Clinical manifestation and microbial profiling of recurrent MDR microorganisms associated with head and neck infection- a retrospective study

Smarita Lenka,[1] Debasmita Dubey,[2] Shakti Rath,[3] Somadatta Das,[4] Santosh Kumar Swain[5]

[1]Department of Otorhinolaryngology, IMS & SUM Hospital, Siksha O Anusandhan deemed to be University, Kalinga Nagar, Bhubaneswar, Odisha; [2]Department of Medical Research, IMS and SUM Hospital, Siksha 'O' Anusandhan Deemed to be University, Kalinga Nagar, Bhubaneswar, Odisha; [3]Central Research Laboratory, Institute of Dental Sciences, Siksha 'O' Anusandhan Deemed to be University, Kalinga Nagar, Bhubaneswar, Odisha; [4]Central Research Laboratory, IMS and SUM Hospital, Siksha 'O' Anusandhan Deemed to be University, Kalinga Nagar, Bhubaneswar, Odisha; [5]Department of Otorhinolaryngology, All India Institute of Medical Sciences, Bhubaneswar, Odisha, India

Abstract

Head and neck infection (HNI) can lead to life-threatening complications, including death. The purpose of this study is to look at the entire clinico-demographic profile of patients with HNI as well as the microbiologic profile of recurring bacterial infection cases with a variety of symptoms. A retrospective cross-sectional study was conducted on 1080 HNI patients in a tertiary care hospital in Bhubaneswar, Odisha, India, from January 2018 to December 2022. Of the 1080 cases, 771 (71.39%) were males, 309 (28.61%) were females, and 603 (55.83%) were from rural areas reporting to a tertiary care hospital. 62% of the cases were between the ages of 31 and 60. Neck abscesses account for 570 (52.78%) of all cases, with parotid abscesses accounting for 233 (21.57%), peritonsillar abscesses accounting for 170 (15.74%), otitis media 32 (2.96%), and oral cavity infection accounting for 26 (2.41%). In 854 (79.07%) cases, the etiology was odontogenic, followed by sinus in 188 (17.41%) and otogenic in 38 (3.52%). The most common presenting features were neck swelling in 537 (49.72%) cases and face swelling in 238 (22.04%) cases, followed by jaw pain in 26 (2.41%) cases and others. Patients were hospitalized for an average of 11.82±4.38 days. Treatment and recurrence had a strong significant relationship (p 0.001). Microbiologic investigation of recurrent patients revealed 12 microorganisms, including bacteria and fungus, mainly multidrug-resistant in given ascending order *Staphylococcus aureus* (26.74%), *Klebsiella pneumoniae, Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Escherichia coli*, *Candida albicans* (4.65%), *Aspergillus fumigatus*, *A. flavus*, *A. niger*, *C. tropicalis*, *C. glabrata*, *C. krusei*. Apart from colistin, almost all antibiotics were highly resistant to gram-negative bacteria, whereas against *S. aureus*, benzylpenicillin, and oxacillin showed 100% resistance, followed by erythromycin (91.3%), levofloxacin (86.96%), and ciprofloxacin (82.61%). This exploratory study would aid in determining the HNI burden and epidemiology, as well as their treatment status.

Introduction

Head and neck infections (HNI) commonly arise through the odontogenic, oral, or otological region and come up with various complications.[1-3] The treatment procedure is developing, but the infection rate is also increasing instead of its downfall. It may be initiated by poor hygienic habits, smoking, alcohol consumption, or environmental factors like polluted air and water.[4] Different studies have shown the mirror of these factors to society, but there have yet to be successful mass effects. Infections involving the sites are initially much more complicated to diagnose as their anatomical construction is a little complex. Patients of all ages, particularly children and young adults, frequently have facial and cervical infectious processes, which pose a clinical concern. A complication of infection increases when it spreads beyond the primary site of origin, like the oral cavity, odontogenic region, rhinitis, or otitis media, where the infection is only at cellulitis or abscess formation adjacent to the sites of infection.[5,6]

