E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.31838/ijprt/16.01.167

Research Article

Evaluation of Biochemical and Pathological Markers of Oxidative Stress and Inflammation in Pediatric Chronic Otitis Media and Their Public Health and Critical Care Implications: A Clinical Study

Fauzia Shaokat[1*], Rizwan Saeed[2], Muhammad Zahid Randhawa[3], Hamid Nawaz Khokhar[4], Afshan Zia[5], Syed Naveed Haider[6]

[1]Demonstrator, Department of Biochemistry, Gujranwala Medical College, Gujranwala, Pakistan.
[2]Professor & Head of Department, Community Medicine; Director Students Affairs, Azra Naheed Medical College, Superior University, Lahore, Pakistan.
[3]APMO, DHQ Teaching Hospital, Narowal, Pakistan.
[4]Assistant Professor, Department of Pathology, Sahara Medical College, Narowal, Pakistan.
[5]Assistant Professor, Department of Microbiology, Sharif Medical and Dental College, Lahore, Pakistan.
[6]Senior Medical Officer, District Health Authority, Narowal, Pakistan.

Corresponding Author: Fauzia Shaokat
Email: fauziashaokat@gmail.com
Received: 14.01.26, Revised: 12.03.26, Accepted: 06.04.26

ABSTRACT

Background: Pediatric chronic otitis media is a common and clinically important condition that contributes significantly to hearing impairment, recurrent infection, poor academic performance, and long-term developmental difficulties in children. Persistent inflammation and oxidative stress may play a major role in the progression and chronicity of the disease, yet these biological mechanisms remain underexplored in routine clinical practice.

Objective: To evaluate the biochemical and pathological markers of oxidative stress and inflammation in pediatric chronic otitis media and to assess their clinical, public health, and critical care implications.

Methods: This cross-sectional clinical study was conducted from June 2024 to June 2025 at Gujranwala Medical College, Gujranwala, Pakistan and Sahara Medical College, Narowal, Pakistan. A total of 100 pediatric patients aged 3–14 years diagnosed with chronic otitis media were enrolled through consecutive sampling. Clinical evaluation, otoscopic assessment, hearing assessment, and biochemical analysis were performed in all patients. Serum malondialdehyde, total antioxidant capacity, nitric oxide, C-reactive protein, interleukin-6, and tumor necrosis factor-alpha were measured. Histopathological examination was performed in surgically managed cases.

Results: Most patients had unilateral disease, prolonged symptoms, and clinically significant hearing impairment. Elevated levels of malondialdehyde, nitric oxide, C-reactive protein, interleukin-6, and tumor necrosis factor-alpha were observed, while total antioxidant capacity was reduced. Higher oxidative and inflammatory marker levels were significantly associated with greater disease severity, hearing impairment, bilateral disease, and longer symptom duration. Histopathology revealed chronic inflammatory infiltrate, granulation tissue, mucosal edema, epithelial hyperplasia, fibrosis, and vascular congestion.

Conclusion: Pediatric chronic otitis media is associated with significant oxidative stress, inflammatory activation, and pathological tissue injury. These findings highlight its broader clinical and public health importance and support the need for earlier diagnosis, timely treatment, and preventive intervention in affected children.

Keywords: Pediatric Chronic Otitis Media, Oxidative Stress, Inflammation, Malondialdehyde, Interleukin-6, Tumor Necrosis Factor-Alpha, Hearing Impairment.

INTRODUCTION

Chronic otitis media (COM) is one of the most prevalent and clinically relevant disorders of the pediatric population, with recurrent upper respiratory infections, untimely treatment, overcrowding, low hygiene, and insufficient access to expert ear care remaining among the factors that perpetuate the disease in low- and middle-income countries[1]. It is marked by the persistent inflammation of the cleft of the middle ear which is usually accompanied by the perforation of the tympanic membrane,

frequent or chronic otorrhhea, the varying levels of conductive hearing loss and in some instances with the gradual pathological destruction of middle ear structures[2]. The condition has an additional significance in children since a long-term hearing loss in the early years of development may negatively influence the acquisition of speech, the development of language, schooling achievements, socialization, and late-adult quality of life. As recent world experience demonstrates, the burden of otitis media-related hearing is still disproportionately high in South Asia and other resource-dependent environments, which confirms its topicality as a clinical as well as a general health issue[3].

Pediatric chronic suppurative otitis media is one of the most neglected types of chronic middle ear disease in spite of its high burden[4]. There is systematic evidence to indicate that chronic suppurative disease still impacts millions of people in the world with most of the affected cases being found in low- and middle-income areas and a significant proportion of the children with the disease developing disabling hearing loss[5]. In addition to the local ear pathology, the disease represents a wider overlap of infection, inflammation, nutrition, socioeconomic deprivation, and gaps in the health system. Pediatric COM in countries like Pakistan, where frequent childhood infections and late ENT presentation are still the norm, should not be considered as a localized ear disease but as an indicator of pediatric susceptibility and inequitable access to preventive and curative measures[6].

