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Original Article

Frequency and Distribution of Complications in Cholesteatoma Patients: A Tertiary Care Hospital Study

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ABSTRACT

Background: Cholesteatoma, a benign epithelial lesion, progresses with time, necessitating surgical intervention. The most common surgical treatments are canal wall up (CWU) and canal wall down (CWD). CWU, though preserving ear canal anatomy, has a higher risk of recurrence, prompting a need to evaluate the frequency and nature of complications arising from cholesteatoma to improve treatment outcomes.

Objective: This study aims to identify the frequency and types of complications in patients diagnosed with cholesteatoma at a tertiary care hospital.

Methods: Conducted as a cross-sectional analysis at the Department of ENT, Jinnah Postgraduate Medical Centre, Karachi, from August 10, 2019, to February 9, 2020, this study included 210 diagnosed patients. Through otoscopy, audiologic evaluations, and microscope examinations for selected cases, patients with signs of persistent disease underwent mastoid exploration. Surgical interventions were tailored based on disease extent and type. Statistical analysis employed descriptive statistics, stratification, and Chi-square tests for significance (P-value ≤0.05).

Results: Of the participants, 57.6% were male, and 42.4% were female, with an average age of 31.30±8.75 years and a mean disease duration of 8.73±3.63 months. Extracranial complications were identified in 29% of patients, with 12.4% experiencing ossicular damage. Intracranial complications were found in 18.1% of patients, with meningitis constituting 8.6% of these cases. A total of 5.7% presented with multiple complications. No significant associations were found between the complications and variables such as gender, age, BMI, and disease duration.

Conclusion: Extracranial complications, notably ossicular damage, were most common, followed by intracranial complications and multiple complications, underlining the necessity for early diagnosis and targeted treatment strategies.

Keywords: Cholesteatoma, Cholesteatoma complications, Complications, Extracranial complications, Intracranial complications, Ossicular damage, Surgical treatment.

INTRODUCTION

Cholesteatoma, a benign but progressive epithelial lesion characterized by the growth of keratinizing squamous epithelium within the middle ear and/or mastoid region, presents a significant clinical challenge. This condition, which tends to manifest more aggressively in children (1-2), originates typically from the retraction of the eardrum, a process widely acknowledged as the primary step in the development of primary acquired cholesteatoma (3). Understanding the etiology of cholesteatoma is crucial for its effective management, as the lesion can enlarge over time, causing bone erosion, infections, and potentially leading to complications such as hearing loss, dizziness, and facial paralysis (4). Pediatric cholesteatoma, in particular, is noted for being more frequently associated with infections, exhibiting a more aggressive growth pattern, and carrying a less favorable prognosis compared to its adult counterpart (5-7).

The clinical behavior of pediatric acquired cholesteatoma differs markedly from that observed in adults, primarily in terms of its aggressiveness and response to treatment (5). The main objectives of surgical intervention for cholesteatoma are to completely remove the lesion, ensure a dry ear with minimal risk of recurrence, and to the extent possible, preserve or restore hearing while minimizing the need for ongoing mastoid cavity maintenance and water activity restrictions (4). Among the surgical techniques employed, canal wall reconstruction tympano-mastoidectomy with mastoid obliteration (CWR) has demonstrated a low recurrence rate and the ability to preserve ear canal anatomy (5,8). Historically, canal wall up (CWU) and canal wall down (CWD) surgeries have been the predominant methods for treating cholesteatoma. While CWU offers the benefit of maintaining normal ear anatomy and middle ear space, it is associated with a significantly higher recurrence rate in children (40–60%) and adults (20%) (9-11). On the other hand, CWD surgery provides better exposure for treatment and a lower recurrence rate (7–17%), but necessitates lifelong mastoid bowl cleanings, limits water activities, and often results in poorer conductive hearing outcomes (12-13).

