Upper respiratory infection and otitis media are clinically and microbiologically associated

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Abstract
Background: Although a significant improvement has been achieved in term of antibiotic care, otitis media (OM) continues to be a worldwide health problem that may develop a serious complications. This study aimed to detect the growth of organisms and to find out the most susceptible factors related to OM among Iraqi population.

Methods: A cross-sectional prospective study was conducted at the out-patient department (OPD) of Ear, Nose and Throat (ENT) at the Baquba teaching hospital at the Faculty of medicine, Diyala University from November 2017 to March 2018. A total of 300 ear samples collected from 87 (29.0%) patients of acute otitis media (AOM), 104 (34.7%) patients of otitis media with effusion (OME) and 109 (36.3%) patients of chronic otitis media (COM). A standard microbiological procedures were recruited to investigate the samples using aerobic and anaerobic culture methods.

Results: The highest incidence of OM 218 (72.7%) was observed among age group of less than ten years old. The most common bacteria isolated were Pseudomonas aeruginosa (35.0%), Staphylococcus aureus (25.0%), Proteus spp. (24.0%), Escherichia coli (7.0%), Streptococcus pneumonia (6.0%), Klebsiella pneumonia (2.0%) and Streptococcus pyogenes (1.0%). It was found that upper respiratory infection (URTI), adenoid inflammation with (URTI), adenoid inflammation, the practices of complementary and alternative medicine (CAM), and the accident or trauma are the main factors related to OM in about (42.0%), (31.0%), (11.0%), (10.0%) and (6.0%) of cases respectively.

Conclusion: Our findings suggest that OM was effectively related to URTI and adenoid inflammation with (URTI) in about 73.0% of cases. More attention should be given to early diagnosis and treatment of URTI before progressing to undesirable OM.

Keywords: Acute otitis media, chronic otitis media, otitis media with effusion, URTI, Baquba, Diyala, Iraq

Background
The term “Otitis media” (OM) is used to describe the inflammatory process occurring in the middle ear. Clinically OM covers a wide spectrum of illnesses such as acute otitis media (AOM), otitis media with effusion (OME) and chronic suppurative otitis media (CSOM) [1]. Unfortunately, OM is one of the most common cases among children that require outpatient department (OPD) visit and is frequently preceded by or accompanied with some types of upper respiratory infections (URIs) [2], however the main causes that may participate in OM are not well understood. Anatomically, the well-known Eustachian tube (ET) runs between the nasopharynx and the middle ear. Usually the young age group is more prone to have ear infection than adults, because ET is shorter, narrower and more horizontal in children compared to older age group [3,4]. The vital small size ET may get plugged resulting in a case called Eustachian tube dysfunction (ETD). The blocked ET or ETD is commonly being a target for many viral and bacterial infections or the normal flora moving from the upper respiratory tract and eventually attack the middle air [5]. Furthermore, the risk factors related to allergy towards some kinds of foods, environmental, social, racial, host, immunological and genetic factors are found to be significantly related to high incidence of OM [6-8].

In fact, URIs with nasopharyngeal colonization are strongly related to OM [9]. The risk of AOM among children would be more likely to increase if the bacterial growth was positive in the nasopharynx [10]. The viral infection was indicated to be the initial cause of URIs in most cases of OM, however...
superadded infection of both viral and bacterial infection has been widely seen [11]. Although OM is not life threatening disease, however a list of serious acute and chronic complications such as labyrinthitis, mastoiditis, facial nerve palsy and intracranial complications have been reported [12,13]. Different microorganisms have been isolated from different cultures of the ear discharge, however the Streptococcus pneumoniae, Streptococcus pyogenes, Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, Klebsiella spp. and Proteus spp. were the most common pathogens knowing to cause OM and usually come from contaminated water [14]. This study aimed to investigate the growth of (aerobic and anaerobic) organisms and to find out the most important related factors of OM among Iraqi population.

Methods
Study design and subjects
A cross-sectional descriptive analytical study was conducted at the OPD of Ear, Nose and Throat (ENT) of Baquba teaching hospital at the Faculty of medicine, Diyala University. A prospective data of three hundred (300) diagnosed otitis media (OM) patients of all ages and either gender were collected during the period of 1st November 2017 to 30th March 2018. A convenience sampling technique was recruited, however only one sample was allowed for each patient to avoid selection bias. Moreover, one sided sample was considered in all cases presented with bilateral infection.