Infection symptoms and signs are clinically apparent in the head and neck, allowing for a presumptive diagnosis. The most frequent cause in children and young people is a tonsillar infection, but the most frequent cause in older is an odontogenic infection. The other potential head and neck infection sources are salivary glands, nasal sinuses, middle ear, mastoids, cervical lymph nodes, and trauma.[7] Head and neck infections are becoming more common and have significant death rates and consequences. It can migrate from the skull base to the mediastinum and affect the other spaces. Nevertheless, it is clinically difficult to identify the implications, such as acute air-

Correspondence: Shakti Rath, Central Research Laboratory, Institute of Dental Sciences, Siksha 'O' Anusandhan Deemed to be University, Kalinga Nagar, Bhubaneswar, Odisha, India.
E-mail: dr.shaktirath@gmail.com

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way obstruction and mastoids, cervical lymph nodes, and trauma.[8-11]

Patients with diabetes, compromised immune systems, and advanced age are more susceptible to complex head and neck infections.[4] According to a study conducted in the US, 11% adult population is diagnosed with sinusitis, and 2.1% of the population accounts for sore throat, which is an early sign of a significant head and neck infection.[12] Particularly in diabetic individuals, it has been demonstrated that there is a higher risk of suppuration, multi-space infections, and the requirement for numerous surgical treatments. Refusing to have head and neck abscesses surgically treated sooner increases the risk of complications and lengthens hospital stays.[5,13] In these populations, for the prompt identification of clinical problems, better analysis of epidemiology, and to fix problems regarding treatment failure, there should be analytical, clinical profiling of recent year visiting patients for a new step towards better treatment. Various analyses were done worldwide to estimate the overall clinical profiling of head and neck infections. Still, in some regions, it needs to be addressed by people underestimating the severity beyond the infection or sometimes by self-medications which may increase infected cases and recurrence and tend to mild to moderate and then severe.[15] Moreover, most infectious diseases re-occurred due to the multidrug resistance activity of associated microorganisms.[16-18] In this case, the infection can be controlled only through region-specific epidemiology of pathogen identification and their drug susceptibility pattern for early diagnosis and therapeutic purposes.

Literature regarding individual head and neck infection sites is readily available as most studies aim to solve it independently concerning their expertise area. But this retrospective study covers almost all clinical profiles and other necessary information of patients suffering from any sites of HNI attending the Department of Otorhinolaryngology, IMS & SUM Hospital, Bhubaneswar, Odisha, India.

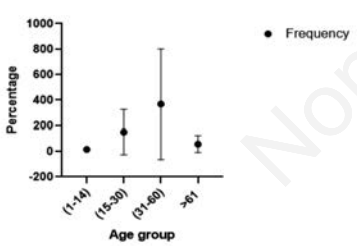

Figure 1. Age distribution of patients.

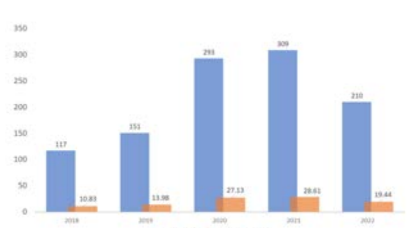

Figure 2. Yearly distribution of patients diagnosed with head and neck infection.

Materials And Methods

Study subjects

This hospital-based retrospective study was conducted with all age groups of head and neck infection patients who attended both the out-patient department (OPD) and in-patients department (IPD) of Otorhinolaryngology (ENT) in this hospital from January 2018 to August 2022. Patients only suspected of infection were included and associated with thyroid gland cysts, infection due to external cervical injury (traumatic or surgical), neoplastic pathology, tumor-associated cases, and clinical cases with insufficient information were excluded from this study. Patients were categorized into four groups that were compared: pediatric (aged 1-14 years), young (aged 15-30 years), adult (aged 31-60 years), and seniors (aged 61 years above). A comparison of data from patients with different sites of infection and their associated factors was performed.