An international study highlighted that among patients with cholesteatoma complications, 56.55% presented with extracranial complications, 40% with intracranial complications, and 9.65% with multiple concomitant intracranial and extracranial complications. It was found that 86.2% of these patients had undergone radical tympano-mastoidectomy (CWD), while 7.5% received a combination of simple mastoidectomy and tympanoplasty (CWU), and 6.2% had simple mastoidectomy (CWU) alone (14). Another investigation revealed that a wet ear was the most common presentation (73.75%), with extracranial complications including ossicular damage (13.5%), mastoid abscess (1.17%), exposed facial nerve (1.76%), exposed sigmoid sinus (1.17%), and Bezold's abscess (0.58%). Intracranial complications were less frequent, with meningitis (1.17%), brain abscess, and sigmoid sinus thrombosis each occurring in 0.58% of cases (15).

Given the scarcity of data on cholesteatoma complications within the Pakistani population, this study aims to ascertain the frequency of such complications in patients treated at a tertiary care hospital. Identifying the prevalence of complications will inform the development of protocols for early treatment and management, ultimately improving patient outcomes.

MATERIAL AND METHODS

This research was structured as a cross-sectional study to explore the incidence and variety of complications among cholesteatoma patients, conducted at the Department of ENT, Jinnah Postgraduate Medical Centre, Karachi, between August 10th, 2019, and February 9th, 2020. In determining the sample size, the study anticipated a complication prevalence rate of 9.65%, adopting a 4% margin of error and employing WHO software for sample size calculation, ultimately selecting 210 patients under a 95% confidence interval. The approach to sampling was a non-probability consecutive method, ensuring a systematic inclusion of participants that met the study criteria.

Participants eligible for this study were individuals aged between 15 and 50 years, diagnosed with cholesteatoma, and who consented to participate. The study meticulously excluded patients with a history of previous cholesteatoma surgery, compromised immune systems, or diagnoses of malignant diseases, to minimize potential biases and confounders. Following the approval of the study's synopsis by the CPSP, the research proceeded with data collection, adhering strictly to the outlined inclusion and exclusion criteria. Each participant's consent was obtained prior to their inclusion, ensuring ethical compliance and respect for patient autonomy.

Diagnostic procedures included otoscopy and audiological assessments for all participants, supplemented by microscopic examination in selected cases. Conservative treatment was initially provided to all patients, with those exhibiting persistent disease, recurrent foul-smelling ear discharge, and marginal perforation being considered for mastoid exploration. The choice of surgical procedure was determined based on the type and extent of the disease, ensuring a tailored approach to patient care. The principal investigator recorded all data on a predesigned proforma, maintaining rigorous standards to mitigate bias and control for potential confounders.

For the analysis of collected data, SPSS version 21 was utilized. Qualitative variables such as gender, presence of diabetes mellitus, extracranial and intracranial complications, and the types of surgical procedures undertaken were represented through frequencies and percentages. Quantitative variables, including age, height, weight, BMI, and duration of disease, were expressed as mean ± SD. The study further employed stratification to control for effect modifiers such as age, gender, BMI, ansd disease duration, with the Chi-square test applied to assess the impact of these modifiers on the study outcomes. A p-value of ≤0.05 was designated as the threshold for statistical significance, ensuring rigorous standards for the evaluation of findings and the establishment of conclusions based on empirical evidence.