At the time of study, patients presented with “acute bacterial infection of the middle ear of less than 6 weeks duration” are diagnosed with AOM, however when “infection persists in the middle ear space for more than three months and is associated with a chronic perforation of the tympanic membrane” referred to CSOM. Cases of OM presented with “fluid in the middle ear without signs or symptoms of inflammation” are defined as OME. Most of OME occur just prior to or persist after an infection for a few days or up to many weeks [3,13,15]. Table 1 presents the inclusion and exclusion criteria.

Collection of the sample
Each eligible patient has undergone to scientific standard procedure. All measures have been taken to avoid sample contamination. A sterile cotton with normal saline (0.85% NaCl) was used to remove the contaminated discharge in the outer part of the infected ear. Then, under Bull’s lamp with head mirror, a sterile cotton swab containing test tube was recruited to take pus sample from the deep region close to tympanic membrane through a sterile ear speculum.

Transport of sample
Consideration was taken to maintain the viability of microorganisms. An ice box was used to keep all collected samples in sterile test tubes and sent within 1 hour to the microbiology department of Baquba teaching hospital. Individual patient data such as name, date and age was included in the corresponding labelled test tubes.

Stain and culture process
All the swabs were Gram stained (GS) to identify the pathogenetic organisms. Only the positive GS swabs were directly inoculated in a suitable culture media. Three types of agar (Blood, Chocolate and MacConkey agars) were used to culture the organisms. According to the standard microbiological methods [16,17], “Five percent sheep blood agar and MacConkey agar plates were incubated aerobically, while chocolate agar was incubated under 5% CO2 atmosphere at 37°C for 24–48 h” [14].

Otitis media related factors
Patient was diagnosed as URTI if clinically “presented with an episode of common cold along with one of the following symptoms: (i) cough; (ii) rhinorrhea; (iii) nasal congestion or if presented with common cold, pharyngitis or tonsillitis” [18-20].

Adenoids (pharyngeal tonsils) are groups of lymphatic tissues located in the throat just behind the nose. Adenoid and the tonsils are the first line of defense against bacteria and viruses invasion. Adenoid inflammation is “the enlargement of the nasopharyngeal tonsils” [21] and “clinically presented with or without typical adenoid facies and difficulty in breathing, repeated upper respiratory tract infection, snoring, mouth breathing, secretory otitis media, nasal speech and sometimes obstructive sleep apnoea” [22].

Information on the complementary and alternative medicine (CAM) options for OM treatment were collected from the participants. In this study, participants were asked if they tried any of CAM (acupuncture, homeopathy, herbal medicine / phytotherapy, osteopathy, chiropractic, xylitol, ear candling, vitamin D supplement, and systemic and topical probiotics) in the form of introduction of unconventional ear drops and concoctions such as oil and honey, etc. into the middle ear [23,24].

Different types of trauma (accident) such as foreign objects, barotrauma and concussive trauma may directly or indirectly affect the ear. Foreign objects were the most common ear trauma that may cause damage or perforation to the tympanic membrane (TM) or eardrum as a result of introducing objects such as keys, hairpins, paperclips, and swabs. Both of barotrauma and concussive trauma result from rapid change in pressure between the middle ear and the outside air. Sudden and

Table 1 Inclusion and exclusion criteria.

<table>
<thead>
<tr>
<th>Inclusion and exclusion criteria</th>
<th>AOM</th>
<th>OME</th>
<th>COM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impaired hearing</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Pain (otalgia)</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Tenderness</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Purulent drainage (otorrhea)</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Systemic symptoms (ie, fever, malaise)</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Current antibiotic therapy</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>(topical or systemic) use or used in the preceding 2 weeks</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Recent ear surgery or an in-situ grommet or tympanostomy tube</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mastoid surgery in the preceding 12 months</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Congenital ear, Obstructed middle ear (eg, polyp) and hearing problems</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Patients with ear discharge due to cholesteatoma</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

OME: Otitis media with effusion; AOM: Acute otitis media; COM: Chronic otitis media.
(+): referred to inclusion criteria; (-): referred to exclusion criteria.
extreme change in pressure around the TM may occur following driving up and down in the mountains or scuba diving blow to the ear. Also when flying and water skiing or when exposed to the sound of an explosion or the concussion from a gunshot near the ear.

