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DEMOGRAPHIC, CLINICAL AND ANTIBIOTIC SUSCEPTIBILITY ANALYSIS OF PIGMENTED AND NON-PIGMENTED SERRATIA MARCESCENS : A COMPARATIVE STUDY AT A TERTIARY CARE CANCER HOSPITAL

Clinical Microbiology

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ABSTRACT

Introduction: Serratia marcescens (S. marcescens) are diminutive, motile, gram-negative bacilli. They are distinguished by their ability to ferment glucose, mannitol, mannose, salicin, and trehalose, producing acid and occasionally gas. They are indole-negative, urease-negative, and can grow on Simon's citrate medium, with certain strains producing a red non-diffusible pigment. Non-pigmented S. marcescens biotypes are also known to occur and cause serious infections. These strains have increased lethality due to cytotoxin synthesis and their resistance to commonly used antibiotics. **Methods:** A retrospective investigation was conducted in the Department of Microbiology, at Tata Memorial Hospital to ascertain and analyze the antibiotic susceptibility patterns in non-pigmented isolates of Serratia marcescens and compare it across the pigmented strain. **Results:** 115 isolates were included in this study, 80 of which were non-pigmented against 30 that were pigmented. A greater incidence 34.78% (40/115) of infections due to S. marcescens was observed among middle age (51 – 60 years) males, of which majority 62.5% (25/40) were non-pigmented. **Conclusion:** The non-pigmented strains were more resistant to routinely prescribed antibiotics. The hazards associated with infections due to Serratia marcescens in immunocompromised people are significant; thus, the early detection, accurate detection and treatment of such infections is of utmost importance.

KEYWORDS

Non-pigmented, Serratia marcescens, antimicrobial resistance pattern, Epidemiology

INTRODUCTION

Serratia was first described by Bartolemeo Bizio, an Italian pharmacist, in 1819 as the cause of the red discoloration of boiled cornmeal, thereby discrediting the claim that the growth was due to the miraculous appearance of blood. [1] Military experiments, primarily used the red pigment from a biological warfare perspective. [2] This bacterium was considered a soil-water pathogen, until the late 20th century when it started causing nosocomial infections. The important reservoirs in epidemics are the digestive tract, the respiratory tract, the urinary tract, and the perineum of neonates and the artificial nails of adults and health care workers.[3] Researchers also linked them to an increasing number of healthcare-associated infections, primarily in sick patients.[4]

S. marcescens is the most important member of the genus Serratia. It is often associated with a variety of human infections, like pneumonia and septicemia in patients with reticuloendothelial malignancies who are receiving chemotherapeutic agents.

Serratia marcescens can secrete virulence factors, including DNase, prodigiosin, lipase, hemolysin, proteases, chitinase, and biosurfactants, and form biofilms through Quorum Sensing regulation. [5] Prodigiosin, which is a non-diffusable pigmented imparts the characteristic red colour to the colonies. It is produced by cells aerobically at temperatures upto 32 . The main antimicrobial action of prodigiosin is by membrane damage.[6] Only a small proportion, usually <10 %, of the strains responsible for infection are pigmented.[7] Some strains have the ability to produce pigment, while others inhibit pigment production by decreasing prodigiosin levels. Such non-pigmented strains also produce toxins thus contributing to their virulence. Regulation of pigmented production is modulated by quorum sensing.[6] Starting in the 1960s, uncolored strains of S. marcescens were more common in clinical settings than colored strains.

Recently, cytotoxin production was detected in non-pigmented isolates of S. marcescens , and this characteristic has been considered an important virulence factor in several species of bacteria.[8] The healthy human being does not often become infected by Serratia, whereas the hospitalized patient is frequently colonized or infected.[9] Serratia marcescens could be said to be an opportunistic pathogen but it is difficult to determine its contribution in progression of disease.[10]

Earlier, fluoroquinolones with aminoglycosides and third-generation cephalosporins were used for treatment of infections with Serratia marcescens. Some types of beta-lactams and tetracyclines do not work on Serratia spp., but quinolones and aminoglycosides can hurt them. [11] However recent development of resistance by various mechanism has been seen in these bacteria. Two Polish hospitals conducted a study in 1996–2000 and found that 19% (67/354) of S. marcescens isolates produced ESBL. [12] A systematic review done by Zivkovic Zarik R et al[13] concluded that treatment should be done by a combination of carbapenems or aminoglycosides with third-generation cephalosporins. Cotrimoxazole is the most effective option in infections of the urinary tract.

