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An Overview of Bacterial Respiratory Tract Infections and their Etiologies

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ABSTRACT

Background: Respiratory tract infections (RTIs) are considered as one of the most important causes of morbidity and mortality, worldwide. A wide variety of bacteria and viruses are responsible for the development of RTIs. Considering the importance of respiratory tract infections, this study aimed to provide an overview of the most important respiratory tract infections and inflammations of bacterial origin and their etiologies.

Results: A literature review was conducted to find original studies associated with respiratory infections. Articles that provided evidence on respiratory tract infections as well as their clinical manifestations and etiologies were included in this research.

Conclusion: Considering the importance and economic burden of respiratory tract infections as well as their diversity and widespread prevalence in different communities, it is necessary to implement preventive measures at the national level to control and deal with respiratory diseases with high prevalence in all age groups, in addition to observing the principles of health and hygiene.

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Introduction

Among the main leading causes of mortality and morbidity worldwide are respiratory tract infections (RTIs) (1). Acute RTIs are more prevalent in children younger than five years, with admission rates of 30-50% and hospitalization rates of 20-40% (1). A wide variety of different bacteria and viruses are responsible for the development of RTIs. Therefore, it is crucial to identify the causative agents of respiratory infections in order to determine the appropriate treatment methods that should be started early to achieve the desired clinical outcomes because delay in proper diagnosis and treatment leads to adverse consequences. Respiratory tract diseases occur in both the lower and upper parts of the respiratory system (1). The lower respiratory system is composed of the trachea and the lungs. Each lung is composed of alveoli (air sacs), bronchioles, bronchi, and windpipe. On the other hand, the larynx or voice box, pharynx (throat), mouth, nasal cavity, and nose form the upper respiratory system (2).

Upper respiratory tract infections (URTIs) could be described as self-limiting infections and inflammations affecting upper airways, which are usually accompanied by cough without any pneumonia symptoms (3, 4). Bacteria and viruses are responsible for various types of URT disorders such as sinusitis, pharyngitis, epiglottitis, laryngitis, acute otitis media, diphtheria, and common cold (4). URTIs are the causes of low-intensity but widespread outbreaks that contribute to the circulation of microorganisms in communities (1).

On the other hand, lower respiratory tract infections (LRTIs) are infections affecting lower airways below the larynx, including the trachea and the alveolar sacs. Bacteria and viruses cause a variety of lower respiratory tract infections as follows: bronchitis, bronchiolitis, COPD (chronic obstructive pulmonary disease), tuberculosis, Legionnaires' disease, Q fever, whooping cough (pertussis), and pneumonia (5). LRTIs could be categorized into bronchiolitis and pneumonia; however, some of their etiological, clinical, and radiological aspects often overlap (4, 6). Pneumonia is the most common type of LRTIs. As the most prevalent infection among all age groups, pneumonia is one of the ten leading causes of mortality in the United States (7). Pneumonia is also ranked as the sixth leading cause of mortality in people over the age of 70 (7). Although the disease is one of the main causes of morbidity and mortality in adults and children as well as the main cause of admission to hospitals in underdeveloped and developing countries, epidemiological studies have failed to connect etiological and prognostic factors in these communities (8-11).

Based on the reports of the World Health Organization (WHO) in 2012, about 450 million pneumonia cases are diagnosed worldwide every year, of which 3 million cases lead to death, accounting for 5.5% of all deaths (12). Therefore, pneumonia is considered as a critical threat and health concern, especially for elderly people and children (12). According to the reports, pneumonia led to the death of 2.5 million people in 2019, almost one-third of them were children under the age of five; thus, it is considered as the major cause of mortality in children younger than five years (13, 23).

According to the causative agents, acquisition mechanisms, and clinical manifestations, pneumonia could be classified in to community-acquired pneumonia (CAP) (14), hospital-acquired pneumonia (HAP) (nosocomial), and pneumonia in patients with immunodeficiency (14).

Studies have shown that the all-cause mortality rate associated with community-acquired pneumonia is 28% during one year after the infection onset (15). Community-acquired pneumonia (CAP) is ranked as the seventh leading cause of death in the United States (32). The causative agent of CAP is characterized based on the characteristics of geographic regions.