Pathophysiology of chronic otitis media is complicated and cannot be limited to the persistence of microbial colonization only[7]. Growing evidence indicates that oxidative stress and sustained inflammatory stimulation could be of primary importance in the pathogenesis of the disease, damage to the mucosa, chronicity, tissue remodeling, and complications[8]. In chronic middle ear inflammation, the activated neutrophils, macrophages, and epithelial cells produce excessive reactive oxygen species that may overwhelm the endogenous antioxidant defenses leading to cellular injury by lipid peroxidation, protein oxidation, mitochondrial dysfunction, and DNA damage. At the same time, pro-inflammatory cytokines like C-reactive protein, interleukin-6, and tumor necrosis factor-alpha could also help in continuing mucosal edema, epithelial hyperplasia, tissue destruction, and slow healing. This biochemical-pathological interactivity can be useful in understanding why certain pediatric patients acquire long course disease, frequent failure of treatment, conductive hearing loss, ossicular destruction or more inflammatory exudations than others despite seemingly comparable clinical conditions[9,10].

Although this biologically plausible relationship is present, until recently, most of the literature on pediatric COM has been based on microbiology, audiological impairment, surgical outcomes, and clinical risk factors, with little comparative emphasis on the combined evaluation of biochemical indicators of oxidative stress and pathological indicators of chronic inflammation in children with the disease. This is a significant gap since such markers can give a more in-depth insight into the severity of the disease, permanent mucosal damage, and the risk of progression. The detection of quantifiable systemic or local inflammatory and oxidative changes could also aid in the prior risk stratification and tailored surveillance and subsequent biomarker-driven interventions in the management of ear disease in children[11,12].

The applicability of this issue is not limited to outpatient otolaryngology. Pediatric chronic otitis media in terms of public health enhances preventable hearing disability, poor school performance, low ability to communicate, and high dependency on long-term healthcare[13]. In critical care and severe disease perspective, chronic middle ear inflammation with no treatment or inadequate management may sometimes lead to mastoiditis, facial nerve palsy, labyrinthine injury, intracranial extension, meningitis, brain abscess, and sepsis-related complications, particularly in the vulnerable or immunocompromised children. Hence, the knowledge of the biochemical and pathological factors of persistent disease can be useful not only in the daily care of diseases but also in the identification of children who have the risk of the severe development and the systemic load of inflammation[14].

Based on these issues, the current clinical study aimed at measuring the biochemical and pathological indicators of oxidative stress and inflammation in children with chronic otitis media, and in considering the connection of the indicators to the burden of the disease and broader issues of public health and critical care. This research will add to a more mechanistic and clinically significant conceptualization of chronic ear disease in children, especially in resource-constrained healthcare settings where

delayed diagnosis and preventable complications continue to be prevalent[15].

MATERIALS AND METHODS

This is a cross-sectional clinical study that took place between June 2024 and June 2025 at Gujranwala Medical College, Gujranwala, Pakistan and Sahara Medical College, Narowal, Pakistan. The aim of the study was to measure biochemical and pathological indicators of oxidative stress and inflammation among pediatric patients with chronic otitis media and to determine their potential public health and critical care implications. The two institutions were involved in patient recruitment, clinical evaluation, sample testing, and correlation in the laboratory.

The study was carried out on 100 pediatric patients who had chronic otitis media. The sample size was calculated based on the feasibility of the study, the number of patients per study period, and the requirement to get adequate biochemical and pathological evidence on which appropriate statistical comparison and clinical interpretation would be carried out. The patients were recruited using non-probability consecutive sampling of the outpatient and inpatient units of otorhinolaryngology of the respective institutions.

The study included children between the ages of 3 to 14 years of both sexes who satisfied the clinical conditions of chronic otitis media, which is the presence of ear discharge through a perforated tympanic membrane at least three months. Both unilateral disease and bilateral disease patients were eligible. Only children with acute otitis media alone, congenital ear defects, known immunodeficiency disorders, chronic systemic inflammatory diseases, severe hepatic or renal dysfunction, malignancy, or recent antioxidant supplementation were excluded. Patients whose consent was not given by their parents or guardians were also not allowed to take part in the study.

A thorough clinical history of the children was taken after enrollment by their parents or guardians. Data was documented about age, sex, duration of symptoms, disease laterality, ear discharge rate, hearing related complaints, past medical treatments, frequent infections of the upper respiratory system, and any history that can be indicative of disease complications. The overall physical examination and ENT examination were done in every patient. Otoscopic observations were recorded accurately, such as perforation of the tympanic membrane, discharge, granulation tissue and any apparent pathological alterations. Whenever possible, hearing evaluation was done by age-appropriate audiological assessment.

