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Rare Diseases in Developing Nations: Addressing the Global Health Disparities, Hurdles of Diagnosis, Treatment and Policy Implementation

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ABSTRACT

Compared to other diseases, rare diseases (RDs) are conditions that only affect a small percentage of the general population. Rare diseases have recently drawn attention on a global scale. Their prompt diagnosis and therapeutic management are challenging due to the scarcity of reliable epidemiological data and the limited availability of clinical information. The production of medications, medical diagnosis, and social services, developing nations have significantly lagged behind. Unfortunately, there is a dearth of pertinent research in developing nations, and there is no accurate estimate of the precise burden of the majority of RDs. The Indian government frequently struggles with how to develop a National Health Policy with a healthcare budget for 1.3 billion people due to the excessive cost of orphan drugs, challenges in diagnosis, and treatment. Numerous surveys were undertaken to find out the general public's understanding of RD in India and throughout the world. Due to a lack of suitable clinical and diagnostic resources in the area, many suspected instances of genetic diseases, unfortunately, go untreated or receive the wrong diagnosis, leaving patients to deal with severe psycho-socioeconomic problems and frequently live with their illness for the rest of their lives. The main difficulties with RDs that regulatory authorities face both in India and throughout the world are generally emphasized in this review. Moreover, at last, some rare diseases like Alice in Wonderland Syndrome (AIWS) and Chronic Pulmonary Aspergillosis (CPA) are discussed briefly in this review.

Keywords: *Rare disease, Orphan disease, Orphan drugs, Alice in Wonderland Syndrome (AIWS), Chronic Pulmonary Aspergillosis (CPA)*

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INTRODUCTION

In contrast to other common diseases, rare diseases (RDs) are heterogeneous clinical conditions that affect a small proportion of people in the general population but are still progressive, chronically disabled, and/or life-threatening [1]. It is also named as *Orphan disease*. Due to a lack of research and development, these diseases are often poorly understood, and there may be limited effective treatments. They, however, are currently acknowledged as one of the most significant global public health issues. According to estimates, a larger proportion of the world's population overall suffers from rare diseases (translating to billion individuals). Rare diseases are frequently genetic, which means that mutations to a person's DNA are the causative factors. There are many different ways that rare diseases can appear, and their symptoms can range from minor to severe, or even life-threatening. Due to their low prevalence, rare diseases can be challenging to diagnose, and patients may face difficulties accessing appropriate care and support. In addition, the small patient populations make it difficult for researchers to conduct clinical trials and develop new treatments. As a result, many rare diseases remain incurable, and treatment options may be limited to symptom management. However, in recent years, there has been increased awareness and attention given to rare diseases, leading to advances in research, diagnosis, and treatment. Researchers, healthcare professionals, patients, and advocacy organisations have worked together to better understand rare diseases and improve patient outcomes. Despite numerous international initiatives to address the

problems caused by rare diseases, significant work still needs to be done to address this underdeveloped area of healthcare [2]. For decades, clinicians have been interested by the clinical presentation, natural history, pathophysiology, and sometimes unexplained character of rare diseases. Rare diseases offer unique possibilities to examine human physiology and biomedical research. Investigating rare diseases has resulted in significant scientific advances that have frequently focus attention on more prevalent disorders. Many rare diseases are typically poorly understood because of their rare commodity, and there may only be a few treatment options available. **Table 1** describes definition of rare diseases in different countries as per the patient ratio.

Table 1. Definitions of rare disease in different countries as per patient ratio [3-7]

Countries	Patient Ratio as Defined	Patient Ratio Standardized For Comparison
Brazil	65 in 100,000	1 in 1,538
USA	<200,000 in population	1 in 1,659
Australia	5 in 10,000	1 in 2,000
Colombia	1 in 2,000	1 in 2,000
Mexico	5 in 10,000	1 in 2,000
Singapore	1 in 2,000	1 in 2,000
Switzerland	5 in 10,000	1 in 2,000
UK	1 in 2,000	1 in 2,000
Japan	<50,000 in Population	1 in 2,507
Peru	1 in 100,000	1 in 100,000