Sample collection and processing

Using Stuart's transport medium, swab samples were collected and transported from recurrent patients from infection sites. They were cultured using blood agar for bacterial growth and Sabouraud dextrose agar for growing fungus. The culture was subjected to Vitek 2 for accurately identifying and analyzing antibiotics' minimum inhibitory concentration (MIC) against individual microorganisms.

Statistical analysis

The collected data were analyzed using the Statistical Package for the Social Sciences (SPSS, version 29.0.0.0). Comparisons between groups of categorical variables were made using the Chi-square test, and a multiple linear regression model was performed using Graph pad Prism 9 to predict or analyze other variables like sites of infection and annual distribution. The significance p value <0.05 was considered statistically significant.

Results

Demographic details of patients

According to their clinical manifestation, 1080 head and neck infection patients were selected during the five years of the study period. Out of the total head and neck infection registered patients, 771 (71.39%) were male, and 309 (28.61%) were female in a ratio of (247:301), where males predominated in all infected age groups. Out of 1080 cases, 28 (2.59%) patients belonged to the pediatrics age group, 275 (25.46%) to the young age group, 674 (62.41%) to the adult age group, and 103 (9.54%) of senior citizens (Figure 1) and the mean ±SD of all age group of patients are 41.18±15.04 (Table 1).

Yearly, seasonal, and regional information

The highest peak of head and neck infection patients was throughout the study period 309 (28.61%) in 2021 (Figure 2). The distribution of patients with head and neck infection revealed seasonal variation:

Table 1. Demographic, social status of patients suffering from head and neck infection.

Demographic Social status			
Gender	**Number**	**Percentage**	**Mean±SD**
Male	771	71.39	-
Female	309	28.61	-
Age			
Pediatric (1-14)	28	2.59	6.64±4.75
Young (15-30)	275	25.46	24.57±3.77
Adult (31-60)	674	62.41	45.39±8.18
Seniors (> 61)	103	9.54	67.15±6.15
Locality			
Urban	477	44.17	-
Rural	603	55.83	-

395 (36.57%) during summer > 303 (28.06%) during rainy > 277 (25.65%) in spring > and 105 (9.72 %) in winter (Table 2). There 603 (55.74%) HNI patients enrolled were from rural areas, and 477 (44.17%) were from the urban population of patients (Table 3).

Detail evidence on sites and origins of infection

For easier infection distribution, infection locations associated with HNI were divided into compartments such as the ear, nasal, neck, and oral. But individual sites of infection were analyzed individually from the complete data set. Neck abscess was the most prevalently diagnosed with 570 (52.78%) patients, followed by parotid abscess 233 (21.57%) and peritonsillar abscess 170 (15.74%). The location of HNI varied among the different age groups. Neck abscesses occurred in all age groups, but the average group of age mean±SD (41.38±14.71) suffered from neck abscesses which are near to the mean±SD of the overall age group 41.18±15.04. Therefore, neck abscess was diagnosed higher times than other infection sites in all age groups (Table 4). The predisposing cause of HNI was determined that otological infection 38 (3.52%), sinus infection 188 (17.41%), and odontogenic infection 854 (79.07%) were the origin of initiation, where the odontogenic infection was the highest cause of origination of HNI that includes dental infections and oropharyngeal infection as well (Table 4).

Clinical manifestation, including all symptoms of HNI, indicated infection at which the diagnosis process started. Face swelling, ear pain, headache, jaw pain, neck pain, sore mouth, swollen neck, and throat pain were the common clinical characteristics with all populations where most of the patients were highly symptomatic with swollen neck 537 (49.72%), followed by face swelling 238 (22.04%) and throat pain 180 (16.67%) (Table 3). In the sites of

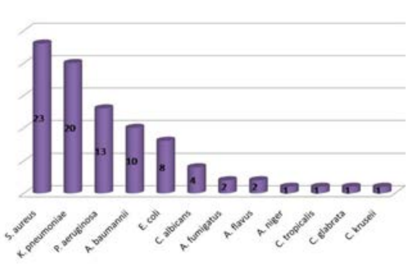

Figure 3. Frequency of microorganisms isolated from recurrence patients.