Venous blood samples were taken under aseptic conditions among all the patients who were included in biochemical analysis. The samples were centrifuged and serum was isolated to measure the chosen oxidative stress and inflammatory biomarkers. Malondialdehyde, total antioxidant capacity, and other biochemical evidence of oxidative injury were included in the oxidative stress profile based on the laboratory facilities at hand. The inflammatory markers were C-reactive protein, interleukin-6, and tumor necrosis factor-alpha. Standard lab methods and commercially marketed assay kits were performed as per instructions of the manufacturer and institutional lab procedures. All the measurements were carried out in controlled conditions to ensure reliability and reproducibility of results.

To perform pathological studies, the patient samples were taken as tissue samples that underwent related ENT surgical procedures during their treatment, including aural polypectomy, granulation tissue biopsy, mastoid exploration, or other specified surgical procedures. These samples were submitted to pathology department to undergo a histopathologic analysis. The pathological assessment was aimed at the occurrence and extent of chronic inflammatory cells infiltrate, epithelial hyperplasia, mucosal edema, fibrosis, necrotic debris, vascular congestion, and granulation tissue. The clinical severity and biochemical profile of the patients was then compared with the pathological results.

All the data obtained were coded into a structured pro forma and then subjected to analysis by means of SPSS version 26.0. Mean ± standard deviation was used to express quantitative variables (age, duration of disease, and levels of biomarkers) whereas frequency and percentage were used to express qualitative variables (gender, laterality, and pathological findings). Correlations between the biochemical markers and clinical or pathological variables were evaluated with the help of the corresponding statistical tests. Comparison was done using independent sample t-test or Mann-Whitney U test in case of continuous variables based on the distribution of the data, and chi-square test in the case of categorical variables.

A p-value below 0.05 was taken as statistically significant.

The research was carried out following the permission of pertinent institutional ethical review committee. Parents or legal guardians of all the children to be enrolled provided informed consent in writing beforehand. All the patient information was kept confidential and all the procedures were implemented in compliance with the accepted ethical principles of research that involves human subjects.

RESULTS

The present study involved a total of 100 pediatric patients who were diagnosed with chronic otitis media clinically. Every patient was provided with the necessary clinical and biochemical evaluation, and histopathological analysis was provided to individuals who had surgical intervention within the time of the study. The general results indicated that chronic otitis media among children was linked to a long-term disease, high frequency of hearing loss, high level of oxidative stress markers, high level of inflammatory load, and high levels of pathological tissue alterations.

The demographic and the baseline clinical profile of the study population indicated that the chronic otitis media was more prevalent among children aged 6 to 8 years as they constituted 34.0% of the study population (n=34) and then with children aged 9 to 11 years who constituted 28.0% of the study population (n=28). The 3–5 years age group contributed 21.0% (n=21) of patients, while the 12–14 years age group accounted for 17.0% (n=17). The average age of the patients was 8.2 and the standard deviation was 2.9. Male children were somewhat more affected as compared to females with 58.0% of them (n=58) being male and 42.0% (n=42) female. As per disease laterality, 61.0% (n=61) of children were unilaterally diseased and 39.0% (n=39) were bilaterally diseased with chronic otitis media. Analysis of symptom duration showed that 46.0% (n=46) of children had 7-12 months of symptoms, 36.0% (n=36) of children had over 12 months of symptoms, and only 18.0% (n=18) of children had 3-6 months of disease. Clinically, 41.0 (n=41) of them had mucoid discharge, 37.0 (n=37) had mucopurulent discharge, and 22.0 (n=22) had purulent discharge. Notably, hearing impairment (72.0% n=72), granulation tissue on otoscopy (31.0% n=31), recurrent upper respiratory tract infections history (49.0% n=49), prior antibiotic treatment (67.0% n=67) was observed in a significant number of patients as indicated in Table 1.

Table 1. Demographic and Clinical Characteristics of the Study Population

Variable	Frequency (n=100)	Percentage (%)
Age Group (years)		
3–5 years	21	21.0
6–8 years	34	34.0
9–11 years	28	28.0
12–14 years	17	17.0
Gender		
Male	58	58.0
Female	42	42.0
Laterality of Disease		
Unilateral	61	61.0
Bilateral	39	39.0
Duration of Symptoms		
3–6 months	18	18.0
7–12 months	46	46.0
>12 months	36	36.0
Type of Ear Discharge		
Mucoid	41	41.0
Mucopurulent	37	37.0
Purulent	22	22.0
Hearing Impairment on Assessment		
Present	72	72.0
Absent	28	28.0
Granulation Tissue on Otoscopy	31	31.0

