Treatment and prevention of acute respiratory infections among Iranian hajj pilgrims: a 5-year follow up study and review of the literature

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Abstract

Background: Respiratory diseases/syndromes are the most common causes of referring to physicians among pilgrims in Hajj. They lead to high morbidity, impose high costs on the health system and are among the major obstacles for pilgrims to perform Hajj duties. The main aim of our study was to determine types, frequencies, etiologies, and epidemiologic factors of respiratory diseases among Iranian Hajj pilgrims and to suggest some preventive and treatment strategies.

Methods: To determine the types and frequencies of respiratory syndromes, we implemented a syndromic surveillance method in Iranian health care system for Hajj during 5 consecutive years. To achieve the etiology of these diseases, we performed 4 concurrent before and after studies. We also evaluated efficacy of the flu and pneumovax vaccines among Iranian Hajj pilgrims in 2 studies. To determine some other epidemiological factors, we conducted 4 additional studies.

Results: The most common problem was common cold like syndrome. Origins of the most upper respiratory problems were infections, and allergies were less involved. Among infectious agents, viruses were the most common agents and their frequencies were as follows respectively: Adenoviruses 38 (36.2 %), Rhinoviruses 31 (30%), Influenza type B virus 21 (20%). Bacteria were often the secondary causes and their frequencies were as follows respectively: Intestine bacillus 69 (19.4%), Chlamydia pneumonia 20(15.8%), Haemophiluses 32 (9.1%) and Streptococcus (A,C and G) 30 (8.5%). We introduced some epidemiological factors as effective in creating respiratory diseases.

Conclusion: In this paper, we suggested some applied points for prevention, treatment, and correction of common malpractices in the treatment of respiratory diseases of the pilgrims.

Keywords: Respiratory tract infections, Prevention and control, Islam, Iran, Saudi Arabia.

approximately, 100,000 Iranian pilgrims have participated in hajj rituals each year in recent years (8).

In this regard, the following questions are raised:

What forms of respiratory diseases have been emerged? What is the most common form? What are the etiological causes of these diseases? Do these diseases have infectious origin? If they are infectious, what class of infectious agents (viruses, classic bacteria, atypical bacteria, and air dispersed fungal spores) is more effective on creation of the diseases? In case of infections, which organisms play a more important role? What are the roles of respiratory allergies? What are the roles of physical factors such as weather dryness, direct exposure to cold air, drinking cold liquids in sweating? Does the gastroesophageal reflux play a role in causing the diseases? What are the common errors which occur in management of the diseases? What are the best therapeutic methods?

The aim of our study was to determine types, frequencies, etiologies, and some of other epidemiologic factors of respiratory diseases among Iranian Hajj pilgrims and to suggest some preventive and treatment strategies based on our 10 years of experience and literature review.

Methods

To determine the types and frequencies of respiratory syndromes, we implemented a syndromic surveillance method, proposed by the Center for Control and Prevention of Diseases (CDC) (9) in Iranian health care system for Hajj. Consequently, we reviewed the physicians’ reports about respiratory diseases of 254,823 Iranian pilgrims between 2004 and 2009 (10).

To study the etiological causes of respiratory diseases in Hajj, we conducted 4 concurrent before and after studies in 2004 (11-14). Six educational departments (microbiology, virology, immunology, mycology, social medicine, statistics and epidemiology, all affiliated to Tehran University of Medical Sciences) cooperated with this study. We evaluated 1,018 serum samples (509 samples before and 509 samples after the journey) for serological assessments, 357 samples for studying pharyngeal classic bacteria, 105 pairs of samples for studying pharyngeal secretions in terms of viruses, 130 pairs of fresh blood samples for studying Nitro Blue Tetrazolium test (NBT) and immunological tests, 128 pairs of serum samples for studying atypical bacteria and 146 samples for studying antibody of respiratory fungi and 500 questionnaires for evaluating the epidemiological issues. Serum samples were gathered at the time of departure from the country and 3 weeks after their return to the country, and were kept at -20ºC. Fourfold increase of antibodies values were considered as acceptable for confirmation of changes. Laboratory tests which were used for detection of organisms were as follows:

Direct smear assessment, culturing the organisms in specific medias, hemagglutinin inhibition test, immune-fluorescence tests, ELISA, specific medias and tests for viruses such as DMEA media and Dako kits, count immune electrophoresis, Latex agglutination tests, and NBT for investigating fresh blood.