RESULTS

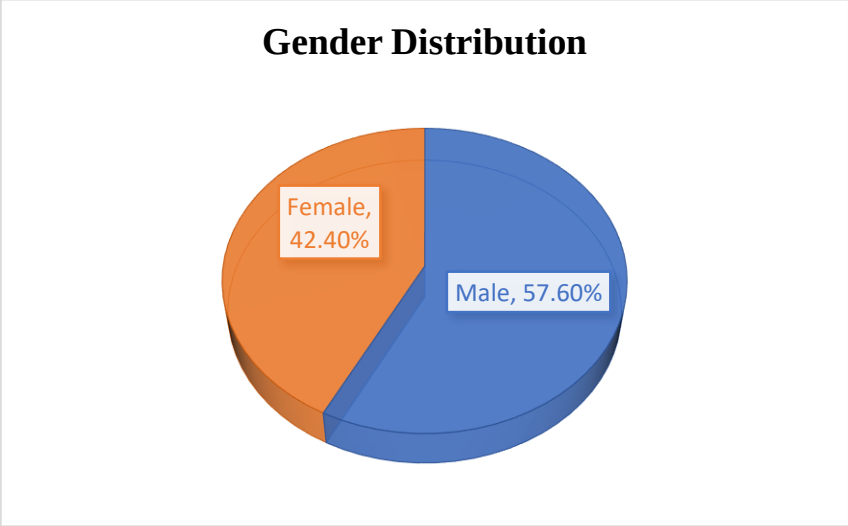

Figure 1: Gender Distribution Among 210 Patients

In our study, 210 patients of either gender with age 15 years to 50 years meeting inclusion criteria of study were evaluated to determine the frequency of complications among patients presented with cholesteatoma at tertiary care hospital. The gender distribution among 210 patients, indicating that 57.60% were male (n=121 patients) and 42.40% were female (n=89 patients) (figure 1).

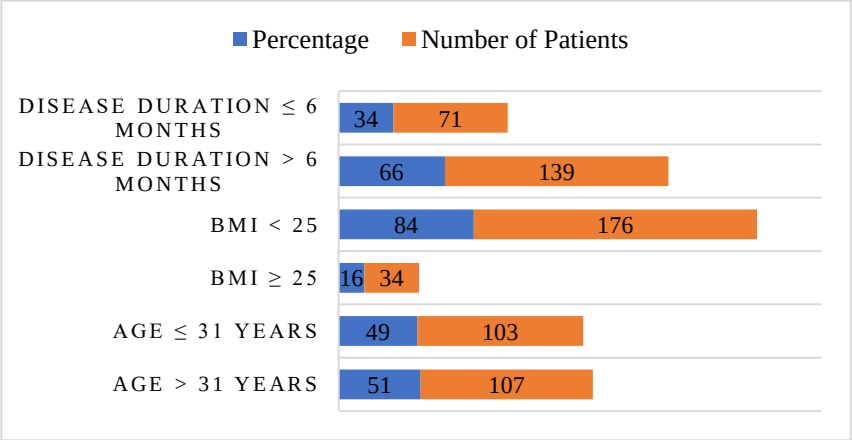

Figure 2: Patient Distribution by Demographic and Health Criteria

The figure 2 outlines the distribution of patients based on age, BMI, and disease duration. For age, 51% of patients are older than 31 years, while 49% are 31 years or younger. Regarding BMI, 16% of patients have a BMI of 25 or higher, with 84% falling below this threshold. Additionally, 66% of patients have a disease duration exceeding 6 months, while 34% have a duration of 6 months or less.

The table 1 presents descriptive statistics for various variables including age, weight, height, body mass index (BMI), and disease duration. The mean age of the sample population is 31.30 years, with a standard deviation of 8.75 years. Weight has a mean of 48.71 kg, with a standard deviation of 8.84 kg, while height has a mean of 153.89 cm with a standard deviation of 11.49 cm. The body mass index (BMI) has a mean of 20.67 kg/m2, with a standard deviation of 3.76 kg/m^2. Disease duration, on average, lasts for 8.73 months, with a standard deviation of 3.63 months.

Table 1: Descriptive Statistics of Study Population

Variable	Mean	SD	Median	Range	Minimum	Maximum
Age (Years)	31.30	8.75	31.00	31	17	48
Weight (kg)	48.71	8.84	47.00	64	33	97
Height (cm)	153.89	11.49	152.00	50	132	182
BMI (kg/m2)	20.67	3.76	20.10	28.20	15.50	43.70
Disease Duration (Months)	8.73	3.63	9.00	12	3	15

The table 2 illustrates the prevalence of extracranial and intracranial complications among patients diagnosed with cholesteatoma. Among extracranial complications, 29.05% of patients exhibited some form of complication, with ossicular damage being the most frequent at 12.38%. Mastoid abscess, exposed facial nerve, exposed sigmoid sinus, and Bezold's abscess were also observed, with

percentages ranging from 1.90% to 5.71%. Intracranial complications were found in 18.10% of patients, with meningitis being the most prevalent at 8.57%. Brain abscess and sigmoid sinus thrombosis were also identified, with percentages of 6.19% and 2.86%, respectively. Additionally, 5.71% of patients experienced multiple complications.