Table 2. Seasonal and monthly distribution of patients.

Seasonal distribution	Monthly distribution	Number	Percentage
Spring	Jan	59	5.46
	Feb	77	7.13
	Mar	141	13.06
		277	25.65
Summer	April	135	12.50
	May	120	11.11
	Jun	140	12.96
	395	36.57	
Rainy	July	162	15.00
	Aug	97	8.98
	Sep	44	4.07
		303	28.06
Winter	Oct	40	3.70
	Nov	38	3.52
	Dec	27	2.50
		105	9.72

Table 3. Clinical manifestation in accordance with internal and external symptoms.

Clinical manifestation	Number	Percentage
Internal symptoms		
Airway blockage	2	0.19
Fever	3	0.28
Jaw pain	26	2.41
External jaw swelling	1	0.09
Sore throat	4	0.37
Throat pain	180	16.67
Ear pain	32	2.96
Headache	8	0.74
Neck pain	29	2.69
External symptoms		
Face swelling	238	22.04
Jaw swelling	1	0.09
Sore mouth	19	1.76
Swollen neck	537	49.72
Swollen throat	1	0.09

Table 4. Origin, complications, and diagnosis of infections.

Origin of infection	Number	Percentage
Otological infection	38	3.52
Odontogenic infection	854	79.07
Sinus infection	188	17.41
Complication		
Biofilm formation	276	25.56
Mold formation	38	3.52
Pus deposit	766	70.93
Diagnosis	**Number**	**Percentage**
Hypopharyngeal abscess	2	0.19
Laryngitis	4	0.37
Neck abscess	570	52.78
Oral cavity infection	26	2.41
Otitis media	32	2.96
Parapharyngeal abscess	1	0.09
Parotid abscess	233	21.57
Parotid gland infection	8	0.74
Peritonsillar abscess	170	15.74
Retropharyngeal abscess	6	0.56
Sinusitis	10	0.93
Submandibular gland infection	18	1.67

infection, complications like biofilm formation were 276 (25.56%), mold formation was 38 (3.52%), and pus deposit was 766 (70.93%; Table 4).

Rate of severity, implementation of treatment, and recurrence

The majority of populations, 695 (64.35%), had a moderate rate of infection in the same way 311 (28.80%) were a mild rate, and 74 (6.85%) had a severe rate of infection. Hospitalization was needed by 650 (60.19%) patients having a severe and moderate rate of infections, and 430 (39.81%) were not hospitalized as some of them were treated with minor surgery, 142 (13.15%) and empirical antibiotic therapy 297 (27.50%). Nearly all patients who underwent surgical drainage (59.35%) were hospitalized for a mean±SD, 14.03±3.23 period. Recurrent HNI was observed in 86 (7.96%) patients, 5 in the pediatric group, 19 in the young age group, 53 in the adult group, and 8 in the old age (senior) group (Table 5). Patients who underwent surgical treatment had a more significant number of days of hospitalization compared to minor surgery and those who were implicated by empirical antibiotics. There was a significant association ($p<0.001$) between sites of infection (compartments) and all treatment procedures. 7.96% of recurrences were noted after completion of treatment, whereas 6.11% of recurrences were patients with treated empirical antibiotics, and there was also a significant association ($p<0.001$) between treatment and recurrence. However, no significant difference in gender ($p=0.5$), local status ($p=0.8$), and age group ($p=0.2$) with recurrence.

Among 86 (7.96%) recurrence patients, 66 (6.11%) patients were implemented with empirical therapy, and 20 (1.85%) patients went through surgical drainage (both minor and major surgery). The microbiological investigation (through Vitek 2) of recurrent patients revealed 12 different types of microorganisms (Figure 3), including bacteria and fungus, and according to their drug susceptibility pattern, almost all antibiotics are resistant to most patients.

Table 5. Treatment and management details of HNI patients.