Etiological factors that were examined in this study were as follows:


Immunological Tests include: NBT, immunoglobulin (A-G-M-E), interleukin 4, and gamma interferon.

We also evaluated the efficacy of the flu and pneumovax vaccines among Iranian
Hajj pilgrims in 2 studies (15-16). To determine some of other epidemiological factors, we conducted 4 additional studies (4-5, 8, 17). We used the results of above mentioned studies and reviewed the literature, and offered a guideline for the treatment and prevention of acute respiratory infections (ARIs) in Hajj.

**Statistical Analysis**
We used independent-t, paired t-tests and ANOVA for numerical data, Mann-Whitney U, Wilcoxon and Kruskal-Wallis as non-parametric tests, chi-square and fisher exact tests for nominal data and odds ratio for evaluating the efficacy of vaccines.

**Results**
The frequencies of symptoms and types of reported respiratory disorders through syndromic surveillance system were as follows (Each patient may suffer from more than one disorder) (5):

- Respiratory disorders with each types and causes: 181,433 (71.2%)
  - Common cold like illness: about 120,149 (47.15%)
  - Influenza like illness: 27,215 (10.68%)
  - Sinusitis and sinobronhitis: 25,609 (10.05%)
  - Pneumonia: 1146 (0.45%)
  - Respiratory allergic syndrome (respiratory signs with allergic manifestations): 44,211 (17.35%)
  - Asthma and COPD: about 4841 (1.9%)
  - Early exudative pharyngitis or complications of respiratory disorders: 19,774 (7.76%)
  - Early infectious conjunctivitis or complications of respiratory disorders: about 2%

- Intestine bacillus: 69 (19.4%)
- Pseudomonas: 4 (1.1%)

The above mentioned items had been extracted from oropharygeal discharge and sputum cultures in acute phase of diseases (5).

- Chlamydia pneumonia: 20 (15.8%)
- Legionella pneumophila: 8 (6.6 %)
- Mycoplasma pneumonia: 2 (1.1%)

**Etiology**

**Microbiological investigations**
1. Bactria (N=357 samples):
   A: Common classic bacteria:
   - Streptococcus (A,C and G): 30 (8.5%)
   - Haemophilus: 32 (9.1%)
   - Intestine bacillus: 69 (19.4%)
   - Pseudomonas: 4 (1.1%)

   B: Common atypical bacteria (128 pairs of serum samples before and after the journey):
   - Chlamydia pneumonia: 20 (15.8%)
   - Legionella pneumophila: 8 (6.6 %)
   - Mycoplasma pneumonia: 2 (1.1%)

**Immunological investigations**
- NBT test: The test was used for the function of neutrophils, the defensive cells in body against infections. The before and after the travel difference was statistically significant (p=0.001).
- Gamma interferon: This agent significantly enhances the phagocytic ability of neutrophils. The before and after the travel difference was statistically significant. (p=0.001). In the other word, these two agents were investigated as infection markers which showed statistically significant differences (14).
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- Interleukin 4: No statistically significant difference was observed.
- IgE: This immunoglobulin increases in allergies. There was not statistically significant difference between before and after titers.
- IgA: This immunoglobulin plays an important role in mucosal defense. No statistically significant difference was observed \((p=0.49)\).
- IgG: This immunoglobulin could be a marker for chronic or previous infections. There were no statistically significant difference between the before and after tests \((p=0.93)\).
- IgM: This marker has a role in acute infections. The difference between before and after tests was statistically significant \((p=0.046)\).

The above tests were performed on 130 pairs of before and after the travel serums.

Other epidemiological investigations
- In this part, the behavioral and environmental factors, affecting the occurrence of respiratory diseases among the pilgrims were studied. Some of these factors included:
  - Use of the flu and pneumovax vaccines (solely or combined) before the trip. Based on our study published in 2004, the effectiveness of influenza vaccine was 50%. We found that injection of influenza vaccine could decrease the Influenza-Like Illness (ILI) incidence \((15)\). We also conducted a similar study in 2005 which showed that the effectiveness of the flu vaccine was not statistically significant \((p=0.93)\).
  - We reported some epidemiological factors affecting the occurrence of respiratory diseases among Iranian pilgrims in 2005 \((17)\). These factors were as follows:
    - Increase in the age: The higher the age of the pilgrims, the higher the percentage of respiratory diseases was.
    - Increase in the vulnerability of the pilgrims: Respiratory diseases raised with the increase of the number of high risk pilgrims in the caravans.