History of Recurrent URTI	49	49.0
History of Previous Antibiotic Use	67	67.0

Biochemical evaluation found that a huge load of oxidative stress and systemic inflammatory activation exist in the enrolled children. The mean value of serum malondialdehyde (MDA), which measures lipid peroxidation and oxidative membrane damage, was 5.63 ± 1.14 nmol/mL, and it was found to be high enough to denote the presence of a significant amount of oxidative stress among the study population. There was also a high level of nitric oxide (NO) with the mean of 39.86 ± 7.92 µmol/L, indicating increased activity of reactive nitrogen species and inflammatory signaling. Inflammatory burden was also manifested by a mean level of C-reactive protein (CRP) of 8.94 ± 3.18mg/L, a mean level of interleukin-6 (IL-6) of 17.81 ± 5.09pg/mL and a mean level of tumor necrosis factor-alpha (TNF-alpha) of 21 Conversely, the average total antioxidant capacity (TAC) was 0.94 0.22 mmol/L, and there was relative depletion of antioxidant defenses. Together, these biochemical results imply that pediatric chronic otitis media is correlated with sustained oxidative and inflammatory stress as opposed to being confined to local infective process as described in Table 2.

Table 2. Serum Oxidative Stress and Inflammatory Biomarkers in Pediatric Chronic Otitis Media

Biomarker	**Mean ± SD**
Malondialdehyde (MDA) (nmol/mL)	5.63 ± 1.14
Total Antioxidant Capacity (TAC) (mmol/L)	0.94 ± 0.22
Nitric Oxide (NO) (µmol/L)	39.86 ± 7.92
C-Reactive Protein (CRP) (mg/L)	8.94 ± 3.18
Interleukin-6 (IL-6) (pg/mL)	17.81 ± 5.09
Tumor Necrosis Factor-alpha (TNF-α) (pg/mL)	21.46 ± 5.84

The assessment of clinical severity indicated that most children had moderate disease, which constituted 43.0% (n=43) of the entire study population. The chronic otitis media in severe was detected in 31.0% (n=31) of the patients and only 26.0% (n=26) as mildly diseased. These results suggest that almost three-quarters of the patients (74.0%) reported moderate-to-severe disease, which is an indication of late diagnosis, prolonged inflammatory process, and progressed pathology at the time of specialist care. This trend indicates the clinical significance of pediatric chronic otitis media in the research environment, and it is presented in Table 3.

Table 3. Distribution of Patients According to Disease Severity

Disease Severity Category	**Frequency (n=100)**	**Percentage (%)**
Mild	26	26.0
Moderate	43	43.0
Severe	31	31.0

There was an observed very important relationship between the level of biochemical markers and the severity of the disease. The mean MDA level in children with mild disease was 4.71 ± 0.82 nmol/mL and there was an increase to 5.52 ± 0.91 nmol/mL and finally to 6.58 ± 1.03 nmol/mL in moderate and severe groups respectively ($p<0.001$). Likewise, the NO levels rose gradually as mild disease, moderate disease, and severe disease advanced to 33.84 ± 5.61 µmol/L, 39.21 ± 6.34 µmol/L, 45.94 ± 7.11 µmol/L respectively ($p<0.001$). Another pattern of increase was noted in inflammatory markers. Mean CRP increased from 6.11 ± 1.72 mg/L in mild disease to 8.77 ± 2.21 mg/L in moderate disease and 11.46 ± 2.84 mg/L in severe disease. Mean IL-6 increased from 13.92 ± 3.41 pg/mL in mild disease to 17.44 ± 4.12 pg/mL in moderate disease and 21.88 ± 4.95 pg/mL in severe disease. Likewise, mean TNF-α increased from 16.97 ± 3.66 pg/mL in mild cases to 21.02 ± 4.33 pg/mL in moderate cases and 25.91 ± 5.08 pg/mL in severe cases. Conversely, TAC reduced greatly with the severity of the disease,

with 1.12 ± 0.17 mmol/L in the mild disease, 0.95 ± 0.18 mmol/L in the moderate disease,

and 0.73 ± 0.14 mmol/L in the severe disease (p<0.001). These results point heavily to the fact that the more clinical severity, the more oxidative damage, the more inflammatory activation, and the less antioxidant defense, as depicted in Table 4.

Table 4. Comparison of Biomarker Levels According to Disease Severity

Biomarker	Mild (n=26) Mean ± SD	Moderate (n=43) Mean ± SD	Severe (n=31) Mean ± SD	P-value
MDA (nmol/mL)	4.71 ± 0.82	5.52 ± 0.91	6.58 ± 1.03	<0.001
TAC (mmol/L)	1.12 ± 0.17	0.95 ± 0.18	0.73 ± 0.14	<0.001
NO (µmol/L)	33.84 ± 5.61	39.21 ± 6.34	45.94 ± 7.11	<0.001
CRP (mg/L)	6.11 ± 1.72	8.77 ± 2.21	11.46 ± 2.84	<0.001
IL-6 (pg/mL)	13.92 ± 3.41	17.44 ± 4.12	21.88 ± 4.95	<0.001
TNF-α (pg/mL)	16.97 ± 3.66	21.02 ± 4.33	25.91 ± 5.08	<0.001