The aim of this study was to explore the epidemiology and antibiotic susceptibility pattern in Non-pigmented strains of Serratia marcescens at a tertiary care cancer hospital and compare it against the pigmented strains.

MATERIAL AND METHODS

We conducted a retrospective study and identified 115 clinical isolates of S. marcescens from various units during the period of June 2023 to February 2024. The identification of the strains was done with help of Vitek 2 Compact system and determined their antibiotic susceptibility susceptible, intermediate, or resistant, in accordance with CLSI[14] guidelines. The antibiotics included in this study were amikacin, ceftazidime, Cefoperazone-sulbactam, piperacillin-tazobactam, ciprofloxacin, cefotaxime, and gentamicin. Majority of the infections were caused in outpatients.

RESULTS

A total of 115 Serratia marcescens isolates were analysed comprising 30.43% (35/115) pigmented and 69.56% (80/115) non pigmented strains from the samples received in the lab.

Majority of isolates, both pigmented and non-pigmented, were recovered from Surgical oncology 93.91% (108/115) compared to 6.08% (7/115) from Medical oncology.

Category	Sub-category	Pigmented (n=)	Non-Pigmented (n=)	P- value
Age	41-60 years	22	42	0.281
	>60 years	8	17	0.281

	15-40 years	3	20	0.281
	<14 years	1	2	0.281
Gender	M	23	43	0.217
	F	11	38	0.217
Location	IPD	15	31	0.718
	OPD	17	42	0.718
	ICU	2	8	0.718
Sample type	Wound swab	13	21	0.275
	BAL/Sputum	11	28	0.275
	Body fluid	8	13	0.275
	Tip	1	7	0.275
	Tissue/Pus	1	7	0.275
	Blood	0	5	0.275
Antibiotic Sensitivity	AN	31	60	0.07
	CAZ	30	63	0.297
	CFS	32	65	0.112
	CIP	29	57	0.148
	GM	30	64	0.366
	IPM	32	65	0.112
	MEM	32	65	0.112
	TZP	32	65	0.112

Majority of pigmented isolates were recovered from OPD 51.30% (59/115) followed by IPD 40% (46/115) and least by the ICU 8.70% (10/115).

Majority of pigmented strains of Serratia marcescens were recovered from middle age group patients 62.8% (22/35) followed by elder age group 22.85% (8/35). The non pigmented strains showed similar results in age distribution. Statistical analysis revealed no significant difference in the age distribution between pigmented and non-pigmented strains. (p=0.282)

Among the pigmented strains, 65.71% (23/35) isolates were from males and 31.42% (11/35) were from females, while non-pigmented strains included 53.75% (43/80) isolates from males and 38.75% (31/80) from females. No significant difference was observed in the gender distribution. (p=0.217)

Among the pigmented strains, the most frequent source was Wound swabs (n=13), while non-pigmented strains were predominantly isolated from BAL/Sputum (n=28). No significant difference in specimen distribution type was noted. (p=0.275)

The sensitivity rates for the isolates displayed a difference where pigmented isolates exhibited higher sensitivity rates across most antibiotics compared to non-pigmented isolates. Amikacin showed a difference of sensitivity 91.4% (31/35) in pigmented and 73.75% (60/80) in non-pigmented strains, followed by Ciprofloxacin showing sensitivity of 85.7% (29/35) in pigmented opposed to 70% (57/80) in non-pigmented strains. No significant difference in sensitivity of Amikacin (p=0.070) and Ciprofloxacin (p=0.148) was noted.

Cefoperazone showed lower comparable rates of sensitivity as, 91.4% (32/35) in pigmented compared to 78.75% (65/80) in non-pigmented, which was also the response in case of Imipenem and Meropenem. No significant difference was noted in the sensitivity of Cefoperazone, Imipenem and Meropenem. (p=0.11)

DISCUSSION

Serratia spp, is a motile Gram negative bacillus, belonging to the Enterobacteriaceae family. It is a known cause of infection in humans especially in immunocompromised individuals. Amongst the pathogenic strains, S. marcescens is the most common followed by S. liquefaciens complex.

While a variant of S. marcescens produces a red pigment called prodigiosin, there are other which fail to be pigmented.