Table 2: Frequency Distribution of Complications among Patients with Cholesteatoma

Complication Type	Frequency	Percentage
Extracranial Complications		
Yes	61	29.05
No	149	70.95
Total	210	100.00
Types of Extracranial Complications		
Ossicular Damage	26	12.38
Mastoid Abscess	12	5.71
Exposed Facial Nerve	11	5.24
Exposed Sigmoid Sinus	8	3.81
Bezold's Abscess	4	1.90
Total	61	29.05
Intracranial Complications		
Yes	38	18.10
No	172	81.90
Total	210	100.00
Types of Intracranial Complications		
Meningitis	18	8.57
Brain Abscess	13	6.19
Sigmoid Sinus Thrombosis	6	2.86
Total	37	17.62
Multiple Complications		
Yes	12	5.71
No	198	94.29
Total	210	100.00

The table 3 provides a breakdown of extracranial complications based on gender, age, BMI, and disease duration among 210 patients. Notable findings include a higher prevalence of Ossicular Damage among males (69.2%, n=13) compared to females (30.8%, n=5). Mastoid Abscess is more frequently observed in patients older than 30 years (83.3%, n=10) compared to those aged 30 years or younger (16.7%, n=2). Exposed Facial Nerve complications predominantly occur in patients with a BMI of less than 25 kg/m2 (90.9%, n=10), while Exposed Sigmoid Sinus complications are more common in patients with a disease duration exceeding 6 months (87.5%, n=7). Bezolds Abscess is observed exclusively in patients with a BMI of less than 25 kg/m2 (100%, n=4).

Table 3: Frequency Distribution of Extracranial Complications According to Gender, Age, BMI, and Disease Duration (n=210)

Extracranial Complication	Male (%) (n)	Female (%) (n)	≤30 years (%) (n)	>30 years (%) (n)	<25 kg/m2 (%) (n)	≥25 kg/m2 (%) (n)	≤6 Months (%) (n)	>6 Months (%) (n)
Ossicular Damage	69.2 (13)	30.8 (5)	53.8 (14)	46.2 (12)	76.9 (20)	23.1 (6)	46.2 (12)	53.8 (14)
Mastoid Abscess	41.7 (7)	58.3 (5)	16.7 (2)	83.3 (10)	91.7 (11)	8.3 (1)	33.3 (4)	66.7 (8)
Exposed Facial Nerve	63.6 (7)	36.4 (4)	54.5 (6)	45.5 (5)	90.9 (10)	9.1 (1)	54.5 (6)	45.5 (5)
Exposed Sigmoid Sinus	62.5 (5)	37.5 (3)	25 (2)	75 (6)	75 (6)	25 (2)	12.5 (1)	87.5 (7)
Bezolds Abscess	50 (2)	50 (2)	25 (1)	75 (3)	100 (4)	0 (0)	25 (1)	75 (3)

In our study, across different demographic and clinical factors, the frequency distribution of intracranial complications reveals noteworthy trends. Among males aged 30 or younger, meningitis emerges as the most prevalent, affecting 50% of cases in this age group, particularly those with a BMI below 25 kg/m², where it reaches 88.9%. Brain abscesses also exhibit substantial occurrence rates among males with a BMI below 25 kg/m², standing at 84.6%. Conversely, in females over 30 years old, meningitis shows a higher prevalence, affecting 55.6% of cases, especially among those with intracranial complications lasting over six months (72.2%). Similarly, brain abscesses are more common among females with complications lasting over six months, affecting 69.2% of cases (table 4).