Treatment and management		Number	Percentage
Procedure	Surgical drainage	641	59.35
	Minor surgery	142	13.15
	Empirical antibiotic	297	27.50
Severity	Mild	311	28.80
	Moderate	695	64.35
	Severe	74	6.85
Hospital stay	Yes	650	60.19
	No	430	39.81
Recurrence	Yes	86	7.96
	No	994	92.04
Observation period	(1-5)	149	13.80
	(5-10)	265	24.54
	(11-15)	509	47.13
	(16-20)	142	13.15
	(21-25)	14	1.30
	(26-30)	1	0.09

Table 6. Details of all organisms isolated with antibiotic susceptibility pattern.

Sl.No.	Name of organisms	Frequency (n)	Percentage	Resistance to Antibiotics/antifungals drugs in percentage
1	*Staphylococcus aureus*	23	26.74	BEN-PEN -100; OX -100; GEN -26.09; CIP -82.61; LE -86.96; E -91.3; CD -60.87; LZ -17.39; DAP -17.39; TEI -13.04; VA -4.35; TE - 21.74; TGC -0; NIT -0; RIF -21.74; TMP -65.22
2	*Klebsiella pneumoniae*	20	23.26	AMP -ND; AMX -ND; TI -100; PI -100; CEF -100; CEFAX -ND; CIS -100; CFS -ND; CPM -100; ETP –ND; IMP -60; MRP -100; AK -85; GEN -60; NA -ND; CIP –95; TGC -85; NIT -ND; CL-20; TMP-90
3	*Pseudomonas aeruginosa*	13	15.12	AMP -ND; AMX -ND; TI -100; PI -92.3; CEF -100; CEFAX -ND; CIS -92.3; CFS -ND; CPM -84.61; ETP –ND; IMP -92.3; MRP -92.3; AK -84.61; G EN -84.61; NA -ND; CIP –84.61; TGC -100; NIT -ND; CL-30.76; TMP-ND
4	*Acinetobacter baumannii*	10	11.63	AMP -ND; AMX -ND; TI -100; PI -100; CEF -100; CEFAX -ND; CIS -100; CFS -ND; CPM -100; ETP –ND; IMP -100; MRP -100; AK -90; GEN -100; NA -ND; CIP –100; TGC -0; NIT -ND; CL-10; TMP-80
5	*Escherichia Coli*	8	9.30	AMP -100; AMX-100; TI -100; PI-100; CEF-100; CEFAX -100; CIS-100; CFS -100; CPM -100; ETP – 100; IMP-100; MRP-100; AK-100; GEN-100; NA-100; CIP – 100; TGC -12.5; NIT -37.5; CL-50; TR-75
6	*Candida albicans*	4	4.65	KT -75; IT- 100; FLC-75; AMP- 75; COT-100; MIC- 100; NS-50
7	*Candida tropicalis*	2	2.33	KT -100; IT- 100; FLC-100; AMP- 100; COT-100; MIC- 100; NS-100
8	*Candida glabrata*	2	2.33	KT -100; IT- 100; FLC-0; AMP- 100; COT-100; MIC- 100; NS-100
9	*Candida krusei*	1	1.16	KT -100; IT- 100; FLC-100; AMP- 0; COT-0; MIC- 100; NS-100
10	*Aspergillus fumigatus*	1	1.16	KT -100; IT- 100; FLC-0; AMP- 50; COT-100; MIC- 100; NS-100
11	*Aspergillus flavus*	1	1.16	KT -50; IT- 100; FLC-100; AMP-100; COT-100; MIC- 100; NS-100
12	*Aspergillus niger*	1	1.16	KT -100; IT- 100; FLC- 0; AMP-0 COT- 100; MIC- 100; NS-100