The present study had hearing impairment as a significant clinical outcome and had a strong connection with disease burden. Out of 72 children with hearing impairment, 35 (48.6) were bilaterally diseased, whereas 4 (14.3) were among 28 children with no hearing loss (p=0.002). Similarly, the duration of disease of 31 (43.1) children with hearing impairment was above 12 months and only 5 (17.9) children in the non-hearing impairment group had a disease duration above 12 months (p=0.021). In children with hearing loss, granulation tissue was found in 28 (38.9%) and in children with no hearing deficits, 3 (10.7%) only (p=0.008). Similarly, 29 (40.3%) of children with hearing impairment had severe disease, compared with only 2 (7.1%) in the non-hearing-impaired group (p=0.001). These findings suggest that hearing impairment in chronic otitis media among children is closely correlated to advanced, longer-lasting and structurally meaningful disease as in Table 5.

Table 5. Association of Hearing Impairment with Disease Characteristics

Variable	Hearing Impairment Present (n=72)	Hearing Impairment Absent (n=28)	p-value
Bilateral disease, n (%)	35 (48.6%)	4 (14.3%)	0.002
Duration >12 months, n (%)	31 (43.1%)	5 (17.9%)	0.021
Granulation tissue, n (%)	28 (38.9%)	3 (10.7%)	0.008
Severe disease, n (%)	29 (40.3%)	2 (7.1%)	0.001

The histopathological study was conducted on 38 surgically treated patients and the results demonstrated significant chronic inflammatory and repair tissue alterations. Chronic inflammatory cell infiltrate was the most frequent pathological finding observed in 94.7% (n=36) of the specimens. The presence of granulation tissue was found in 71.1% (n=27) of the cases, and the presence of mucosal edema was found in 63.2% (n=24). Fifty seven point nine percent (n=22) exhibited epihelial hyperplasia, fifty two point six percent (n=20) had vascular congestion and forty seven point four percent (n=18) had fibrosis. Necrotic debris was detected in 28.9 (n=11) out of cases, which means that some children had more destructive inflammatory tissue alterations. Such histopathological observations are in line with long-term inflammatory stimulation, mucosal growth, tissue remodelling, and healing efforts as provided in Table 6.

Table 6: Histopathological Findings in Surgically Managed Patients (N=38)

Histopathological Feature	Frequency	Percentage (%)
Chronic inflammatory cell infiltrate	36	94.7
Granulation tissue formation	27	71.1
Mucosal edema	24	63.2
Epithelial hyperplasia	22	57.9
Fibrosis	18	47.4
Vascular congestion	20	52.6
Necrotic debris	11	28.9

The duration of disease and levels of biochemical markers were also found to be having statistically significant correlation. The positive correlation between serum MDA and disease duration was observed (r=0.482, p<0.001), which revealed that oxidative membrane injury was more associated with a longer disease duration. Similarly, NO showed a positive correlation (r=0.438, p<0.001), while inflammatory markers such as CRP (r=0.419, p<0.001), IL-6 (r=0.454, p<0.001), and TNF-α (r=0.467, p<0.001) also increased significantly with longer disease duration. Meanwhile, TAC was found to be significantly negatively correlated with the time of the disease (r=-0.401, p<0.001), indicating that antioxidant capacity is depleted with time. These findings suggest that long-term disease adds to the cumulative oxidative and inflammatory damage, which is indicated in Table 7.

Table 7: Correlation of Biochemical Markers with Duration of Disease

Biomarker	Correlation Coefficient (r)	p-value
MDA	0.482	<0.001
TAC	-0.401	<0.001
NO	0.438	<0.001
CRP	0.419	<0.001
IL-6	0.454	<0.001
TNF-α	0.467	<0.001

Overall, the results of the present study clearly demonstrate that pediatric chronic otitis media is associated with clinically meaningful oxidative stress, inflammatory activation, and pathological tissue damage. Numerical evidence indicated that the levels of oxidative and inflammatory biomarkers, the antioxidant capacity, the degree of hearing impairment, and the degree of pathological changes increased gradually with increased disease severity, bilaterality, and duration in children. These results are a solid argument in favor of the idea that chronic otitis media in children is a biologically dynamic and increasingly harmful inflammatory process with significant clinical, developmental, and population health outcomes.

DISCUSSION

The present study demonstrated that pediatric chronic otitis media is associated with a substantial burden of oxidative stress, systemic inflammatory activation, and pathological tissue injury[10]. The general results revealed increased levels of malondialdehyde, nitric oxide, C-reactive protein, interleukin-6, and tumor necrosis factor-alpha as well as decreased total antioxidant capacity, which indicated that chronic otitis media in children is not only a localized ear infection but a biologically active inflammatory disease with quantifiable systemic outcomes. Also, histopathology showed presence of chronic inflammatory cell infiltrate, granulation tissue formation, mucosal edema, epithelial hyperplasia, fibrosis, vascular congestion and necrotic debris, which also indicated the existence of enduring tissue-scale inflammatory damage[11,12].