Score of management: We developed a new scoring system for evaluating managerial performances in each caravans. The percentage of respiratory diseases among pilgrims of related caravan decreased as the managerial performance scores in each caravan increased.

Score of health management: We also developed a new scoring system for evaluating the physicians of caravans. As the health management scores of the physicians increased in each caravan, the percentage of respiratory diseases among pilgrims of the caravan decreased.

Screening of the pilgrims: Screening of the pilgrims before the journey was an effective way for reducing respiratory tract disorders.

Discussion

CDC in a paper entitled "Syndromic surveillance: an applied approach to outbreak detection" has suggested a method for immediate and easy identification of diseases. In this method, by establishing a documented, telephonic or electronic reporting system, health managers can find manifestations and trend of the diseases via collecting symptoms of patients \((9)\). The method has been used several times and has many different names such as:

- Early warning systems
- Prodromal surveillance
- Outbreak detection systems
- Information system-based sentinel surveillance
- Bio-surveillance systems
- Health indicator surveillance
- Symptom-based surveillance \((18)\).

Using the above mentioned method, in this study the most common respiratory syndrome was common cold like syndrome. Allergy just mimics the symptoms of common cold. Thus, it can lead to over diagnosis or malpractice. In this condition, the main question is whether the respiratory involvements of pilgrims in Hajj have infectious or allergic origin? The following
points suggest that the pilgrims' respiratory problems had mostly infectious origin.

- Significant difference values of NBT test before and after travel showed that respiratory diseases of pilgrims might have infectious origins.

- Significant difference values of Gamma-Interferon before and after the travel, also showed that respiratory diseases of pilgrims could be infectious. (14).

- The difference between the levels of interleukin 4 in serum before and after the travel was not statistically significant. So, the respiratory diseases in Hajj pilgrims could not have allergic origin.

- The levels of IgE in serum before and after the travel did not show a statistically significant difference. So, the respiratory diseases were not allergic.

- The differences in the values of immunoglobulin A, G were no statistically significant before and after the journey, supporting the infectious origin for the diseases (5).

Unfortunately, more than 90% of the physicians in caravans assumed that respiratory problems of the pilgrims were originated from allergy and they attempted to prescribe corticosteroids for their patients (4, 14). This not only did not help the patients, but it also caused loss of immunity and deteriorated the patients’ conditions.

Viral infections are more prevalent than bacterial infections. Fungal infections do not play any role in respiratory infections (11). Therefore, considering the absence of the effect of antibiotics on viruses, irrational prescription of antibiotics has no scientific basis. Prescription of antibiotics without paying attention to the indication, disturbs the normal flora of mouth and throat, which play an effective role in defending the body against other organisms.

Among the viruses, Adenoviruses were more prevalent than the other viruses which have no special treatment (12). Transmission of this virus is perhaps one of the reasons for the prevalence of severe conjuncti-

vitis in outbreaks.

In our study, most frequent viruses were: Adenoviruses, Rhinoviruses and Coronavirus. Currently there are no treatments available for these viruses.

Another common virus is the influenza virus which has a special treatment. However, it is not easy to confirm it in Hajj ceremony.

In a study by Al-Tawfiq et al., most common respiratory tract infection viruses were influenza and rhinoviruses (19). In a study by Alborzi et al. on 255 patients in Hajj, the rates of viral causes were reported as follow: influenza 9.8%, parainfluenza 7.4%, rhinovirus 5.9%, adenovirus 5.4%, enterovirus 2%, and RSV 1.6% (20).

In another study by Moattari et al. it was stated that both seasonal and pandemic influenza infections occurred among the Iranian Hajj pilgrims; seasonal viruses were more common than the pandemic viruses even though all pilgrims were vaccinated against seasonal influenza (21). The findings of this study are in line with our findings.

Among atypical bacteria, chlamydia pneumoniae plays a more prominent role in respiratory diseases of the pilgrims than the other atypical bacteria. By comparing serum values of IgG and IgM antibodies against chlamydia pneumonia, we found that this organism plays an evident role in respiratory infections of the pilgrims (11).