Antibiotics used: AK, Amikacin, AMP, Ampicillin, AMX, Amoxicillin, BEN-P- Benzylpenicillin, CD, Clindamycin, CEF, Cefuroxime, CEF-AX, Cefuroxime Axetil, CFS, Cefoperazone, CIP, Ciprofloxacin, CIS, Ceftriaxone, CL, Colistin, CPM, Cefepime, DAP, Daptomycin, E, Erythromycin, ETP, Ertapenem, GEN, Gentamicin, IMP, Imipenem, LE, Levofloxacin, LZ, Linezolid, MRP, Meropenem, NA, Nalidixic Acid, NIT, Nitrofurantoin, OX, Oxacillin, PI, Piperacillin, RIF, Rifampicin, TE, Tetracycline, TEI, Teicoplanin, TGC, Tigecycline, TI, Ticarcillin, TMP, Trimethoprim, VA, Vancomycin. Antifungals used: AMP, Amphotericin B, COT, Clotrimazole, FLC, Fluconazole, IT, Itraconazole, KT, Ketoconazole, MIC, Miconazole, NS, Nystatin.

Investigation of microbial specimens collected from recurrent patients

Investigation of microbiologic specimens through the Vitek 2 identification procedure gives five different genera and species of bacteria. Only *S. aureus* was gram-positive, and the rest 4 were gram-negative. But the prevalence of *S. aureus* (n=23) was higher than other bacterial and fungal isolates (Table 6). The prevalence of bacterial isolates was high compared to fungal isolates. Only 12 (n=12) cases were identified with fungal cultures, which include *Candida spp.*(n=7) and *Aspergillus* spp. (n=5) (Figure 3). A maximum number of antimicrobial agents were resistant to their respective bacteria/fungi. Apart from Colistin, almost all antibiotics were highly resistant against gram-negative bacteria, whereas in the case of *S. aureus*, benzylpenicillin, and oxacillin revealed 100% resistance, followed by erythromycin (91.3%), levofloxacin (86.96%) and ciprofloxacin (82.61%) (Table 6). Among 12 fungal isolates, there were 4 (n) *C. albicans,* and the rest of 3 (n) *Candida spp.* were identified with single species such as *C. tropicalis* (n=1), *C. glabrata* (n=1), *C. krusei* (n=1). There were 5 (n) *Aspergillus spp*. including *A. fumigatus* (n=2), *A.flavus* (n=2) and *A. niger*(n=1). All fungal isolates were resistant to most of the antifungals (ketoconazole, itraconazole) rather than some of the antifungals like fluconazole and amphotericin B were intermediate against two isolates of *A. fumigatus,* and one isolate of *A. niger* (Table 6).

Discussion

Head and neck infections are an uncommon but severe problem in all age groups. Although intravenous antimicrobial therapy might help reducing the incidence of primary and secondary HNIs, life-threatening complications may arise if not diagnosed or treated promptly. At an early stage, it may have very subtle signs and symptoms, which demand a high index of suspicion and specific diagnostic examination, which may reduce the severity and significant complications. Around 57% of the cases in the age group of 11 to 40 years were reported with HNI by Dudhe P *et al*., 2022,[19] whereas a mean±SD of age 41.18±15.04 was reported in our closely relevant study. Distribution of patients according to seasonal variation revealed a higher number in summer, but this can be different in a different climate.

No significant differences were found in demographic distributions on the HNI of our study with other studies. Unlike our study, there was a high prevalence of male patients (55.26%) compared to females (44.74%) and primarily admitted from a rural background.[20] It is reasonable that HNIs may predominate in specific anatomic spaces according to the initiation of infection. As such, studies[21,22] showed that odontogenic and otogenic etiological factors are responsible for spreading HNI, and pain and swelling were the most common presenting features, followed by fever. This may not be the proportion in the present study, but the association was valid in all clinical presentations. Previously reported that retropharyngeal infection and peritonsillar abscesses are frequently diagnosed in children and the young.[23,24] Due to potentially life-threatening complications, hospitalization is advised for patients at a severe stage. The duration of treatment should be individualized depending on the clinical response, like pus deposition, biofilm formation, or mold formation. Empirical broad-spectrum antibiotic treatment should be started immediately to prevent the infection, and microbial diagnosis takes 24 to 72 hours, depending on the availability of the nearest laboratories. Still, some cases might not respond as they would be at their moderate to severe stage of infection and need surgical drainage. It was supported by Boscolo-Rizzo *et al*., 2012[10] that only 61.9% of their patients responded to intravenous antimicrobial therapy, and 38.1% were gone for surgical drainage. Here, 59.35% of our registered patients were treated with surgical drainage, which was closely relevant to the previous study. However, 27.50 % were treated with antimicrobial therapy, which needs to be considered as a future problem of the resistance mechanism of intravenous antimicrobials.

