

50 years of Pediatric Pulmonology: Progress and Future

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Development of Pediatric Pulmonology as a speciality in India is steadily improving over past few decades. Present profile of Indian pediatric chest services include: asthma, recurrent infections, bronchiectasis, etc. It is expected to change and the emerging pulmonary illnesses include: human immunodeficiency virus (HIV infection) associated pulmonary illnesses, cystic fibrosis, primary ciliary dyskinesia, bronchopulmonary dysplasia, interstitial lung diseases, gastroesophageal reflux diseases, neuromuscular illnesses, sleep disorders, disorders due to malformations and opportunistic pulmonary infections.

Respiratory infections constitute major load in pediatric outpatient services and are the leading cause of mortality in under-five children. To reduce morbidity and mortality due to respiratory tract infections, Indian Academy of Pediatrics (IAP) has developed Respiratory Tract Infection Group Education Module (RTIGEMS). After initial increase in prevalence of asthma, it seems to have stabilized now but going by the numbers, it will remain a major health problem in India. Diagnosis of pulmonary tuberculosis was always a challenge to pediatricians and with emergence of drug resistant tuberculosis, it is even more challenging.

Presently few centers are providing specialized Pediatric pulmonology services in India. There is a need to develop more centers to enhance services including (a) assessment of pulmonary physiology by performing pulmonary function testing in all age groups, (b) improving diagnostic and therapeutic role of bronchoscopy and bronchoalveolar lavage, (c) sweat testing, (d) molecular diagnostics for various respiratory illnesses, and (e) utilizing advance imaging and minimally invasive technologies for diagnosis and treatment of respiratory illnesses. At present there is no degree course in Pediatric Pulmonology in India. Initially middle level pediatricians wanting to pursue their career in pediatric pulmonology should undergo training in existing centers. Trained persons should develop a network to collect data and answer relevant research questions.

Key words: *Acute respiratory tract infection, Cystic fibrosis, India, Interstitial lung diseases, Pulmonology services, Training.*

Respiratory system is vital organ system of body, illnesses of which may affect function of body as a whole. Respiratory tract illnesses are of variable etiology and may be acute, sub-acute or chronic. Development of Pediatric Pulmonology as a speciality in India is steadily improving over past few decades. Formation of separate chapter with name of "Respiratory Chapter" of Indian Academy of Pediatrics has improved interaction among pediatricians who are practicing Pediatric pulmonology or are interested in childhood respiratory illnesses. With regular meetings, more young persons are getting attracted to this speciality.

BURDEN OF RESPIRATORY ILLNESSES

In a recent estimate, about 1.682 million children younger than 5 years died in 2010 in India. Of these, 0.397 million (24%) died due to pneumonia alone [1]. It has been reported that outpatient attendance attributed to acute respiratory infections is as high as 20-40% of all outpatients and 12-35% of in-patients [2]. Burden of asthma in school going children varies from 4%-20% in different parts of India [3]. Apart from these illnesses, drug sensitive and drug resistant pulmonary tuberculosis and

Human immunodeficiency virus (HIV) associated pulmonary illnesses also add to the burden of respiratory illnesses. Other emerging diseases like cystic fibrosis, bronchopulmonary dysplasia, interstitial lung diseases and opportunistic infections in group of immunocompromised hosts, though do not form a significant burden now, but are emerging as future challenges.

Acute respiratory tract infections

Acute respiratory tract infections (ARI) are one of the leading causes of morbidity and acute lower respiratory tract infection is the leading cause of mortality in children [1]. Government of India launched ARI control program in the 1980s and it showed improved survival in infants and under-five children. However, its impact is less than desired. This is a major challenge for pulmonologists and public health experts to reduce pneumonia-related mortality in under-five age group. There is need to identify risk factors for pneumonia related mortality and prevent deaths by appropriate efforts. Emergence of drug resistance to commonly used drugs like cotrimoxazole in common respiratory pathogens is one of the important challenges [4,5]. Reasons for emergence of drug resistance

include indiscriminate use of antibiotics in respiratory tract infection. Majority of upper respiratory tract infections (URTI) are due to viral infections and do not need antibiotics. To reduce unnecessary use of antibiotics in URTI, there is need to sensitize pediatricians for its harmful effect. In this direction, IAP Respiratory Chapter developed Respiratory Tract Infection Group Education Module (RTIGEMS) that aims to educate pediatrician about rationale use of antibiotics [6].

World Health Organization recommended the identification of community acquired pneumonia by clinical features (cough with difficulty in breathing) and administration of antibiotics to these patients. In ARI control program, children with wheeze may also get treated with antibiotics unnecessarily. To overcome this problem, modification in algorithm has been found to be useful [7] and same has been suggested by an expert group [8].

Identification of causative microbial agents for various respiratory tract infections is difficult and not cost effective at present. Earlier bacterial pathogens were being recognized by an invasive procedure like lung puncture [9]. Viral agents can be identified by obtaining nasopharyngeal aspirates [10] and bacterial pathogens by demonstration of antigen in urine [11] or by blood culture [10]. With use of molecular diagnostic tests, it may be feasible to identify causative agents for respiratory tract infection [12]. With improvement in molecular diagnostics, it may be possible to make informed decision for starting antibiotics in respiratory infection in future.

