBL) enzymes were of the TEM type , diversification of these enzymes occurred in the first decade of the second millennium with the emergence of CTX-M enzymes, as was observed concurrently in other Enterobacterales such as Escherichia coli (E. coli) and Klebsiella pneumoniae (K. pneumoniae). CTX-M enzymes can be divided into five distinct groups based on the sequence of essential amino acids (groups 1, 2, 8, 9, and 25). Typically, the production of broad-spectrum beta-lactamase (ESBL) enzymes is acquired by Proteus spp. bacteria. elevated resistance to ceftazidime, cefotaxime, and aztreonam. In 1999, a French study revealed the first P. mirabilis bacteria that produced ESBL (De Champs et al., 2000). The frequency of Proteus species that produce ESBLs. Spain produces 1.3% of ESBL enzymes, France produces 3.3%, Greece

produces 5.9%, Croatia produces 12.6%, Poland produces 14.5%, and Italy produces 16.3%.For instance, strains of Proteusia mirabilis that produce broad-spectrum beta-lactamase (ESBL) were found in a hospital in Hong Kong (Tonkić et al., 2010 ;Nijssen et al., 2004;Ho et al., 2005) Between 1999 and 2002, the percentage of these strains rose from 0% in 1999 to 18.5% in 2001 and subsequently to 25.8% in 2002 (8 out of 31 Proteusia mirabilis isolates). Broad-spectrum beta-lactamase enzymes, such as SHV-5, TEM-11, CTX-M-13, and CTX-M-14, were more varied in these isolates (He et al., 2005). According to reports, 7% of Proteus mirabilis bacteria in Eastern Europe, 10% in Latin America, and 2.2% in North America are ESBL-producing bacteria. In a large-scale investigation conducted in 2013 with 8,800 gut bacterial isolates from the United States, 8.4% of the bacteria produced broad-spectrum beta-lactamase enzymes. Although the majority of the bacteria in this study that produced broad-spectrum beta-lactamase enzymes were Escherichia coli (49.5%) and Klebsiella pneumoniae (40.1%), they only made up 5.2% of the Proteusia mirabilis isolates (Castanehira et al., 2015).

In many countries, carbapenems (imipenem, ertapenem, meropenem, doripenem) are still considered "last resort" antibiotics for treating severe infections caused by intestinal bacteria that produce broad-spectrum beta-lactamase enzymes. the latest emergence and prevalence of carbapenemase-producing enteric bacteria (CPE) has become a main public health issue due to the limited clinical treatment options available. These bacteria frequently cause invasive infections that are linked to a higher death rate. Among the acquired carbapenemases found in Proteus spp. bacteria are. The following: (A) Carbapenemases of the Ambler A class, including KPC-2, (B) metallo-beta-lactamases (MBLs, Ambler B class), include NDM-1, VIM-1, and IMP-type (C) OXA-48 or, more intriguingly, OXA-23, OXA-40, and OXA-58 (carbapenemases have been particularly found in Acinetobacter spp.) are examples of Ambler D class carbapenem-degrading beta-lactamases (CHDLs). KPC, NDM, VIM, and OXA-48 are the most prevalent forms of carbapenemase in Europe. KPC and IMP are the most prevalent carbapenemases in the US and Japan, respectively (Naas et al., 2008; Ohno et al., 2017).

6-Genomic Similarity Of P.Mirabilis Between Animal And Human

Increased genetic similarity was spotted among P.mirabilis isolates from human to animal , and linked with product and environment . Pet isolates were shown to have a significant degree of genetic similarity to human isolates, with some strain pairings originating from individuals and pets living in similar households. Using urine samples from 76 humans and 107 pets suffering from UTIs, Marquez et al. created a phylogenetic tree based on PFGE genotyping to assess the genetic relatedness of the isolates (Marquez et al., 2019). Of the (39) groups (17) contained for to humans and animals isolates, with genetic same ranging from (80- 100%). the canines isolates of P.mirabilis shows a perfect match (100%) With human isolation, while with feline isolation showed a match of over 90% with a human strain (Marquez et al., 2019).