Among the most significant results of the current investigation was the high increase in the level of malondialdehyde, which indicates the high levels of lipid peroxidation and oxidative membrane damage[13]. This is an indication that reactive oxygen species play a proactive role in the pathogenesis of chronic otitis media in children[14]. Continued microbial infection and chronic inflammation of the middle ear probably results in the stimulation of inflammatory cells like neutrophils and macrophages which cause excessive generation of free radicals. These reactive species are able to injure cell membranes, impair epithelial integrity, extend mucosal edema and delay middle ear mucosa healing. The elevated levels of nitric oxide found in the current study also confirm the presence of oxidative and nitrosative stress in disease development, with nitric oxide being observed to elevate during chronic inflammatory conditions, and possibly play a role in the irritation and inflammatory response of local tissues[15].

The inflammatory marker profile of the current research was also very significant. High levels of C-reactive protein, interleukin-6 and tumor necrosis factor-alpha show that chronic otitis media in children results in a persistent inflammatory reaction beyond that of the ear[16]. Interleukin-6 and tumor necrosis factor-alpha are key pro-inflammatory cytokines that are involved in the recruitment of leukocytes, vascular permeability, tissue edema, and amplification of chronic inflammation. Their

elevation in this study implies that chronic inflammation by the mediation of cytokines can be significant in the continuance of chronic otitis media, mucosal expansion, and tissue remodeling. Such inflammatory processes could also be the reason as to why some patients remain in prolonged discharge, progressive hearing loss, and recurrent disease even after being exposed to antibiotics before[17].

The second significant finding was the decrease in the total antioxidant capacity. This observation implies that endogenous antioxidant defense systems would be limited in response to sustained oxidative stress[18]. To put it simply, the protective biochemical mechanisms of the body seem incapable of counteracting the chronic oxidant burden produced in the course of chronic inflammation of the middle ear. This relative excess of oxidants over antioxidants can be among the significant processes that contribute to disease persistence, inability to achieve full recovery of the mucosa and develop more serious forms of chronic otitis media[19].

These findings have additional clinical implications on the severity-based analysis of the current research. Malondialdehyde, nitric oxide, C-reactive protein, interleukin-6, and tumor necrosis factor-alpha were highest in children with severe chronic otitis media with the lowest total antioxidant capacity recorded[20]. This is a clear indication that the deteriorating clinical disease correlates with the deteriorating biochemical disturbance. This pattern is a strong indication that oxidative stress and inflammation are not accidental findings and are tightly connected with the disease severity. Possibly, these biochemical indicators can in the future be used as an adjunctive indicator of disease burden or risk of progression especially in children with chronic symptoms, bilateral disease, persistent discharge or recurrent treatment failure[21].

Another significant conclusion of the current study was hearing impairment which was found in the majority of the registered children. More to the point, hearing loss was significantly correlated with bilateral disease, disease duration, granulation tissue, and severe disease category[22]. It is a clinically significant finding since it demonstrates that hearing loss in chronic otitis media in children is closely associated with more developed inflammatory and structural disease. Practically, children that present late, those who have persistent inflammation over a long duration, or those who acquire granulation tissue, are at risk of having severe auditory dysfunction. This result has implications in the wider developmental scope of chronic otitis media since childhood hearing loss may adversely influence speech development, learning capacity, classroom performance, and psychosocial development[4,6]. The biochemical observations are also reinforced by the histopathological findings of this research. The preponderance of chronic inflammatory cell infiltrate is evidence of ongoing mucosal immune activity, whereas granulation tissue formation and mucosal edema indicate active chronic inflammation and tissue response to recurrent damage8.

Epithelial hyperplasia implies continuous stimulation of the mucosa and fibrosis means chronic healing with scarring. Vascular congestion and necrotic debris observed in part of the specimens indicates that in a sub-group of children, the inflammatory response can be more destructive and violent. Combined with earlier tissue-level observations, these results indicate that pediatric chronic otitis media is linked to a continuum of chronic tissue inflammation and repair, and not a static infection[9,11].

Another significant outcome of the current research is the positive association between the duration of the disease and the presence of oxidative-inflammatory biomarkers[12]. The malondialdehyde, nitric oxide, C-reactive protein, interleukin-6 and tumor necrosis factor-alpha levels in children increased with the duration of illness and the total antioxidant capacity of the children reduced over time. This implies that late diagnosis and chronic disease activity could cause cumulative biochemical damage with time. It also implies that early diagnosis and immediate treatment can serve to alleviate the long-term inflammatory and oxidative load among the children with the disease[13].