Rare disease as per Jurisdictions

Rare diseases are often known as 'single gene disorders' or 'monogenic disorders' because they are brought on by one or more variations in a single gene that disrupt its function. There is not a common definition of the prevalence of recognized rare diseases [3]. The World Health Organization (WHO) has defined a basic prevalence estimate for rare diseases of about 1 in 2,000 individuals [4]. However, many nations define the prevalence of rare diseases differently, based on the disease's prevalence among their own people, the state of their healthcare system, and the availability of resources. In contrast to the United States, where the incidence rate for rare diseases is 7 or less per 10,000 people and a genetic condition that is common in the European Union (EU) is only considered rare if it affects 5 or fewer individuals per 10,000 people. Using these statistics, one in ten people in North America and over 30 million people in Europe are estimated to have one of the known rare diseases. According to estimations, there are 2.5 incidences per 10,000 people in Japan and 1 case per 10,000 people in Australia [5]. Drug research for patients with rare diseases has been stopped by pharmaceutical companies due to a lack of profitability. The Orphan Drug Act (ODA) was developed in the USA in 1983 as a means of promoting pharmaceutical companies. Several countries all over the world turned to ODA as a symbol of renewal. While there were fewer than ten orphan drugs available before the ODA, the FDA had authorised more than 450 pharmaceuticals by the end of 2017 for 668 orphan indications [6,7]. Due to import limitations, excessive pricing, etc., In India, these orphan drugs are not accessible. Moreover, patients in India are not provided with either an ODA or any other provisions.

The Indian Scenario

Research on rare diseases has been complicated in developing countries such as India by a lack of advanced clinical resources. It has been proposed that the major cause of India's genetic diversity is the country's ancient history of migration and its very diversified population designs are is separated by social, physical linguistic, and religious separation [8]. In India, however, genetic diseases may be more common than in other countries due to the biological isolation of multiple endogamous population subgroups. The remaining rare diseases might be raised on by environmental factors such as mesothelioma or Jamaican vomiting sickness, as well as infectious (maternofetal measles) or immunological (such as children's chronic arthritis) [4]. Because there are no epidemiological data, there are inappropriate implications on the burden of rare illnesses as well as the morbidity and mortality linked to them. Over 450 uncommon illnesses have been discovered so far at India's tertiary care institutes. [9]. The most prevalent rare diseases include sickle-cell anaemia, haemophilia, thalassemia, auto-immune diseases, primary immunodeficiency in children, and lysosomal storage disorders like pompe disease, hirschsprung disease, hemangiomas,

cystic fibrosis, gaucher's disease, and specific types of muscular dystrophy. In India, there is a lack of knowledge about rare diseases among the general public, medical professionals, and policymakers. Insufficient documentation of rare diseases within the health sector and a lack of expertise and specialized institutions demonstrates significant obstacles to accessing diagnostic and support facilities. There is no reliable data on the epidemiology of uncommon diseases in the nation because there is no comprehensive disease-specific repository and data collecting facilities. Indian Organization for Rare Diseases (IORD) is an inclusive patient association designed to cover India's rare diseases and sufferers. Its vision is to develop awareness, advocate government policies, promote pharma companies to produce drugs, educational establishments to developing diagnostic equipment [10]. IORD has been serving the Indian rare disease community for the past 14 years. They are conscious that rare diseases have an impact on the entire community (the 92% of non-orphan patients) on a physical, emotional, and economical level. The number of people with rare disorders who suffer from them are constantly topics of discussion among policymakers in India. In India, there is no defined definition of rare diseases, making it difficult to determine the approximate number of persons affected. Hence, it is complicated for policymakers to develop a healthcare service that effectively addresses patient demands, offers the pharmaceutical industry incentives to manufacture new drugs, and develops tertiary infrastructure for the therapy of patients with rare diseases. A policy document was published by the Indian government in 2017, but there were obstacles with its implementation [11]. Many studies were carried out in developed countries over the years. However, they regularly concentrate on particular issues, such as information relating to orphan drugs, the function of patient organisations for rare diseases in research, difficulties faced by patients, problems faced by carers for rare diseases. IORD conducted a 'first-of-its-kind' survey to establish a broad understanding of rare disease in the country. No government or agency in any country has ever carried out a survey like this. A country having several states, various languages, and economic and social disparities, and a number of other factors makes it impractical and impossible to survey billions of people. One would anticipate that a survey that has an adequate sample would provide useful data rapidly and efficiently. Also, the objective of this research was to provide a broad picture of rare diseases in the community in the form of a picture. The survey's outcomes will be combined and written up in a report that is accessible to everyone. The study was expected to generate a national discussion on providing care and support for families of people with rare diseases and raising awareness of how these conditions affect communities [12].
In India, rare diseases are categorized under the following groups **(Figure 1)**