Table 4: Frequency Distribution of Intracranial Complications by Gender, Age, BMI, and Disease Duration

Intracranial Complications	Gender	Age	BMI	Disease Duration
	Male	≤30 years	<25 kg/m²	≤6 Months
Meningitis	8 (44.4%)	9 (50%)	16 (88.9%)	5 (27.8%)
Brain Abscess	7 (53.8%)	7 (53.8%)	11 (84.6%)	4 (30.8%)
Sigmoid Sinus Thrombosis	4 (66.7%)	4 (66.7%)	5 (83.3%)	3 (50%)
	Female	>30 years	≥25 kg/m²	>6 Months
Meningitis	10 (55.6%)	9 (50%)	2 (11.1%)	13 (72.2%)
Brain Abscess	6 (46.2%)	6 (46.2%)	2 (15.4%)	9 (69.2%)
Sigmoid Sinus Thrombosis	2 (33.3%)	2 (33.3%)	1 (16.7%)	3 (50%)

The frequency distribution of extracranial complications, intracranial complications, and multiple complications was analyzed concerning gender, age, BMI, and disease duration (table 5,6,7). Notably, in extracranial complications, there were no significant differences observed in gender distribution (p=0.569) or BMI groups (p=0.863). However, for intracranial complications, similar results were found regarding gender (p=0.492) and BMI (p=0.632). Age groups also showed no significant differences for both extracranial (p=0.135) and intracranial complications (p=0.397). Moreover, the occurrence of multiple complications didn't exhibit significant differences concerning gender (p=0.080), age (p=0.262), BMI (p=0.469), or disease duration (p=0.971). These findings suggest that in this study, gender, age, BMI, and disease duration did not significantly influence the occurrence of extracranial complications, intracranial complications, or multiple complications.

Table 5: Frequency of Extracranial Complication According to Gender, Age, BMI and Disease Duration

Extracranial Complication		Yes (n=61)	No (n=149)	Total	P-Value
Gender	Male	37 (30.6)	84 (69.4)	121	0.569**
	Female	24 (27)	65 (73)	89	
Age Group	≤30 years	25 (24.3)	78 (75.7)	103	0.135**
	>30 years	36 (33.6)	71 (66.4)	107	
BMI Group	<25 kg/m2	51 (28.8)	126 (71.2)	177	0.863**
	≥25 kg/m2	10 (30.3)	23 (69.7)	33	
Disease Duration Group	≤6 Months	24 (33.8)	47 (66.2)	71	0.278**
	>6 Months	37 (26.6)	102 (73.4)	139	
Chi Square Test was applied. P-value ≤0.05 considered as Significant. **Not Significant at 0.05 levels.					

Table 6: Frequency of Intracranial Complication according to Gender, Age, BMI And Disease Duration

Intracranial Complication		Yes (n=38)	No (n=172)	Total	P-Value
Gender	Male	20 (16.5)	101 (83.5)	121	0.492**
	Female	18 (20.2)	71 (79.8)	89	
Age Group	≤30 years	21 (20.4)	82 (79.6)	103	0.397**
	>30 years	17 (15.9)	90 (84.1)	107	
BMI Group	<25 kg/m2	33 (18.6)	144 (81.4)	177	0.632**
	≥25 kg/m2	5 (15.2)	28 (84.8)	33	
Disease Duration Group	≤6 Months	12 (16.9)	59 (83.1)	71	0.748**
	>6 Months	26 (18.7)	113 (81.3)	139	
Chi Square Test was applied. P-value ≤0.05 considered as Significant. **Not Significant at 0.05 levels.					

Table 7: Frequency of Multiple Complications According To Gender, Age, BMI And Disease Duration

Multiple Complication		Yes (n=12)	No (n=198)	TOTAL	P-Value
Gender	Male	4 (3.3)	117 (96.7)	121	0.080**
	Female	8 (9)	81 (91)	89	
Age Group	≤30 years	4 (3.9)	99 (96.1)	103	0.262**
	>30 years	8 (7.5)	99 (92.5)	107	
BMI Group	<25 kg/m2	11 (6.2)	166 (93.8)	177	0.469**
	≥25 kg/m2	1 (3)	32 (97)	33	
Disease Duration Group	≤6 Months	4 (5.6)	67 (94.4)	71	0.971**
	>6 Months	8 (5.8)	131 (94.2)	139	
Chi Square Test was applied. P-value ≤0.05 considered as Significant. **Not Significant at 0.05 levels.					