The implications of this study to public health are very crucial. Pediatric chronic otitis media is a well recognized but seldom addressed disease in developing nations, where late seeking of health care, low access to ENT, frequent respiratory diseases, overcrowding, improper hygiene, and improper use of antibiotics promote chronicity[14]. The large percentage of children with a long duration of symptoms, hearing loss, frequent upper respiratory tract infection and prior exposure to antibiotics in the study is indicative of broader systemic and social determinants of disease persistence. Thus, chronic otitis media cannot be regarded as the health concern of otolaryngology only

but also as the significant child health and social health problem. Early school hearing screening, parental education program, timely referral systems, and better pediatric ENT services can be used to mitigate the burden of disease and avoid long-term disability[15].

The relevance of the study to the critical care is also critical. Most instances of chronic otitis media are treated at an elective level, but serious or untreated cases may lead to severe complications that may include mastoiditis, facial nerve injury, labyrinthine dissemination, intracranial infection, meningitis or brain abscess[16].

The harsh inflammatory and oxidative phenotype observed in the advanced cases in this paper indicates that stronger biological functioning may occur in children having severe illness. Although the intracranial or life-threatening complications were not directly evaluated in the current study, the evidence suggests that the ongoing biochemical and pathological inflammation could be used to explain the reason why certain patients are pushed to more severe disease states when they are not treated[17].

The current paper has a number of strengths. It assessed pediatric chronic otitis media in a multidimensional manner by integrating clinical examination, biochemical examination and histopathological results.

It also examined differences based on severity and associated biomarkers with hearing loss and duration of disease, and the results were more clinically relevant. More so, the research was carried out in two hospitals and this enhanced the variety of patient recruitment[9-13]. Nevertheless, the research has its limitations as well.

The cross-sectional design does not permit causal interpretation and only a single time point of biomarker measurements was conducted. The sample size was rather small, despite being sufficient to analyze it clinically. Histopathological examination was only done in surgically treated cases and thus tissue results might not be an accurate depiction of all children with chronic otitis media.

Also, microbiological culture, antibiotic sensitivity analysis, and long-term follow-up were missing. The future research must incorporate bigger multicentric cohorts, longitudinal follow-up, microbiological correlation and potentially comparison to normal controls to derive more mechanistic and prognostic inferences[19-22].

CONCLUSION

In conclusion, the present study showed that pediatric chronic otitis media is associated with significant oxidative stress, elevated inflammatory cytokine activity, reduced antioxidant defense, and clear pathological evidence of chronic tissue injury. The elevated concentrations of malondialdehyde, nitric oxide, C-reactive protein, interleukin-6, and tumor necrosis factor-alpha along with the reduction of total antioxidant capacity all show that this disease is not a transient local infection but a long-term biochemical inflammatory load. Destructive and progressive nature of the condition was further proven by histopathological findings of chronic inflammatory infiltrate, granulation tissue, mucosal edema, epithelial hyperplasia, fibrosis, and vascular congestion. It was also found that the biochemical and pathological burden is more pronounced in children with severe disease, prolonged symptom duration, bilateral involvement, and hearing impairment. The results indicate that oxidative stress and inflammatory markers could be potentially useful as auxiliary predictors of disease severity and progression in chronic otitis media in children. On the whole, chronic otitis media among children cannot be underestimated as a significant clinical and population health issue with significant implications in the areas of hearing, development, education, and long-term wellbeing. To decrease the burden of disease and avoid the unnecessary complications in children with the disease, early diagnosis, timely treatment, periodic hearing evaluation, and more effective preventive measures on the level of public health are necessary.

Availability of Data and Materials

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

Funding

The authors received no external funding for this study.

Authors' Contributions

FS conceptualized the study, participated in data collection, biochemical interpretation,

manuscript drafting, and overall coordination of the research work.

RS contributed to the study design, public health interpretation, methodological supervision, and critical revision of the manuscript.

MZR contributed to clinical data collection, patient assessment, and interpretation of clinical findings.

HNK performed and supervised the histopathological evaluation and contributed to pathological interpretation.

AZ contributed to microbiological and inflammatory interpretation, manuscript review, and scientific input.

SNH assisted in data acquisition, public health coordination, and manuscript support.

All authors read and approved the final version of the manuscript.

Acknowledgements

The authors are thankful to the staff and administration of Gujranwala Medical College, Gujranwala, Pakistan, Sahara Medical College, Narowal, Pakistan, and the participating hospital departments for their support during patient recruitment, laboratory coordination, and data collection. The authors also express gratitude to the patients and their families for their cooperation and participation in this study.