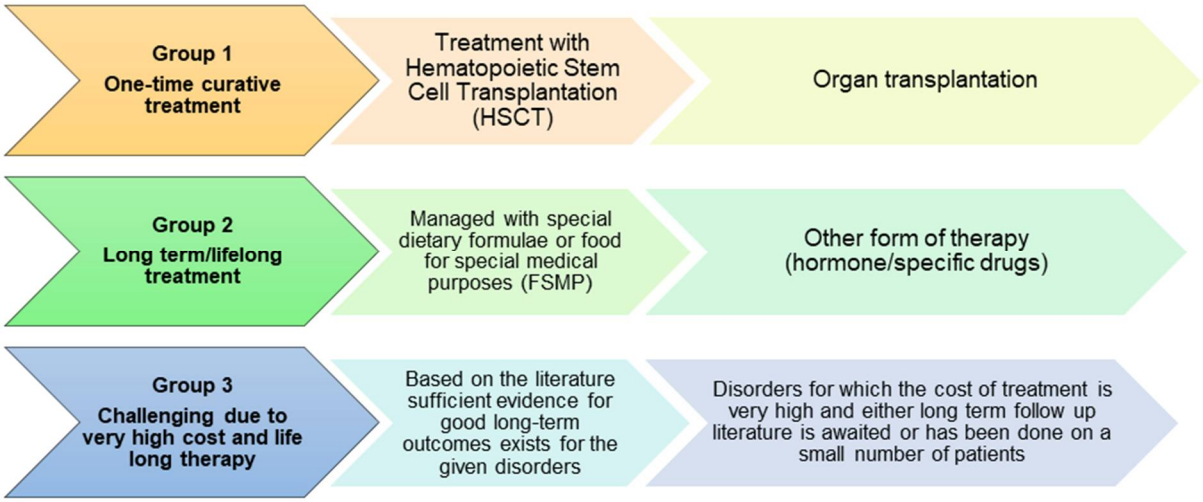

Figure 1. Rare diseases categories in India as per ministry of health and family welfare guidelines [12]

Cause of rare disease

Many rare diseases have no recognized etiology. However, the majority of the problems may be traced back to single gene mutations or alterations. These are known as rare genetic disorders. This helps to explain why some rare disorders tend to run in families since many of these genetic variants may be passed down from parent to child. Rare illnesses can be affected by diet, smoking, and chemical exposure, among other factors. The aforementioned variables may directly contribute to diseases or interact with genetic factors to aggravate or develop diseases.

The prevalence of rare diseases as a public health concern

Despite the fact that rare diseases sometimes only affect a small percentage of individuals, they can still represent a serious threat to public health. A rare disease in the United States refers to one that affecting fewer than 200,000 people. A rare disease in Europe is one that impacts less than 1 in 2,000 people [13,14]. There are some reasons why rare diseases can be a public health issue:

Inadequate epidemiology data

One of the challenges associated with rare diseases is an insufficient amount of statistical information. Epidemiological data refers to information about the occurrence, distribution, and causes of a particular disease in a specific population. Rare diseases, by definition, affect a small number of people. As a result, it can be challenging to collect enough data to accurately determine the incidence and prevalence of the disease. This can limit our understanding of the disease and our ability to develop effective treatments. Since rare diseases are not well-known, there is often no central database or registry that tracks cases of the disease. This can result in fragmented data collection, making it difficult to accurately determine the incidence and prevalence of the disease [15]. The lack of data can make it difficult to advocate for funding for research and treatment of rare diseases. Without funding, it can be challenging to improve our understanding of the disease and develop new treatments. Overall, the lack of epidemiological data on rare diseases highlights the need for increased awareness and research. By improving our understanding of rare diseases, we can develop better treatments and support for those affected by these conditions.

Diagnosis of rare disease

Diagnosing a rare disease can be challenging, as many healthcare providers may not have encountered the condition before. It is important to note that diagnosing a rare disease can be a long and complex process, and it may require a multidisciplinary approach involving several healthcare professionals. Due to the complexity of the diagnostic procedures and the lack of medical awareness, it takes years. There are many rare diseases for which there are no diagnostic techniques or resources. As a result, the doctor will take a thorough medical evaluation, physical assessment, imaging scans, and laboratory testing by taking various samples of the patient and their family members to look for any clues or patterns that may suggest a rare disease and then guess the required study of gene [16]. If the test is negative, more expensive and time-consuming testing is needed. Both the general people and healthcare experts are not well-informed about rare diseases Many clinicians are not adequately trained or aware of how to diagnose and treat these diseases in a reasonable timeframe. There is an urgent need to raise public awareness, educate patients and their families, and train physicians to make better diagnoses and standardise diagnostic processes, create new diagnostic tools, enhance clinical trials, and invest in gene therapy [17].

Challenges in research and development

Research and development are significantly restricted by the reality that, As the pathogenesis and natural history of the majority of uncommon illnesses are unknown. Due to their occasional incidence and lack of clinical expertise, rare diseases are challenging to study, because of it clinical descriptions of rare diseases may be inappropriate or insufficient. The research and development of treatments for rare diseases pose several challenges, including limited patient populations which raises the limitation of clinical trials and make it difficult to conduct statistically significant studies and to generate sufficient data to support regulatory approval. Then, heterogeneity of disease is also a challenging factor for research as it shows genetic and phenotypic variation among in patients with the same disease which makes it difficult to develop a one-size-fits -all treatment approach. In order to address the effects of these disorders, we must consider regional and international research collaborations, medical professionals working on rare diseases, and patient groups and families [18].