Following Carbone *et al.*, 2012,[25] we found that those cases who underwent surgery had a greater length of hospitalization than those who did only medical treatment. Along with clinico-demographic profiling, close follow-up is mandatory as some patients often show recurrence, which would be challenging for recent treatment procedures. In this study, 7.96% of recurrences occurred, and most of the patients treated with empirical antibiotics were under them, and there was found a significance ($p<0.001$) between treatment and recurrence.

Multiple infection sites have been previously associated with complicated clinical courses and to stated significant multiple space involvement ($p<0.001$).[7] However, there was no statistically significant association between gender ($p=0.5$), local status ($p=0.8$), and age group ($p=0.2$) with recurrence to treatment. But, for those prescribed only antibiotics and those who underwent surgery concerning sites of infection, there was a significant association ($p<0.001$). Unlike all spaces, brain abscess or infection also is part of HNI,[26] but no cases were found in the duration of this study regarding this. The previously reported mortality rate of HNI was 0.3%,[10] which was not recorded in our study.

According to the present evaluation, the incidence of recurrence was n=86 (7.96%) among 1080 attended cases during the five years of retrospective study, which was undoubtedly an increasing point of recurrence compared to past studies.[27-29] The disease and syndromes associated with the respective infection remain the same with the recurrency and their clinical, pathologic, and microbiologic features.[30] In the present study, recurrent patients' complications were more severe than in their last visit. According to Yu *et al.*, *S. aureus* has a prominent genetic cause of biofilm formation, contributing to virulence and immune evasion,[31] and our study got the highest number of recurrent patients identified with *S. aureus* (Table 6). Almost all antibiotics and antifungals were resistant to all bacterial and fungal isolates. Moreover, *S. aureus*, with the highest prevalence among recurrent patients, was 100% oxacillin-resistant, and methicillin/oxacillin-resistant *S. aureus* is a significant pathogen resulting in hospital-acquired infection.[32-35] In this study, the antibiotic susceptibility pattern was analyzed through MIC (minimum inhibitory concentration) of the Vitek 2 system, as MIC can report the breakpoint of antibiotic therapy. However, empirical therapy can only eradicate the infection in the initial stage of colonization with the patient's immune response. Despite their importance, the early recognition of infection still represents an unmet need in clinical microbiology. The present study was based entirely on patients' clinico-demographic profile, and it seems worth underlining that the more severe the complication, the more difficult it may become to treat, but some exceptional cases needed to be considered either for their long-term hospitalization, delay in treatment, or recurrence.

Conclusions

The present study exhibited that diagnosing and treating HNI can sometimes be complicated and confusing. Moreover, treating such infections has become an uphill task with the advent of MDR microorganisms. However, successful results can be achieved without significant complications if the infections are diagnosed sooner. It is evident from the study that the location and duration of infection vary in different age groups according to their immune response. Minute symptoms like toothache and neck pain admission can be identified as possible predictors of complications. There should be a quick attempt at treatment in all age groups who present only fever, or oral or neck mass, even without more specific findings. Intravenous antimicrobial treatment is still one of the most helpful treatment procedures. Still, a quick step with microbial identification with their susceptibility pattern towards isolated microbes is a better way to combat drug resistance and failure of drug therapy. Epidemiology of HNI by their demographic and clinical history is essential to look forward to a bright step of diagnosis and treatment, supporting future research to eradicate any gap.

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