Marquez and other ,found human and dog pair carrying genetically related strains of the bacterium P.mirabilis in a disconnect investigation. The animal-derived clinical strain FMV4938/07, which was isolated from a dog with a UTI, and these strains were 82.5% identical (Marquez et al., 2021). An isolated sample of Proteus mirabilis bacteria from the feces of dog in a separate household showed genetic similarity to two isolated samples of community-acquired urinary tract infection, at 80.9% and 88.9% respectively (Marquez et al., 2021). Wang and colleagues identified the P. mirabilis strain CC16012 from a dog that had diarrhea; this strain was closely related to the US strain Crl143, which originated in humans (Wang et al., 2020).The mrpA gene sequence of P.mirabilis bacteria isolated from pet turtles shows

(94.9%) & (96.4%) same the samples isolated from human respiratory tract infections and urinary tract infections, respectively (Patherana et al., 2018). In animal experiments, Yu et al. isolated Proteus mirabilis bacteria from the feces of diarrheal primates, and showed 99.6% genetic similarity to the HI4320 strain associated with human urinary tract infections (Yu et al., 2015).

Similarly, five duck isolates of Proteus mirabilis showed close genetic affinity with strain HI4320 and other referees strains from different source, based on the atpD gene sequence (Algammal et al., 2021). Isolates from animal product showed increases genetic similarity to those taken from source of human. In 2021 dependent on PFGE analysis , reported that the elevated same spotted between an isolate from a broiler chicken and an isolate from feces of humans was (83.3%) with only two ranges differing (Yu et al., 2021). likewise , Sanchez et al. confirmed the existence of exclusived clonal connection between isolates derived from chickens and those responsible for community-acquired UTIs, especially those in the C01 group . Notably, two strains in this group—one isolated from flesh chicken and the other from a UTI patient—showed 100% genetic similarity to spp. by PFGE (Sanchez et al., 2023). Additionally, strain JZ109's blaNDM-1 gene exhibited 100% nucleotide similarity to SGI1-1NDM, the first clinically documented strain of P. mirabilis from China, with only one base difference (Ma et al., 2022).

7- Interpretation

Proteus mirabilis bacteria is becoming a major source of zoonotic and foodborne illnesses, as evidenced by its high virulence, diverse antibiotic resistances, and dissemination and adaption across a variety of animal hosts and food products. The important need for integrated surveillance systems is highlighted by the widespread finding of clinically significant antibiotic resistance genes, including as blaNDM, mcr-1, and tmexCD3-toprJ1, in isolates from farm animals, pets, wildlife, and animal-based commodities. Global genomic study has demonstrated the spread of antibiotic resistance genes between humans, animal sources, and the environment, underscoring their crucial role in the One Health concept. Antibiotic residues and drug-resistant bacteria found in urban home wastewater and farm animal waste can move to wildlife habitats through environmental media, such as soil and water bodies . The blaSHV-12 gene has been found in strains of wild animals that are in close proximity to urban and agricultural regions, such as wild boars and birds of prey.

This occurrence suggests that populations of wild animals are frequently exposed to environmental contamination with drug resistance brought on by human activity. Additionally, the discovery of resistance genes in contaminated butchery environments and disease vectors like houseflies indicates a still unidentified mode of transmission that calls for greater research. Proteus mirabilis has been demonstrated to cause comparable illnesses in people and animals, indicating a common bacterial pathogenicity mechanism that is not exclusive to any one host. Since horizontal transmission of these genes has been noted among isolates of captive pandas through transmissible gentetic factors, pathogenicity may be disseminated in conjunction with the bacteria and their virulence genes (Yang et al., 2025). Comparative assessments of genetic virulence patterns between the two sources are currently lacking, despite the fact that multiple studies have shown that Proteus mirabilis isolates from people and animals include virulence genes. It should be mentioned that Proteus mirabilis populations are showing increasing levels of diversity, according to genetic studies.

To better comprehend their capacity to cause disease in a variety of hosts, greater research into virulence patterns and a more thorough examination of their pathogenic pathways is crucial. In order to better understand the habitat and evolution of Proteus mirabilis bacteria, future research should concentrate on

a "One Health" strategy that combines data from the Environmental, food, animal, and human sectors. Whole genome sequencing and other molecular epidemiology methods antibiotic resistance analysis, virulence analysis, and comparative genomics will be of large value in tracking the mechanisms of its transmission and modification . Additionally, research on quorum sensing host pathogen interaction , and biofilm development may provide new targets for intervention. Proteus mirabilis bacteria continue to adapted and dispersal under the pressure of antibiotics choice, the need for coordinated international pains to lessen the risk to food safety and public health is becoming to an increasing extent apparent.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/2076-2607/14/2/444 , https://www.mdpi.com/2076 2607/13/9/2060 , Antibiotic resistance of Proteus mirabilis from animals and animal-derived products and other .

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