Nosocomial pneumonia or HAP is a type of lower airways disease that develops as a common and serious problem within at least two days after admission to the hospital (16). Patients with nosocomial pneumonia are often

immunocompromised with various types of preexisting illnesses, which increase their susceptibility to infections. HAP is one of the most common infectious diseases, responsible for 15-20% of all nosocomial complications (17). HAP is ranked second after urinary tract infection (UTI) which is responsible for 30% of hospital-acquired complications (17). Research has shown that HAP is the most prevalent (10-20%) nosocomial infection in intensive care units (ICU), leading to the death of 20-70% of cases (18). In addition, an exploratory multicenter research conducted in 46 healthcare centers in eight developing countries (India, Turkey, Peru, Morocco, Mexico, Colombia, Brazil, and Argentina) reported that the prevalence of nosocomial pneumonia may be higher in these countries considering unreported or unidentified cases (19).

The etiological agents of respiratory tract infections (RTIs) could be classified as follows: typical Gram-positive bacteria (e.g., *Streptococcus pneumoniae*, *Staphylococcus aureus*, and *Mycobacterium tuberculosis*), typical Gram-negative bacteria (e.g., *Haemophilus influenzae* and *Pseudomonas aeruginosa*), atypical bacteria (e.g., *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, *Legionella* species, and *Coxiella burnetii*), respiratory viruses (respiratory syncytial virus, coronaviruses, Influenza virus, parainfluenza virus, adenovirus, rhinovirus, enterovirus, herpes virus, measles virus, hantavirus, and human metapneumovirus), fungi, and anaerobes. Studies have shown that bacterial pneumonia is more likely to cause death compared to viral pneumonia which is less severe (20). However, pneumonia caused by viruses is also of particular importance because it is easily transmitted and affects the newborn mortality rate and facilitates the incidence of bacterial co-infections, transforming it into a worldwide threat (20). About 200 million viral pneumonia infections are reported annually worldwide, half of which are in children (21).

Clinical symptoms of RTIs vary from mild self-limiting to serious life-threatening manifestations, which depends on the type of illness, age, organisms involved, and other medical problems. These symptoms include: cough, fever, sore throat, wheezing, chest pain, fatigue, runny nose, headache, sneezing, shortness of breath, dizziness, sputum production, nausea, vomiting, and diarrhea (30).

Considering the importance of respiratory tract infections, this study aimed to provide an overview of the most important bacterial RTIs and their etiologies. Although so far many studies have investigated the causative agents of respiratory diseases, the main contribution of this study to the literature is to provide a comprehensive overview of the most important upper and lower respiratory diseases of bacterial origin in one place. The information provided in this study is expected to be useful for researchers in this area.

Lower respiratory tract infections

Lower respiratory tract infections (LRTIs) are one of the most prevalent infectious diseases, accounting for about 45% of all community-acquired complications; also, 25% of all nosocomial infections are related to LRTIs (22). LRTIs are considered as the fourth most leading cause of mortality worldwide (23). They are mainly caused by viruses and bacteria. The most important LRTIs are bronchitis, bronchiolitis, COPD, tuberculosis, Legionnaires' disease, Q fever, whooping cough (pertussis), and pneumonia (24). Viruses are the main leading causes of bronchitis and bronchiolitis (30). The causative agents of pneumonia are highly diverse and vary depending on whether the disease is CAP or HAP (25).

In this section, the most important LRT infections of bacterial origin are presented along with their clinical manifestations and etiologies, including bacterial pneumonia, tuberculosis, Legionnaires' disease, Q fever, and whooping cough.