Comparison of the samples before and after the travel indicated no recent affliction of the pilgrims with infections caused by Legionella pneumophila. Also, Mycoplasma pneumoniae did not play any role in respiratory infections of the pilgrims.

The results of this study showed that the most prevalent bacteria were Enteric bacilli (19.4%) and Chlamydia pneumonia (15.8%) (5). Therefore, in case of need for empiric antibiotic therapy, antibiotics of macrolides and fluoroquinolone groups should be used.

Fungi had no role in the respiratory diseases of the pilgrims (13), thus, we should consider this fact in our management.
Some experiences

Our experiences of dealing with patients with respiratory diseases during Hajj period for 10 years are summarized in following suggested statements:

- In most cases, affliction with severe respiratory infections occurs during or after Tashriq days and it seems that the disease spread point is Masharolharam (the holy place for Muslims in Mecca, Saudi Arabia). Anxiety, fatigue, inevitable population density, and low hygienic standards in Masharolharam compared with other locations are probably among the effective factors.

- Based on observations, the most severe side effects emerge at the end of travel.

- According to physicians’ reports, some people refer to the physicians of the caravans for more than 30 times during their travel (means every day of the journey) only for their bothering coughs which were alleviated over time. The finding suggests that the treatments were not completely effective, doctors did not spend a lot of time to explain the trend of diseases for their patients, or the expectations of pilgrims were not matched with the reality of conditions. In these conditions we need to educate pilgrims because, the duration of diseases may take up to 2 weeks (22). A vaccine should be injected to prevent influenza. Sometimes the disease is emerged from a strain other than the strain which vaccine has been made. Therefore, the pilgrims may claim in this subject, particularly individuals who paid for the expenses of their own vaccines. Therefore, we should educate all the pilgrims before the travel.

- It seems that high risk people play some roles in increasing of the affliction rate and spread of respiratory diseases among healthy ones (17). Educating these groups is more important than the healthy pilgrims.

A valuable experience in this case was pilgrimage of 2009 which Iran prevented high risk people to travel due to spread of type I influenza (H1N1 type). According to the Al-Towfiq et al. report, despite the occurrence of pandemic of H1N1 during Hajj period in 2009, the available literature did not show an increased rate of respiratory infection in hospitalized patients in 2009 (19). It might be owing to the screening of high risk groups and the more attention paid to the personal hygiene.

Common therapeutic mistakes in Hajj pilgrimage

Within 10 years (from 1999 to 2008), we have seen some therapeutic physicians’ mistakes on the pilgrims:

- Some syndromes such as exudative pharyngitis and allergy were over-diagnosed.

- Antibiotics were used excessively and irrationally and were early shifted to another antibiotic due to mental pressure of the pilgrims.

- Corticosteroids were excessively prescribed.

- Antibiotics (ceftriaxone, gentamycin, etc.) were prescribed in single dose.

- Prescribing a combination of drugs including tramadol, dexamethasone, and penicillin L.A, named "cocktail", whereas, tramadol was excluded from Iran pharmcopoeia some years ago (the drugs were prepared by physicians themselves).

- Prescribing antacids for the treatment of coughs by diagnosing the reflux (it is true that some coughs are caused by reflux, but we should use the medicines which block the entrance of acids to esophagus instead of prescribing the antacids).

- Homeotherapy and energy therapy were used, whereas, the effectiveness of them should be studied more.

- One of the important and vital factors in bad therapy is continuous mental pressures of the pilgrims. Correction of this problem needs long-term cultural efforts.

Suggested treatment for Hajj pilgrim’s respiratory disorders

1. Treatment of the common cold (23):

- Rest.

- Gargling warm normal saline.

- Drink adequate fluids.
Avoid eating spicy foods.
Administration of a first generation anti-histamine such as chlorpheniramine (every 12 hour, 12 mg until 5 days) for rhinorrhea (administration of ipratropium can also reduce rhinorrhea).
Administration of acetaminophen or one NSAID (e.g. ibuprofen, indomethacin, or naproxen)
Lozenges including topical anesthetics.
Administration of vitamin-C, zinc, vitamin-E, probiotics, hand-washing recommendations and exercising are useful but further investigation is needed.
Administration of expectorants like guaifenesin are not effective for the elimination of cough (20).