DISCUSSION

The investigation into the frequency of complications among cholesteatoma patients revealed a predominance of male subjects over females, with an average age of 31.30 ± 8.75 years and a mean disease duration of 8.73 ± 3.63 months. This study identified that 29% of patients experienced extracranial complications, with ossicular damage being the most prevalent (12.4%), while 18.1% presented with intracranial complications, predominantly meningitis (8.6%). Additionally, 5.7% of the cohort suffered from multiple complications.

Comparative analyses with existing literature underscore the variability in demographic distribution and clinical presentation of cholesteatoma. For instance, other research has indicated a higher incidence of cholesteatoma in younger age groups, particularly among individuals aged 11-20 years, suggesting an earlier onset in some populations (16-17). Moreover, a correlation between lower education levels and increased cholesteatoma incidence was observed, mirroring findings from studies conducted by Ludman H and Chowdhury MA et al, which reported a predominance of illiteracy among cholesteatoma patients (18-19).

Symptomatology across studies largely aligns, with otorrhoea, hearing impairment, and otalgia frequently reported, albeit with varying frequencies. This study's findings on extracranial and intracranial complications also find echoes in previous research, although direct comparisons reveal discrepancies in prevalence rates, possibly attributable to differences in study design, patient demographics, and diagnostic criteria (17, 20).

The unilateral predominance of cholesteatoma, with a slight favor towards the right ear, and the characteristic presentation of discharge, granulation tissue, and specific eardrum perforations align with historical data. These clinical features, notably the foul-

smelling discharge and specific sites of perforation, have been consistently documented, reinforcing the clinical markers essential for diagnosis (17, 18, 21).

Surgical intervention remains a cornerstone of cholesteatoma management, with a significant majority of this study's participants undergoing modified radical mastoidectomy. This surgical preference aligns with the necessity for comprehensive disease eradication while attempting to preserve auditory function, a principle that resonates with broader clinical practice. However, the occasional recourse to radical mastoidectomy, dictated by the extent of intracranial complications, underscores the variable nature of the disease and the need for tailored therapeutic approaches (21-24).

Despite these insights, this study's limitations warrant careful consideration. The constrained sample size and single-center design, coupled with the urban setting of the research, may limit the generalizability of the findings. These limitations highlight the necessity for broader, multi-center studies to validate these observations and enhance the understanding of cholesteatoma's clinical landscape.

This research contributes valuable data to the existing body of knowledge on cholesteatoma, reaffirming some established clinical patterns while also highlighting areas of variability and the need for further study. The emphasis on early diagnosis and intervention emerges as a critical takeaway, underscoring the importance of primary care practitioners in the early detection and management of this potentially complex condition. Moving forward, expanding the scope of research to encompass a wider demographic and geographic sample, alongside exploring the nuances of surgical outcomes, could provide deeper insights into the optimal management of cholesteatoma.

CONCLUSION

The findings from our investigation reveal that extracranial complications, particularly ossicular damage, were more prevalent, with intracranial complications, led by meningitis, following closely. Furthermore, the study identified significant risk factors for complication development, including male gender, age over 30 years, a BMI greater than 25 Kg/m^2, and disease duration exceeding six months. These insights underscore the critical importance of early detection and swift management of cholesteatoma to mitigate its complications, emphasizing the potential to significantly improve patient outcomes and prevent severe consequences.

Implications drawn from this study highlight the necessity for healthcare practitioners to maintain a high degree of vigilance for cholesteatoma, especially in patients presenting with risk factors identified. Strengthening the emphasis on early diagnostic procedures and integrating prompt therapeutic interventions can drastically reduce the progression and complications associated with cholesteatoma, ultimately enhancing patient quality of life and reducing the burden on healthcare systems. This research advocates for an increased focus on education and training for clinicians to recognize and manage this condition effectively, thereby ensuring timely care and minimizing the risk of adverse outcomes.