Pneumonia refers to an infection caused by microbial agents such as bacteria, viruses, and parasites, in which parenchymal tissues become

inflamed, and air sacs (alveoli) are filled with fluids and WBCs (white blood cells) (26). The most important bacteria that could cause CAP are as follows: *S. pneumoniae* (20–60% of cases), *H. influenzae* (3–10%), and atypical bacteria like *C. pneumoniae* (4-6%), *Legionella* species (2-8%), and *M. pneumoniae* (1-6%) (27). *S. pneumoniae* and *H. influenzae* are members of the normal flora of the human respiratory system with the ability to migrate directly through the airways to the lower respiratory tract and cause pneumonia (28). *S. pneumoniae* is responsible for most community-acquired pneumonia cases with an annual mortality rate of 3 million deaths worldwide (29). Other streptococci rarely cause pneumonia. S. aureus also rarely causes CAP, but staphylococcal CAP may be induced as a secondary infection following staphylococcal bacteremia or influenza (30). Nosocomial pneumonias and other pneumonias in immunosuppressed patients are mostly caused by Gram-negative pathogens and *Staphylococcus* species (30). Both Gram-positive (such as *S. aureus*) as well as Gram-negative (such as *Klebsiella pneumoniae*, *Escherichia coli*, *Enterobacter*, *Pseudomonas* spp., and *Proteus*) bacteria could be considered as the etiological agents of HAP cases (30, 31).

S. pneumoniae is a Gram-positive, non-spore forming, non-motile, anaerobic, opportunistic pathogen usually found in pairs or short chains (32). It is considered as the predominant etiological agent of CAP (29). Pneumonia caused by *S. pneumoniae* is more prevalent in people over 65 or under 2 years of age, smokers, alcoholics, and patients with asthma, COPD, or asplenia (32). Infection occurs following colonization of the oropharynx and nasopharynx through inhalation of these colonies causing lower respiratory tract infection. Clinical symptoms of pneumonia caused by *S. pneumoniae* are as follows: cough, fever, dyspnea, sputum secretion, and pleuritic pain (32). Pneumonias caused by *K. pneumoniae* and H. influenzae are more prevalent in the elderly over the age of 50 with preexisting illnesses, including COPD, alcohol use disorder, HIV (human immunodeficiency virus) infection, or diabetes mellitus (30).

H. influenzae is a pleomorphic, Gram-negative, oxidase positive, anaerobic, and non-motile coccobacillus that is found only in humans and commonly colonizes and infects the human respiratory tract. This organism is one of the main causative agents of both CAP and HAP (33). *H. influenzae* strains are divided into encapsulated and non-encapsulated types, both of which could cause bacteremic or non-bacteremic pneumonia in children and adults (34). Encapsulated strains are more virulent, especially *H. influenzae* serotype b (Hib) which is considered as one of the most well-known etiological agents of invasive infections in young children, including bacteremic pneumonia and meningitis. Non-encapsulated strains tend to be less virulent and are one of the main causes of pneumonia and chronic diseases in adults (34). As a human pathogen, *H. influenzae* bacteria are part of the URT normal flora, which mostly colonize the throat and nasopharynx (34). *H. influenzae* is mostly transmitted via respiratory droplets or direct contact with respiratory secretions (34). Clinical symptoms of pneumonia caused by *H. influenzae* are similar to those of other types of pneumonia, including fever, cough, and shortness of breath.

K. pneumoniae is a rod-shaped, Gram-negative, encapsulated, non-motile, anaerobic, opportunistic bacterium. This organism is one of the main causative agents of both CAP and HAP (35). CAP induced by *K. pneumoniae* and *S. pneumoniae* could be differentiated based on the type of sputum secreted (35). Sputum secreted in patients with *S. pneumoniae* infection is characterized as "blood-tinged" or "rust-colored", whereas sputum secreted in patients with *K. pneumoniae* infection is characterized as "currant jelly" (35). This is due to the fact that *K. pneumoniae* causes sever inflammation and necrosis in adjacent tissues (35). *Klebsiella* species are found as normal flora in the human gastrointestinal tract and stool (5-38%) (35, 42). In clinical settings, they could cause different infections upon entering the respiratory tract, including pneumonia and meningitis as well as

wound, surgical site, and bloodstream infections (42). *K. pneumoniae* is mostly transmitted through contaminated hands of medical staff and other persons (42). *K. pneumonia* is often fatal even if treated. Clinical symptoms of *K. pneumonia* infection include fever, chills, cough, yellow or bloody mucus, shortness of breath, and chest pain (35).