**Statistical analysis**

Data was collected and analyzed using Microsoft Excel Spreadsheet. Descriptive analysis was performed concerning the most common related factors to otitis media and the common pathogen isolate.

**Results**

**Descriptive analyses**

Out of 300 collected ear swabs, the vast majority 218 (72.7%) of patients were in age group of less than 10 years old compared to 82 (27.3%) cases of ten or more than ten years old. In general, each of COM (109, 36.3%) and OME (104, 34.7%) constitute separately about two third of the studied sample compare to 87 (29.0%) cases of AOM (Table 2). The primary diagnosis was OME in 86 (28.7%) cases under ten years old, while he COM was diagnosed in 34(11.3%). OM with URTI was found in 126 (42.0%) of cases and 93 (31.0%) of patients were diagnosed OM with adenoid inflammation and URTI (Table 2).

In table 3, the most common organisms isolated were *Pseudomonas aeruginosa* 105 (35.0%), *Staphylococcus aureus* 75(25.0%) and *Proteus ssp.* 72 (24.0%) respectively. However, *Enterobacteriaceae* members such as *Escherichia coli* were isolated in 21(7%) of patients and *Streptococcus pneumoniae* in 18 (6%) of patients respectively (Table 3).

**Discussion**

In this study, three different groups of OM namely: AOM, OME and COM have been diagnosed, however the incident was not much different. COM was in the highest incidence and reported in 36.3% of cases indicating improper medical treatment of AOM and OME in Iraq [25, 26]. Indeed, after US-led invasion of Iraq in 2003, the security, health care services and socio-economic status have been worsened significantly [27]. A great number of Iraqi families who are living in rural regions and even the displaced families who are forced to live in small camps with poor hygiene, malnutrition and overcrowding were more liable to develop different diseases including OM [26,28]. Beside all these factors, the lack or poor implementation of child health care programs such as integrated management of neonate and child health (IMNCH), the insufficient number of trained and specialized staff [27,29] and the deficiency of effective treatment have either led to misdiagnosis or to evolution of OM from acute to chronic status. Moreover, the short and straight ET in children is more likely to ease moving of pathogens directly from nose, adenoids and sinuses to middle ear “particularly during coughing, sneezing, vomiting, and forced feeding commonly practiced in our environment with the child’s nose blocked, while being held head down and half prone” [30,31]. Our clinical findings were agreed with this fact, in which the incidence of OM (AOM, OME and COM) was higher among children under 10 years old. Similar results were reported in Nigari [24], Iraq [26], Nibal [30], Egypt [32], Saudi Arabia [33] and China [34].

In this study a number of contributing factors found to be clinically related in the emerging of OM. The highest percent was among children presented with URTI and OM. Such findings are shedding the light about the role of respiratory diseases in the occurrence of otitis media. Results of this study were supported by earlier findings from studies among Nigerian children [2], and school-aged children in Yemen [35]. In fact, children are prone to URTI due to their immature immune system that minimally protects them against the opportunistic organisms [36]. Although the vast majority of otitis media cases occur in children under the age of 10 years, especially in the first six years of age, the adult population is not immune to this affliction [37].

In this study, the most commonly isolated pathogen was *Pseudomonas aeruginosa* (35.0%) followed by *Staphylococcus aureus* (25.0%) and *Proteus ssp.* (24.0%) respectively. This trend is similar to findings observed in Iraq [38], Gaza Strip, Palestine [14], Kashimir, India [39], Ethiopia [40], and Pakistan [41]. However, other studies reported a reverse sequence to our results where *Proteus ssp.*, followed by *S. aureus* and *Pseudomonas ssp.* were the predominant isolates [42-43]. *Pseudomonas aeruginosa* is known to be the most common secondary bacterium associated with ear infection, because of “its ability to survive in competition with other organisms and resistance to antibiotics” [40]. This may explain partly the reason behind the dominance of *Pseudomonas aeruginosa* in ear infection. “Moreover, *P. aeruginosa* uses its pili to attach to the necrotic or diseased epithelium of the middle ear. Once attached, the organism produces enzymes like proteases to elude the normal defense mechanism of body required for fighting infections”[40,42]. Furthermore, the isolation of fecal pathogens such as *K. pneumoniae* and *E. coli* indicating that the source of infection with these bacteria does not have to be from the nasal pharyngeal canal but can be obtained through fecal contamination of the auditory tube by improperly cleaning the ear and swimming in polluted water.