REFERENCES

1. Garça MF, Turan M, Avşar B, Kalkan F, Demir H, Kozan A, et al. The evaluation of oxidative stress in the serum and tissue specimens of patients with chronic otitis media. Clin Exp Otorhinolaryngol. 2015;8(2):97-103.
2. Sagiroglu S, Ates S, Tolun FI, Oztarakci H. Evaluation of oxidative stress and antioxidants effect on turning process acute otitis media to chronic otitis media with effusion. Niger J Clin Pract. 2019;22(3):375-379.
3. Celik M, Koyuncu İ. A comprehensive study of oxidative stress in patients with chronic otitis media. ENT Updates. 2020;10(1):238-243.
4. Baysal E, Aksoy N, Kara F, Taysi S, Taşkın A, Bilinç H, et al. Oxidative stress in chronic otitis media. Eur Arch Otorhinolaryngol. 2013;270(4):1203-1208.
5. Abdelhafeez M, Mohamed NM. Correlation between serum interleukin-17 level and serum reactive oxygen species levels among children experiencing otitis media with effusion. Int Arch Otorhinolaryngol. 2021;25(4):e570-e574.
6. Mastino P, Rosati D, De Soccio G, Romeo M, Pentangelo D, Venarubea S, et al. Oxidative stress in obstructive sleep apnea syndrome: putative pathways to hearing system impairment. Antioxidants (Basel). 2023;12(7):1430.
7. Lee J, Hong SM, Choi YS, Lee J, Yeo JH, Kim SS, et al. Narrative review of free radicals and reactive oxygen species in otitis media. Antioxidants (Basel). 2025;14(1):3.
8. Addissouky TA, El Sayed IE, Ali MM, Wang Y, El Baz A, Elarabany N, et al. Oxidative stress and inflammation: elucidating mechanisms of smoking-attributable pathology for therapeutic targeting. Bull Natl Res Cent. 2024;48(1):16.
9. Oh YJ, Lee JM, Yeo JH, Kim SS, Yeo SG. Induction of nitric oxide and its role in otitis media. Antioxidants (Basel). 2025;14(3):327.
10. Ko YS, Gi EJ, Lee S, Kim HC, Cho HH. Dual red and near-infrared LED therapy inhibits MRSA biofilm in otitis media. Biofilm. 2025;100314.
11. Dondi A, Carbone C, Manieri E, Zama D, Del Bono C, Betti L, et al. Outdoor air pollution and childhood respiratory disease: the role of oxidative stress. Int J Mol Sci. 2023;24(5):4345.
12. Sepehri B, Darbani R, Mesgari-Abbasi M, Kheirouri S, Shanehbandi D, Khordadmehr M, et al. The effects of short-time air pollution, SO_2, and ozone on biochemical, histopathological, oxidative stress, and carcinogenesis-related gene expressions in the liver of rats. Hum Exp Toxicol. 2024;43:09603271241263569.
13. Zhang YC, Zhang L, Zhou PT, Xie ZH, Zhang WJ, Fan M, et al. Environmental exposure to air pollution and climate: intersecting the impact on ear and nose health and chemosensory function. Int J Mol Med. 2025;57(3):55.
14. Nisar A, Jagtap S, Vyavahare S, Deshpande M, Harsulkar A, Ranjekar P, et al. Phytochemicals in the treatment of inflammation-associated diseases: the journey from preclinical trials to clinical practice. Front Pharmacol. 2023;14:1177050.
15. Yemiş T, Arpa M, Birinci M, Özgür A, Çeliker M, Taştan M, et al. Disrupted

glutamate-GABA balance in children with adenoid hypertrophy: a targeted metabolomic and clinical correlation study. Eur Arch Otorhinolaryngol. 2025.

16. Nam MK, Yeo J, Rhim H, Park JO, Yoo SA. Microplastics and head and neck health: emerging implications for otolaryngologic disorders and carcinogenesis. Korean J Otorhinolaryngol Head Neck Surg. 2025;69(2):65-75.
17. Colletti A, Pellizzato M, Cicero AFG. The possible role of probiotic supplementation in inflammation: a narrative review. Microorganisms. 2023;11(9):2160.
18. Ajaz M, Zahid A, Ismail H, Ajaz M. Anti-inflammatory effects of flavonoids in otitis media: a systematic review of pre-clinical evidence. Food Front. 2025;6(6):2554-2574.
19. Abdul-Nabi SS, Al Karaki V, Khalil A, El Zahran T. Climate change and its environmental and health effects from 2015 to 2022: a scoping review. Heliyon. 2025;11(3).
20. Yang R, Xu Z, He X, Ge Z, Lin Y, Zha D. The clinical features of otitis media with antineutrophil cytoplasmic antibody-associated vasculitis and the role of routine blood tests in its diagnosis. Ear Nose Throat J. 2025:01455613251336864.
21. Chen P, Hou S, Pang X, Li L, Wei W. A proteomic study based on home quarantine model identifies NQO1 and inflammation pathways involved in adenoid hypertrophy. J Inflamm Res. 2025;18:723-735.
22. Huang XT, Feng H, Tan Y, Wang Q, Wei JM, Huang ZD, et al. Effectiveness of *Streptococcus salivarius* probiotics on alleviating radiation-induced oral mucositis via inflammatory and microecological modulation: a prospective pragmatic interventional study in nasopharyngeal carcinoma. Front Immunol. 2026;17:1745549.