Some points
- New non-sedating antihistamines are not more useful than the first generation antihistamines; this may be due to their differences in their passage from brain-blood barrier (BBB).
- NSAIDs reduce headache, malaise, and cough, this may be due to their inhibitory effect on prostaglandins.
- Combination of prescribing first generation antihistamines and NSAIDs alleviate nasal congestion. So, there is no need to prescribe anti-congestions.
- If it is necessary to prescribe decongestants, administration of oral products is preferred to topical drugs such as phenylephrine or oxymetazoline.
- Dextromethorphan and codeine are useful in reducing cough.
- In a large meta-analysis, researchers demonstrated that administration of vitamin-C in prevention of common cold is beneficial (24). However some other literatures confirmed that it has a short term effect on the treatment of common cold and its preventive effect was not confirmed.
Benefit of Echinacea and herbal medicines are not approved and they even might have suppressive effect on CD4 cells. Although it was shown that they were effective in 5 of 6 trials. Evidences suggest that the use of probiotics for prevention or treatment of the common cold had no more benefits (24).

Despite application of the above mentioned medications, we have to wait until the disease course is over.

2. Treatment of influenza or Influenza-Like Illness (ILI):
- Rest
- Intake abundant of fluids
- Gargling warm normal saline
- Administration of analgesics like acetaminophen.
- Administration of amantadine or rimantadine for influenza type A (if confirmed)
- Administration of zanamivir or oseltamivir for influenza types A and B. (if confirmed).

Attention: Oseltamivir is not in pilgrim’s drug list now.

3. Treatment of laryngitis:
- Rest voice
- Humidification with normal saline
- Symptomatic treatment in case of viral laryngitis.
- Administration of antibiotics for viral laryngitis is not helpful. (23)
- If the patient did not feel better after 3 days, it might be non-viral laryngitis and administration of an antibiotic such as azithromycin is useful.

Administration of dexamethasone has temporary effect. So, it is not suggested for routine use. Unfortunately, physicians prescribed corticosteroids in more than 90.3 % of cases (14). They might have temporary effects and could suppress body immune system. Administration of oral or intra muscular dexamethasone (0.3 mg/kg) for the treatment of acute laryngo-tracheobronchitis (croup syndrome) is suggested.

4. Treatment of sinusitis in adults (25):
   * Conservative treatments: For experimental treatment of Acute Community Acquired Bacterial Sinusitis (ACABS), in ad-
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dition to conservative treatment, one of the following drugs can be administered:
- Amoxicillin, 500 to 875 mg per 12 hours
- Co-amoxiclav, 875 to 2000 mg per 12 hours
- Cefpodoxime Proxetil, 200 mg per 12 hours
- Cefdinir, 600 mg per 24 hours
- Cefprozil, 500 mg per 12 hours
- Clarithromycin 500 mg for 3 days
- Clarithromycin 500 mg per 12 hours till 14 days
- Levofoxacin 500 mg every day
- Moxifloxacin 400 mg every day

Unfortunately, some of these medicines are not in the Hajj drug lists.

5. Treatment of acute bronchitis (9, 26-28):
- Acute bronchitis does not need antibiotics administration.
- * A mixture including brompheniramine, naproxen or chlorpheniramine, ibuprofen relieves the cough especially with nasal Interferon alfa.
- Administration of oseltamivir, in case of ILI or approved influenza.
- Administration of azithromycin or other macrolides and quinolones are not useful for bacterial bronchitis caused by Mycoplasma or Chlamydia.
- Early treatment of bronchitis caused by Bordetella pertussis with tetracyclines or macrolides can prevent transmission of disease.
- Conservative treatments.

6. Treatment of COPD with super imposed infections:

Viral causes do not need antibiotics and are not distinguishable from bacterial infections.

7. Treatment of Acute pneumonia (30):
If needed, referring to medical centers for hospitalization. Pneumonia is a significant cause of hospital admission accounting for 20-50% of the admissions (19).