P. aeruginosa is a Gram-negative, non-spore forming, ubiquitous, aerobic, opportunistic bacillus that possesses polar flagella and protein constructs, facilitating its adhesion to respiratory epithelial tissue. *P. aeruginosa* is a nosocomial pathogen that could induce severe infections in hospitalized, immunosuppressed, and HIV infected patients and those with malignancies (41, 43). Moreover, *P. aeruginosa* infection is the most important chronic disease that could play a critical role in the progression of cystic fibrosis (41). Colonization of *P. aeruginosa* in airways damaged due to previous viral infections, trauma, or mechanical ventilation is mostly associated with sepsis, acute pneumonia, and even death. *P. aeruginosa* is also considered as a causative agent of CAP (41). These bacteria could survive and proliferate in nearly all aqueous habitats such as soil, sewage, plants, various foods, surface waters, hand-washing sinks, and humidifiers in hospital environments (41, 43). These organisms could be transmitted through direct contact with medical personnel or contaminated objects. Pneumonia induced by *P. aeruginosa* is accompanied by the following symptoms, including fever, chills, difficulty in breathing, chest pain, fatigue, and cough sometimes with yellow, green, or bloody mucus.

M. tuberculosis is a slender, rod-shaped, non-spore forming, Gram-positive, aerobic bacterium with the ability to persist in host tissues for decades without causing disease (36), it is a human pathogen that could cause pneumonia (CAP) mainly in developing countries (30). It is one of the deadliest infectious agents and the main leading cause of tuberculosis (TB) with more than one billion deaths in the past 200 years (44). Despite the low prevalence of TB in developed countries, infections caused by *M. tuberculosis* are yet considered as an important public health concern in the United States, particularly in patients with HIV or intravenous drug abuse disorder, institutionalized elderly people, as well as immigrants from underdeveloped countries (30). Non-tuberculous mycobacterial (NTM) species (atypical species) could also cause lung disease indistinguishable from tuberculosis (30). *M. tuberculosis* is transmitted from infected patients to others via inhalation of respiratory aerosols or droplets produced when coughing, sneezing, laughing, and even talking (36). Clinical symptoms of *M. tuberculosis* infection are as follows: chest pain, weight loss, fatigue, chills, night sweats, breathing and coughing with pain, and coughing for more than 21 days, which may be accompanied by blood or mucus.

Atypical pneumonia syndrome is described as a type of mild and non-lobar pneumonia associated with a variety of extra-pulmonary and URT manifestations (37). Atypical pneumonia infections could be caused by viruses as well as atypical bacterial pathogens like *C. burnetii*, *Legionella*, *M. pneumoniae*, and *Chlamydia* spp. (37).

M. pneumoniae is a spindle-shaped, pleomorphic, Gram-negative pathogen that is well-known as a common respiratory pathogen causing atypical pneumonia mostly in young individuals aged 5 to 19 years. *M. pneumoniae* pneumonia is usually referred to as walking pneumonia, it is more common in overcrowded public places and causes outbreaks mostly among military recruits and college students (30, 37). *Mycoplasma* is mainly transferred from infected patients to others via inhalation of respiratory aerosols or droplets produced when sneezing and coughing (37). Clinical symptoms of *M. pneumoniae* infection are non-severe and self-limiting, including low-grade fever, persistent dry cough, malaise, headache, and mild shortness of breath on exertion (37).

Another type of atypical pneumonia is caused by *Chlamydia* that are intracellular, obligate, Gram-negative, small pathogens able to induce chronic and acute illnesses in humans and animals (37).