Asthma: Changing Incidence, Treatment Protocols, Future Prospects

Asthma is one of the commonest chronic illnesses for visit to doctor and has significant social and economic impact [13]. First documented studies on asthma prevalence in India include a survey conducted by Indian Council of Medical Research (ICMR) on central government employees and their family members in 1961, and recorded prevalence as 1.8% [14]. A study in Patna documented prevalence of 2.7% in rural area and 1.6% in urban area [15]. More recent reports on asthma prevalence (any wheeze in past 12 months) in school going children in Indian subcontinent in ISAAC 1 and ISAAC 3 studies have reported prevalence of 6.38% and 6.40% [16], suggesting that it has stabilized now. However, going by the numbers, it will continue to remain a public health problem. The treatment followed by pediatricians is still suboptimal. Only one third of asthmatic patients receive standard inhaled therapy [17]. Respiratory Chapter of the Indian Academy of Pediatrics has prepared an evidence based treatment protocol to promote standardized uniform

treatment [18]. This is one step forward to improve care of children with asthma.

With the recognition of various phenotypes of asthma, it is important to identify and treat individuals accordingly. Diagnosis of asthma still remains clinical in most instances. Newer drugs like omalizumab are available in India. Though cost is limiting factor, but is important therapeutic approach that may have potential role in difficult to treat asthma.

Advances in immunotherapy for allergic diseases including asthma has not been assessed to be useful in asthmatic children possibly due to multiple phenotypes of asthma and good response to inhaled steroids along with other medications. It also may have some potential for treatment in selected difficult atopic asthmatic children [19]. Some of the drugs like ciclosporin, long acting beta agonists, leukotriene receptor antagonists (LTRA) etc have not been cleared for use in all age groups. With more safety data they will also become part of therapeutic armamentarium of asthma in India.

Pulmonary Manifestations of HIV Infection

HIV infection in children is a new illness over past three decades. Respiratory illnesses are important cause of morbidity in these children. These patients are at risk of recurrent respiratory infections due to usual and unusual organisms. Apart from the usual organisms (*S. pneumoniae*, *H. influenzae*, *S. aureus*) these children are more prone for infections due to gram negative bacilli, *Pneumocystis jirovecii* (PCP) and fungal infections. In India, tuberculosis is the commonest opportunistic infection in HIV infected children [20]. Non infectious illnesses like lymphoproliferative disorders including lymphoid interstitial pneumonia (LIP) is considered to be AIDS defining illness. Use of anti-retroviral drugs and daily cotrimoxazole in children has reduced respiratory infections due to usual organisms and PCP.

Molecular diagnostic test on induced sputum for identification of PCP is one of the important advances and can be used for management of immuno-compromised hosts, including children with HIV infection [21].

CHRONIC RESPIRATORY DISEASES

In industrialized countries, the bulk of respiratory illnesses in Pediatric Pulmonology services include: cystic fibrosis, interstitial lung disease, gastroesophageal reflux diseases, neuromuscular illnesses, sleep disorders, disorders due to malformations, etc. Present profile of Indian pediatric chest services include: asthma, recurrent infections, bronchiectasis, etc. It is expected, that in future, this profile will change and will become similar to that of industrialized countries.

Cystic fibrosis (CF) is leading, inherited, life-limiting illness in Caucasian population. CF was considered to be nonexistent in India. Recent review suggests that CF is probably under-reported in India [22]. First documented Indian case of CF was reported in 1968 [23]. Due to strong belief that CF is disease of Caucasian population, diagnostic test, (sweat test/mutations/nasal transmembrane potential difference) were not developed and majority of trained pediatrician, may not have seen single case of confirmed CF. Now many centers have developed diagnostic facilities for CF and care of CF patients. This is being reflected in form of sudden increase in number of children with CF from different part of India.

Respiratory management of children with CF requires systemic antibiotics. Another intervention in form of inhaled antibiotics tobramycin/colistin is also available in the Indian market. Mucolytic agent DNase is not available in open market in India. Hypertonic saline has been found to be an inexpensive substitute to DNase [24]. 3% hypertonic saline that is available in market has been found to be equally effective [25]. Gastrointestinal management of CF requires enteric coated spherules of pancreatic enzyme for use in infants and children who cannot swallow enteric coated tablets, and is available since 2004. Though at present there are few centers that provide diagnostic and clinical care services, it is expected that in future there will be need to develop more centers that can provide services for CF patients. With increasing survival, more patients with CF will survive into adulthood and there is need to develop liaison with adult pulmonologists.

Primary ciliary dyskinesia is being recognized as relatively common illness in pediatric respiratory. Earlier the diagnosis was based on classical clinical features and electron microscopy and now genetic defect has been identified. Multiple mutations have been reported in literature. A non-invasive test in form of reduced fraction of exhaled nitric oxide (FENO) in these patients has been used as screening test in some facilities. At present, these patient require supportive care, but in future we expect development of therapeutic intervention.