There is global variability in the distribution of non-pigmented strains of S. marcescens. Earlier, in the study reported by Clayton et al[10], only 1 out of 181 strains were pigmented. Similarly, 100% of strains were pigmented producing in the study by Khanna et al[3]. Earlier few studies were seen on non-pigmented strains of Serratia spp. [15], but as the incidence of infections have increased more research has been done on its role as an opportunistic pathogen. Ewing et al (1962)[16] reported in their study that 27% of the strains were non pigmented which is in comparison to the findings of 30.43% in our study.

Xiang T et al[17] have disserted in a study that the non-pigmented morphotypes possessed a competitive growth advantage over the parent strain. The pig gene which is responsible for red pigment is present completely in non-pigmented strains but altered at transcriptional level.[17]

The grouping of specimen type shows diversification amongst the strains. In contrary to study by Mlynarczyk A et al[18], where 70% of isolated S. marcescens originated from urine, the present study showed that, majority 37% (13/35) of strains of pigmented S. marcescens were recovered from wound swabs. Ilaria et al[19] in their study isolated 125 strains from broncho-aspirates (31.6%), which was in concordance with current study showing 31.42% (11/35) pigmented isolates from respiratory samples.

Serratia spp can survive in harsh conditions including in antiseptics, disinfectants and on moist surface in hospitals. Being commonly found in environmental reservoir, they can easily contaminate wounds and medical devices. Thus patient with compromised immunity are more prone to infections.

In a recent study conducted by Ilaria et al[19] resistance rates were observed at 20.7% for ceftazidime, 25.3% for cefotaxime, and a reduced rate of 8% for cefepime in 2022. Their study also highlighted increasing rates of resistance to Imipenem going from 4,25 to 7.5% during their study period. This was comparable to the resistance rates in the present study, with non-pigmented strains demonstrating higher resistance to most antibiotics. Amikacin showed higher resistance (26.25%) to non-pigmented compared to pigmented (8.57%). Cefotaxime showed a resistance percentage of 25% (non-pigmented) as opposed to 11.43% (pigmented), which was similar to Ciprofloxacin 30% (non-pigmented) against 14.28% (pigmented).

Muto Y et al[20] in their study explained that transfer of R plasmid could be a probable cause for the significant increase of non-pigmented, drug resistant strains of S. marcescens in nature. They also emphasized on the importance of identification of non-pigmented strains of Serratia which may pose an obstacle for effective treatment.

Serratia marcescens produce beta-lactamase, and carbapenem resistance is conferred by AmpC overexpression with carbapenem hydrolysing activity in some strains.[6] The metallo-beta-lactamase GIM-1 and NDM have also been described in S. marcescens.[21] Serratia along with other Enterobacteriaceae fall in the Priority 1(Critical) group of WHO list of pathogens that require research and development for new antibiotics as per November 2017 report.

Infections caused by the organism may be difficult to treat because of resistance to a variety of antibiotics, including ampicillin and first and second generation cephalosporins. This is seen in the case report by Priyamvada Roy [15] where a 64-year-old male patient having squamous cell carcinoma of the left retromolar trigone, soft palate and buccal mucosa, undergoing chemotherapy, presented with fever, cough with expectoration and breathlessness. On culture, Serratia marcescens was isolated which was sensitive to Amikacin, Gentamicin, Piperacillin-tazobactam, Cefotaxime, Cefepime, Ciprofloxacin, Trimethoprim-sulfamethoxazole, Imipenem, Ertapenem and resistant to Cefuroxime axetil, Cefuroxime and Amoxycillin-clavulanic acid.[15]

A case report by Sevencan NO et al[22] showed an 89-yr-old male diagnosed Squamous cell carcinoma, developed ulcerated tumor. On culture, non-pigmented Serratia marcescens was identified sensitive to Ciprofloxacin. They emphasized on the uncommon location of the tumor with simultaneous occurrence of Non pigmented Serratia marcescens.

In contrast to other studies on hospital acquired infections, the current study was unable to determine any effect on patient's clinical outcome.

CONCLUSIONS

Serratia marcescens is an uncommon opportunistic pathogen, essentially more fatal because of the cytotoxin production coupled with higher antibiotic resistance in non-pigmented strains. The risk associated with immunocompromised patients, like in the current study are very high, pertaining to which identification and treatment should be prompt. This study attempted to evaluate a difference between Clinical and antibiotic sensitivity pattern of the two types. Although a difference was seen in the sensitivity pattern it wasn't significant. However, this demands further research to establish a valuable contribution to diagnosis and treatment of infections with Serratia marcescens.

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