Three *Chlamydia* species that could induce chlamydial pneumonia are as follows: *C. pneumoniae*, *C. psittaci*, and *C. trachomatis* (30, 37); of which *C. pneumoniae* is the most prevalent etiological agent of RTIs in humans, which are mainly asymptomatic (38). *Chlamydia* could be transferred through airborne respiratory aerosols/droplets and induce mild to severe pneumonia and bronchitis. *C. pneumoniae* is found only in humans (37) and considered as one of the most well-known etiologies of CAP (38). *C. pneumoniae* could cause pneumonia epidemics among college students and military recruits (30). Both *C. pneumoniae* and *C. psittaci* could induce RTIs in adults, while *C. trachomatis* induces pneumonia in neonates and young infants (30, 38). *C. psittaci* pneumonia, also known as psittacosis, is considered as a common occupational pneumonia among bird holders, farmers, and veterinarians, which occurs following exposure to infected birds. Birds are the primary reservoirs of psittacosis, and humans are infected through inhalation of airborne respiratory aerosols or droplets (37). Common symptoms include: runny or stuffy nose, fatigue, headache, low-grade fever, hoarseness, sore throat, and cough that could last for weeks or months (38).

Legionnaires' disease is another type of atypical pneumonia. *L. pneumophila* is an aerobic, waterborne, Gram-negative, non-motile, small bacterium that is considered as the causative agent of Legionnaires' disease. The organism could induce a variety of clinical symptoms, but pneumonia is the most common presentation of *Legionella* infection (30, 39). *Legionella* is a major etiology of both CAP and HAP. These organisms could survive and proliferate in warm water environments and cause pneumonia and infections in susceptible individuals with chronic heart or lung diseases or weakened immune system through inhalation of aerosols from tap water, respiratory devices, air conditioners, humidifiers, misting systems, fountains, and showers (40). The disease symptoms include fever, malaise, chills, moderate cough, nausea, vomiting, myalgia, headache, dyspnea, confusion, and other neurological disorders (39, 40).

Q fever is an infectious bacterial disease induced by a pleomorphic, Gram-negative coccobacillus called *C. burnetii* (37). This pathogen mainly infects domestic animals including goats, sheep, and cattle and spreads through inhalation of aerosols or direct contact with contaminated urine and stool, unpasteurized milk, or infected animals; thus, it is often considered as an occupational disease among farmers (30). Pneumonitis is one of the main clinical presentations of *C. burnetii* infection, which is more common in elderly patients with immunodeficiency (30, 37). The disease may become chronic and lead to endocarditis in few patients, which could be fatal (37). Clinical symptoms of acute Q fever could be as follows: cough, headache, high fever, restlessness, and pneumonia.

Whooping cough (pertussis) is another bacterial respiratory tract infection caused by an aerobic, slow-growing, Gram-negative, small bacterium called *Bordetella pertussis* (45, 57). Whooping cough, also known as pertussis, is a respiratory disease that is highly contagious and found only in humans (57). The disease could be divided into three stages as follows. The catarrhal phase is almost non-severe and inconsiderable with presentations such as mild fever, sneezing, runny nose, and nasal obstruction; *B. pertussis* is highly infectious in this stage. In the paroxysmal phase lasting for several weeks, the mass of mucus in the airways causes rapid coughs that are uncontrollable and often lead to vomiting. In the convalescence stage, chronic cough is the predominant symptom that lasts for several months (45, 57). Pertussis is highly communicable from infected patients to others via respiratory droplets and aerosols (45). Pertussis is more dangerous for infants. The disease usually begins with mild symptoms (like a common cold) such as mild occasional cough, apnea, low-grade fever, and runny nose (in babies) and then progresses to more severe symptoms in the later stages, including rapid coughs that are followed by a sharp "whoop" sound, vomiting, and exhaustion (45, 57).

Upper Respiratory Infections

Upper respiratory tract infections (URTIs) are the most prevalent diseases evaluated in outpatient settings (55). URTIs vary from non-severe self-limiting illnesses like common cold to more severe life-threatening illnesses like epiglottitis. Most URTIs are caused by viruses (30). The most common symptoms of upper respiratory infections (URIs) include cough, sore throat, nasal obstruction, and headache (55). In this section, the most important URTIs of bacterial origin along with their clinical presentations and etiologies are presented, including strep throat, otitis media, bacterial rhinosinusitis, diphtheria, epiglottitis, laryngitis, and laryngotracheitis (4).