REFERENCES

1. Maniu A, Harabagiu O, Schrepler MP, Catana A, Fanuta B, Mogoanta CA. Molecular biology of cholesteatoma. Rom J Morphol Embryol. 2014;55(1):7-13.
2. Louw L. Acquired cholesteatoma pathogenesis: stepwise explanations. J Laryngol Otol. 2010;124(6):587-93.
3. Shibata S, Murakami K, Umeno Y, Komune S. Epidemiological study of cholesteatoma in Fukuoka City. J Laryngol Otol. 2015;129(2):6-11.
4. Kao R, Wannemuehler T, Yates CW, Nelson RF. Outpatient management of cholesteatoma with canal wall reconstruction tympanomastoidectomy. Laryng Investig Otolaryngol. 2017;2(6):351-7.
5. Kuo CL, Shiao AS, Yung M, Sakagami M, Sudhoff H, Wang CH. Updates and knowledge gaps in cholesteatoma research. BioMed Res Int. 2015;2015:1-17.
6. Dornelles C, Costa SS, Meurer L, Schweiger C. Some considerations about acquired adult and pediatric cholesteatomas. Rev Bras Otorrinolaringol. 2005;71(4):536-46.
7. Bujía J, Holly A, Antolí-Candela F, Tapia MG, Kastenbauer E. Immunobiological peculiarities of cholesteatoma in children: quantification of epithelial proliferation by MIB 1. Laryngoscope. 1996;106(7):865-8.
8. Walker PC, Mowry SE, Hansen MR, Gantz BJ. Long-term results of canal wall reconstruction tympanomastoidectomy. Otol Neurotol. 2014;35(6):954-60.
9. Syms MJ, Luxford WM. Management of cholesteatoma: status of the canal wall. Laryngoscope. 2003;113(3):443-8.

10. Shohet JA. The management of pediatric cholesteatoma. Otolaryngol Clin North Am. 2002;35(4):841-51.
11. Cody TD, McDonald TJ. Mastoidectomy for acquired cholesteatoma: Follow-Up to 20 years. Laryngoscope. 1984;94(8):1027-9.
12. Black B, Gutteridge I. Acquired cholesteatoma: classification and outcomes. Otol Neurotol. 2011;32(6):992-5.
13. Vartiainen E. Ten-year results of canal wall down mastoidectomy for acquired cholesteatoma. Auris Nasus Larynx. 2000;27(3):227-9.
14. Mustafa A, Kuçi S, Behramaj A. Management of cholesteatoma complications: Our experience in 145 cases. Indian J Otol. 2014;20(2):45-7.
15. Baig MM. Prevalence of cholesteatoma and its complications in patients of chronic suppurative otitis media. J Rawalpindi Med Coll. 2011;15(1):16-7.
16. Shenoi PM. Management of chronic suppurative otitis media. In: Scott-Brown's Otolaryngology. 6th ed. Oxford, London, Boston: Butterworth-Heinemann; 1987. p. 215-37.
17. Cody TR, Taylor WF. Mastoidectomy for acquired cholesteatoma: Long term results. In: McCabe BF, Sade J, Abramson M, editors. Cholesteatoma (Active squamous chronic otitis media), 1st International Conference, Birmingham, Alabama: Aesculapius Publishing Co; 1977. p. 33:51.
18. Ludman H. Complications of suppurative otitis media. In: Booth JB, editor. Scott Brown's Otolaryngology. 5th ed. London: Butterworth; 1987. p. 264-91.
19. Chowdhury MA, Alauddin M. Comparative study between tubotympanic and atticoantral types of chronic suppurative otitis media. Bangl Med Res Counc Bull. 2002;28(1):36-44.
20. Kangsanarak J, Fooanant S, Ruckphaopunt K. Extracranial and intracranial complications of suppurative otitis media. Report of 102 cases. J Laryngol Otol. 1993;107(11):999-1004.
21. Roland PS. Middle ear Cholesteatoma [Internet]. Available from: http://emedicine.medscape.com/article/860080-overview.
22. Kemppainen HO, Puhakka HJ, Laippala PJ. Epidemiology and aetiology of middle ear cholesteatoma. Acta Otolaryngol. 1999;119(5):568-72.
23. Nyrop M, Bonding P. Extensive cholesteatoma: Long-term results of three surgical techniques. J Laryngol Otol. 1997;111(6):521-6.
24. Alho OP, Jokinen K, Laitakari K. Chronic suppurative otitis media and cholesteatoma: Vanishing diseases among Western populations? Clin Otolaryngol Allied Sci. 1997;22(4):358-61.