Interstitial lung diseases (ILD), though rare, are an important cause of morbidity. ILDs are important illnesses in Pediatric pulmonology services in industrialized countries. Till now, in India, ILDs are limited to few case series [26-28]. Gold standard for the diagnosis of ILD is lung biopsy. With improvement in imaging/bronchoscopy, now all children with ILD may not need lung biopsy. This will increase the number of patient that will get label of ILD. The treatments of ILD depend on underlying cause. Many children with ILD may need home oxygen therapy/home ventilation and other supportive care. Home oxygen

and ventilation are very poorly developed in India. With increasing number of patient there is need to develop expertise in this direction.

Gastroesophageal disease (GERD) and other syndromes that cause passive aspirations are being recognized more frequently now. Earlier diagnosis was based on endoscopic examination and biopsy of esophagus. Now with availability of pH probe, it has become less invasive and number of children with GERD has increased significantly. Medical management is evolving and some patients may need surgical intervention.

Other aspiration syndromes may be due to malformations, neuromuscular problems or mental subnormality. These patients are under diagnosed due to lack of awareness and burden of other conditions. Management of such patients is challenging and needs a team effort. Many such patients may need gastrostomies or feeding jejunostomies for improving their nutrition and decreasing pulmonary manifestations, and this requires collaborations with pediatric surgeons and pediatric gastroenterologists.

Children born with major malformations like pulmonary hypoplasia/agenesis, congenital diaphragmatic hernia, congenital lobar emphysema, cystic adenomatoid malformation, tracheoesophageal fistula, bronchogenic and duplication cysts etc are now surviving with better supportive care. They have significant morbidity in first few years of life and require management expertise. At present, they are being treated by pediatric surgeons or gastroenterologists. However, these patients are better managed by pediatric pulmonologists and we need to develop awareness and expertise in management of such patients. Children with pulmonary vascular problems, with or without heart disease, are also being recognized and need expertise for management [29,30].

In children, a common cause of obstructive sleep apnea is upper airway obstruction due to adenoidal hypertrophy or maxillofacial dysplasia. These can be corrected by surgical intervention. More and more cases of central apnea are being reported now. With identification of genetic markers for this syndrome, a definitive diagnosis can be made. Screening tests and confirmation for diagnosis by polysomnography are being developed in India.

FUTURE CHALLENGES

Pulmonary function tests: Children older than 5-7 years of age may undergo spirometry for diagnostic and monitoring purpose. Demonstration of reversible airway obstruction is difficult in preschool children. Now with advances in

pulmonary function testing it may be possible to document reversible airway obstruction in infants using tidal breath flow volume loop (TBFVL), rapid thoracic compression (RTC) or raised volume rapid thoracic compression (RVRTC) or whole body plethysmography. For children above 3-4 years of age interrupter technique and impulse oscillometry can also be used. These techniques may not be available for routine use but some of them may have potential for clinical utility in future. Some experience with spirometry documenting normal values of parameters have been reported from different part of India [31-35].

Bronchoscopy and bronchoalveolar lavage: Flexible fibre optic bronchoscopy (FOB) is one of the important techniques in pulmonary services. It is available in few centers and going by the indications, we may need to develop bronchoscopy services in more centers. Some experience of bronchoscopy and its utility has been reported from various part of India [36-39]. At present transbronchial ultrasound and biopsy is possible only with large size bronchoscope (6 mm external diameter), that may not be useful for young children. However, with better technology, it may be available for smaller bronchoscope also. Some centers are using FOB for removal of foreign bodies [40]. In near future, other interventions in form of balloon dilatation, whole lung lavage, etc may be available at some centers.

Sweat testing and mutation analysis for diagnosis of cystic fibrosis: The facility for sweat test has been developed in multiple centers over past one decade. However, going by size of India there is need to develop more centers. Commercially available sweat test equipment use pilocarpine iontophoresis for sweat collection and estimation is done by measuring conductivity or osmolality (Vescor Macroduct sweat collecting system). Some centers are using indigenous method of sweat chloride estimation [41]. More than 1600 mutations have already been identified and the mutations are heterogenous in Indian children with CF [42], and there is no common panel of mutations that can detect all children with CF, sweat chloride still remains gold standard for making a diagnosis of CF. In future with more experience, possibly we may have region specific mutation panel for easy diagnosis of CF.

Radiology and nuclear imaging: These facilities are available in public and private services and pediatricians are using them for diagnosis and management of various respiratory conditions. There is need to create interest among radiologists in each center who are more interested in pediatric pulmonary images to improve diagnostic yield of imaging in children.

Sleep studies: Sleep problems are emerging morbidity in

children. Some centers are performing sleep studies in children. There is need to develop indications for sleep studies in India [43].

At present there is no formal degree course in Pediatric pulmonology. However, going by the burden of illness and scope of subject there is huge scope in pediatric pulmonology specialty. Initially, middle level pediatricians who want to pursue their career in pediatric pulmonology should undergo long term or short term training in existing centers. Trained persons should develop network to collect data and answer relevant research questions.

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