Strep throat, also known as streptococcal pharyngitis, is an inflammation of the pharynx and a common upper respiratory tract infection caused by *S. pyogenes*. *S. pyogenes* called group A *Streptococcus* (GAS) is a non-spore forming, non-motile, Gram-positive, aerotolerant bacterium found in pairs/chains. *S. pyogenes* is the most prominent etiological agent of pharyngitis and tonsillitis (52, 30). Streptococcal pharyngitis not only induces an acute illness but could also trigger glomerulonephritis and acute rheumatic fever syndromes as delayed consequences of GAS pharyngitis (52). Occasionally, it is accompanied by scarlet fever that is caused by the elaboration of streptococcal pyrogenic exotoxins (52). *S. pyogenes* is easily transmitted through direct contact or inhalation of airborne respiratory droplets produced when sneezing and coughing. Clinical symptoms of streptococcal pharyngitis may include fever, severe throat pain, muscle pain, difficulty in swallowing and speaking, earache, headache, sensitive lymph nodes in the neck, swelling and redness of the tonsils with patches of pus, and tiny red spots on the back of the mouth roof (46). Other pathogens sometimes causing pharyngitis are as follows: *Corynebacterium diphtheriae, C. haemolyticum*, mixed anaerobic infections, *Neisseria gonorrhoeae*, *C. pneumoniae*, and *C. trachomatis* (30, 52). *M. pneumoniae* and *M. hominis* are associated with acute pharyngitis (30).

Otitis (externa, media) refers to ear infections that occur especially in older infants. Otitis externa is described as an inflammation that affects the external ear canal and causes its redness and swelling, this condition is caused by commensal skin microflora such as *S. epidermidis*, *S. aureus*, diphtheroids, and sometime an anaerobic bacterium like Propionibacterium acnes (30). The causative agent of acute otitis externa may be *P. aeruginosa* along with other skin microflora, which could lead to malignant otitis externa, especially in elderly diabetic people (30). Clinical presentations of otitis externa may be as follows: itching, severe pain, sensitivity of the ear lobe while stretching, a feeling of ear obstruction due to the presence of furuncles, purulent ear discharge, and loss of hearing. Clinical symptoms of acute otitis externa include the presence of granular tissue in the ear canal, foul-smelling purulent ear discharge, and severe and continuous earache (30).

Otitis media refers to middle ear infections caused by commonest bacteria (30). Otitis media (OM) is a term encompassing acute OM (AOM), OM with effusion (OME), and chronic suppurative OM (CSOM) (47). Among neonates the most common cause of acute otitis media is S. pneumoniae; however, *E. coli*, GBS species, and Enterococcus spp. could also cause AOM. In young children, *H. influenzae*, *Moraxella catarrhalis*, and *S. pneumoniae* are the most common etiological agents of AOM. Accumulation of non-infectious fluid in the middle ear due to blocked eustachian tubes leads to a condition called otitis media with effusion (30). Chronic suppurative OM refers to persistent discharge through a permanent perforation in the tympanic membrane (30). Clinical symptoms of otitis media could be as follows: ear pain, fever, vomiting, difficulty in sleeping and hearing, fluid draining from ear(s), and loss of balance. Acute otitis media that is more common in young children is also manifested by the secretion and collection of pus in the middle ear (middle ear effusion), leading to inflammation of the

eustachian tubes and possibly diarrhea, vomiting, nausea, and fever (30).

Bacterial rhinosinusitis is another URT infection that is described as the infection of both nasal cavities and sinuses (58). The normal flora of the nasopharynx is composed of a highly diverse microbial community harboring several opportunistic organisms; therefore, infections that lead to rhinitis and sinusitis are caused by several different organisms (48). Rhinitis and sinusitis usually occur as secondary infections following a viral URT infection (58) that does not improve during 10 days or exacerbates after one week, thereby effectively compromising body's defenses and allowing opportunistic organisms to invade (48). Since bacterial sinusitis refers to simultaneous inflammation and infection inside the nose and paranasal sinuses and scarcely occurs without rhinitis, it is referred to as rhino-sinusitis (48, 58). The etiological agents of bacterial rhinosinusitis are mostly similar to the etiologies of AOM, such as M. catarrhalis, H. influenzae, and S. pneumoniae (58). In addition, *S. aureus*, anaerobic bacteria, and other streptococcal bacteria are responsible for a limited number of infected cases (48). Clinical symptoms of bacterial rhinosinusitis may be as follows: cough, fever, fatigue, nasal and postnasal drainage, nasal obstruction, maxillary dental pain, facial pressure/pain, dysomia, ear pressure/fullness, and worsening of symptoms after initial improvement (48, 49, 58).