This is study has a number of limitation; because of the limited patient details in term of sociodemographic variables it was impossible to perform further analysis. The main objective was to confirm the clinical relationship between the URTI and OM, so there was no need to make antimicrobial susceptibility testing, however the earlier local study in Iraq found that *P. aeruginosa* were sensitive to imipenem (100%), Amikacin (85.0%) and Ciprofloxacin (62.5%) respectively [38].

**Conclusion**

In conclusion, the present study emphasized that OM and URTIs are clinically and microbiologically related. Otitis media was found to be highly prevalent among children of less than ten years, however adults are not so far from the disease. In this study, commonest pathogens isolated were *Pseudomonas aeruginosa* 105(35.0%), *Staphylococcus aureus* 75(25.0%) and *Proteus ssp.*72 (24.0%) respectively. In Iraq, OM is among the serious health condition that required further research to help understanding the progress of the disease. Scientific and strategic plans are required to formulate better therapeutic and preventive measures.
Table 2 The most common related factors to otitis media (n=300)

<table>
<thead>
<tr>
<th>Related factors</th>
<th>Less than 10 year old</th>
<th>10 years and more</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AOM</td>
<td>OME</td>
<td>COM</td>
</tr>
<tr>
<td>URTI</td>
<td>10</td>
<td>41</td>
<td>39</td>
</tr>
<tr>
<td>Adenoid Inflammation with (URTI)</td>
<td>27</td>
<td>35</td>
<td>11</td>
</tr>
<tr>
<td>Adenoid Inflammation</td>
<td>13</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Complementary and Alternative Medicine (CAM)</td>
<td>5</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>Trauma</td>
<td>2</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>57</td>
<td>86</td>
<td>75</td>
</tr>
</tbody>
</table>

Table 3 Aerobic bacteria isolated from discharging ear.

<table>
<thead>
<tr>
<th>No.</th>
<th>Isolated Bacteria</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pseudomonas aeruginosa</td>
<td>105</td>
<td>35</td>
</tr>
<tr>
<td>2</td>
<td>Staphylococcus aureus</td>
<td>75</td>
<td>25</td>
</tr>
<tr>
<td>3</td>
<td>Proteus sp.</td>
<td>72</td>
<td>24</td>
</tr>
<tr>
<td>4</td>
<td>Escherichia coli</td>
<td>21</td>
<td>7</td>
</tr>
<tr>
<td>5</td>
<td>Streptococcus pneumoniae</td>
<td>18</td>
<td>6</td>
</tr>
<tr>
<td>6</td>
<td>Klebsiella pneumoniae</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>Streptococcus pyogenes</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>300</td>
<td>100%</td>
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Abbreviations


Declarations

Acknowledgement

We render our special thanks to all medical and paramedical staff in Baquba teaching hospital for their help, time and openness during the data collection.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Availability of data and materials

Data will be available by emailing hanan6319@gmail.com

Authors’ contributions

HRH is the principal investigator of the study who designed the study and coordinated all aspects of the research including all steps of the manuscript preparation. She is responsible for the study concept, design, writing, reviewing, editing and approving the manuscript in its final form. SF, RMH and AH contributed in the study design, analysis and reviewed and approved the manuscript. SAAJ contributed in the study design, analysis and interpretation of data, drafting the work, writing the manuscript and reviewed and approved the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

We conducted the research following the Declaration of Helsinki, and the protocol was approved by the Center of Training and Human Resource Development, Diyala Province Health Directorate, Ministry of Health, Iraq (Ref: official letter No. 303 issued in 21st January 2018). Confidentiality was assured with signed informed consent.

Consent for publication

Not applicable

Competing interest

The authors declare that they have no competing interests.

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Table 3 Aerobic bacteria isolated from discharging ear.

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17. CLSI. Performance standards for antimicrobial susceptibility testing, seventeenth informational supplement, document M100-S17, 2007; No 1.