Treatment for outpatients
- In individuals with healthy condition without taking antibiotics: administration of erythromycin
- In individuals with healthy condition with taking antibiotics: azithromycin and co-amoxiclav
- In individuals with history of diseases such as COPD- diabetes mellitus - renal failure – cardiac failure or malignancy, without taking antibiotics: administration of azithromycin
- In individuals with above mentioned diseases and history of taking antibiotics: azithromycin and cefuroxime
- In individuals with pneumonia suspicious to aspiration: co-amoxiclav
- In individuals with pneumonia with a history of influenza: cefuroxime.

Treatment of inpatient pneumonia in ordinary wards
With a history of taking antibiotics: clarithromycin plus ceftriaxone
Preventive points:
- Screening of high risk groups before the journey (3).
- Education is necessary for pilgrims continually before and during the Hajj period (2).
- Reports of previous years indicated that the most prevalent cause of deaths of Iranian pilgrims was cardiac diseases. In addition, about 25.6% of the pilgrims were vulnerable (high risk groups) and were mostly afflicted with critical respiratory diseases (17). Thus, we should emphasis on screening of vulnerable pilgrims for the diseases such as cardiac diseases, cancers, and respiratory disorders before the journey.
- Stress, fatigue, and anxiety cause immunity suppression in human beings (14) and these factors are among the reasons for the establishment and continuation of dis-
eases. Therefore, it is suggested to prevent all the factors which can lead to such conditions.

- Contaminated hands are one of the most common ways of diseases transmission (2,23). Therefore, repetitive hand washing, avoiding from shaking hands with the patients and not touching eyes and respiratory mucus membranes by contaminated hands are among the effective preventive ways.

- It is useful to inject influenza and pneumovax vaccines solely or jointly to reduce respiratory diseases occurrence, mortality, and hospitalization (31-32) particularly in people over 50 years of age, and patients who suffer from diabetes, renal failure, liver failure, cardiac diseases, asthma and COPD at proper time (2 to 3 weeks before the trip). Although a few studies doubted the effectiveness of influenza vaccine (33), other studies strongly recommended vaccination of pilgrims (34-35). These results show that causal patterns of respiratory infections were different in various years and effectiveness of vaccines will also be different and the pilgrims should be educated in this regard.

- To avoid excessive and unreasonable use of antibiotics and corticosteroids for therapeutics or preventive purposes.

- Not attending unnecessary crowded locations such as recommended Tavafs (going around Kabah) in high densities situations (2).

- Correct and timely treatment of pneumonia and its side effects.

- Some specialists recommended sucking antiseptic lozenge before attending the crowds for reducing affliction with respiratory infections but this matter has not been approved by the preliminary studies and should be studied more.

- Garlic tablets and its medicinal derivatives have been suggested for prevention of influenza (36).

- Social distancing is one of the behavioral variables which influence respiratory illnesses (2). It is necessary for the patients to consider distance of longer than 1 meter from healthy individuals or conversely. However, it is impossible under pilgrimage conditions. Therefore, the distance could be considered between beds in pilgrims’ rooms.

- It is unreasonable to use masks for the prevention of viral diseases (33). However, it is useful to prevent entrance of larger particles. It is recommended to use masks especially for patients. The use of masks may reduce exposure to droplet nuclei, which is the main mode of transmission of most respiratory tract infections (19). In a study by Deris et al. on 387 Malaysian Hajj pilgrims it was stated that wearing masks was significantly associated with sore throat and longer duration of sore throat and fever (22). On the contrary, in another study by Al-Jasser et al. on 1507 Saudi Arabian Hajj pilgrims it was showed that occurrence of URTI among the pilgrims who were wearing face mask most of the time was lower than those pilgrims who were wearing them only at some times (37).

The effects of the following factors require further investigations.

- Indiscriminate use of disinfectants such as chlorine compounds in caravans

- Population density of the rooms in caravans

- Distances between the beds in the rooms of the caravans

- Mask usage

- The number of attendances at crowded locations per day

- Use of antiseptic lozenges before attendance at crowded locations

- Repeated hand washing

- Exposure to cold air

- Use of the personal prayer mat

- Repeated consumption of banana or the other substances producing histamine.

Conclusion

In this paper, we reviewed types, frequencies, etiologies, and epidemiologic fac-
tors of respiratory diseases among Iranian Hajj pilgrims and suggested some applied points for prevention, treatment, and correction of common malpractices in the treatment of respiratory diseases of the pilgrims.

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