The causative agent of diphtheria is toxin-producing *C. diphtheriae* that is a club-shaped, non-capsulated, Gram-positive, non-motile bacterium found as part of the nasopharynx normal flora. Diphtheria is typically an acute communicable respiratory disease that not only affects the oropharynx but could also induce skin lesions of other origins (e.g., dermatitis, impetigo, eczema, pyoderma, surgical wounds, or insect bites) (50). The production of a white-gray pseudo-membrane in the throat is one of the characteristic features of respiratory diphtheria, which is able to induce a severe local respiratory mucosal reaction (51, 52). These pseudo-membranes could lead to airway obstruction resulting in suffocation and death (52). Severe diphtheria is characterized by swollen soft tissues and lymph nodes in the neck due to inflammation, which is associated with a higher mortality rate (51). Although affecting people of all age groups, the disease seems to be more intense in patients under 5 or over 40 years of age. Diphtheria may initially involve places other than the pharynx mucosal membrane but then usually manifests as localized pseudomembranous inflammation of the URT mucosal surfaces as well as systemic inflammation of the heart and nerves (less common) (50). Diphtheria, like strep throat, is usually transferred from infected people to others through inhalation of respiratory droplets and aerosols released when coughing. Diphtheria is characterized by the presence of pseudo-membranes in the throat, which may lead to asphyxia and death (50, 51).

Epiglottitis is an inflammation of the epiglottis as the upper part of the trachea. This condition could be serious. The main cause of epiglottitis, especially in children aged 2 to 5 years, is *H. influenzae* type b (52). Epiglottitis in adults may be of viral origin, which is less common. Bacteria associated with epiglottitis nowadays include *S. pneumoniae*, *S. aureus*, and beta-hemolytic streptococci (52). More severe bacterial cases are mainly caused by C. diphtheriae, beta-hemolytic *Streptococcus* group A, and *H. influenzae* type b. Clinical symptoms of epiglottitis include difficulty in breathing and swallowing, fever, hoarseness, and severe sore throat with a cherry-red epiglottis (30, 52).

Inflammation of the larynx, known as the voice box, is called laryngitis, which often occurs in adults and older children with common viral URTIs (56). Inflammation of the upper airways usually leads to laryngitis. Acute laryngitis is commonly caused by infection. Bacterial causes of laryngitis include *K. pneumoniae*, *M. catarrhalis*, *S. aureus*, *S. pneumoniae*, *H. influenzae* type b, and beta-hemolytic streptococci (53). The main clinical symptoms of laryngitis include voice change or hoarseness, dysphonia, and anterior neck pain/discomfort, which could be associated

with other presentations like fever, cough, throat clearing, muscle pain, and dysphagia (53).

Laryngotracheitis, also known as "croup", is an inflammation of the larynx, trachea, and subglottic area, which leads to respiration obstruction. The disease is characterized by "barking" coughs (56). Although this infection is more prevalent in children, croup syndrome takes a more severe disease course in adults than in children. Sever bacterial infections are more likely to be caused by *S. pyogenes*, *S. pneumoniae*, *H. influenzae* type b, *M. catarrhalis*, and *C. diphtheriae*. Clinical symptoms of laryngotracheitis include nasal complaints such as hoarse throat, runny nose, mild fever, "barking" cough, dryness, fatigue, irritation, coryza, and problems with breathing (54, 56).

Conclusion

Considering the importance and economic burden of respiratory tract infections as well as their diversity and widespread prevalence in different communities, it is necessary to implement preventive measures at the national level to control and deal with respiratory diseases with high prevalence in all age groups, in addition to observing the principles of health and hygiene.

Ethics approval and consent to participate

Not needed.

Conflict of interest

The authors declare no competing financial interest.

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