Challenges in the treatment

The treatment of rare diseases poses several challenges including limited knowledge of their causes, symptoms, delayed diagnosis, high cost, regulatory challenges, limited access to treatments and small patient populations which limits the conduction of large-scale clinical trials to test new treatments or to develop specialized healthcare infrastructure [19]. It will need the coordination of patients, researchers, patients' families, health workers, policy makers to identify the possibility of cause of rare disease.

Unavailability of therapy

Despite recent advancements, the majority of rare diseases lack the access to effective or secure treatments. Medicine accessibility and availability are extremely crucial for lowering morbidity and mortality associated with rare diseases. As a result, even after a correct diagnosis has been confirmed, a treatment for the rare disease may not be available. Approximately 95% of rare diseases have no permitted therapy, and fewer than one out of every 10 patients obtain disease-specific diagnosis. Where drugs are available, they are extremely expensive, putting enormous burdens impact the budgets of individuals, families, health-care institutions, and financing organisations alike [20].

Costly Medical Care

Since the number of individuals who suffer from personal rare diseases is small, there is no significant market for pharma companies to design and brought to market drugs for them. Therefore, rare disorders are referred to as 'orphan diseases,' and the treatments used to treat them are referred to as 'orphan drugs'. When firms make pharmaceuticals to cure uncommon diseases, they sell them at exorbitant rates in order to recover their research and development expenses. At the moment, few such pharmaceutical corporations in the world have started developing treatments for rare diseases, and there are no commercial manufacturers in India; even the government has been denied permission to give these drugs free of charge due to their high cost [21]. Besides this, the procedure for analysing rare disease treatment is frequently in the experimental stage, making it difficult to assess clinical relevance and cost effectiveness. Several governments have implemented legislation to give incentives to drugs producers such as the Orphan Drug Act (ODA) to promote them to start manufacturing drugs for rare 14 diseases. The number of reports for orphan drug registration has roughly tripled since 2000. As a result, medication sales and earnings have increased tremendously. In fact, over one-third of rare disease medications now have yearly sales in excess of £1 billion. The global orphan drugs company is anticipated to be worth £144 billion by 2020, accounting for 19% of total branded prescription drug sales; the average yearly cost of rare disease medicine in order to rises above $100,000. According findings, while legislation and restrictions on orphan drug research, such as the US Orphan Drug Act, have stimulated the discovery of orphan pharmaceuticals, they have been unable to regulate the cost of these therapies, raising severe concerns about the health system's sustainability. The cystic fibrosis drug Kalydeco (ivacaftor), for example, costs £14,000 per patient each month. In fact, each of the world's ten most expensive drugs is used to treat a rare disease, with Soliris (eculizumab) being one of the most expensive, costing £340,000 per patient each year [22]. Despite the fact that these treatments are prescribed to fewer people, their extraordinarily high pricing can generate profits comparable to traditional branded drugs. Orphan drug market authorization holders with publicly listed pharmaceutical businesses have better market value and profitability than companies that are not permitted to manufacture medicines for rare diseases. Several medications have been designated as orphan drugs over the years, even if they are not completely new or signify a scientific advance. A low-cost off-patent pharmaceutical licenced by the FDA for one condition but widely utilised as a 'off-label' therapy for a rare disease can be turned into a significant source of profit [23]. The 7 to 10 years of monopoly status that comes with it might cause significant price increases for a treatment that was previously widely used. For example, older drugs for rare diseases, such as imatinib, in affluent countries, the cost of this drug, which is used to treat chronic myeloid leukaemia, can exceed $100,000 per year.

Development of policy for treatment of Rare Disease

Many governmental and non-governmental organisations, as well as their programmes, are working to design an advanced integrated research approach for advanced therapy development for rare diseases such as the Therapeutics for Rare and Neglected Diseases (TRND) programme of the National Institutes of Health (NIH), the Genetic and Rare Diseases (GARD) Information Centre (a collaboration between two NIH centres, the National Human Genome Research Institute (NHGRI) and the National Centre for Advancing Translational Sciences (NCATS), the NIH's Office of Rare Diseases Research (ORDR), and the National Organisation for Rare Diseases etc. have been introduced in recent years to campaign for rare disease patients' demands for national and/or international rare disease policies [24]. These initiatives offer a good framework to solve the issues, patient advocacy, research funding, and the creation of more enhanced amenities are needed associated with neglected rare diseases, with the common goal of disseminating associated data and information to the technological community, as well as establishing their overall use in the treatment and diagnosis of rare disease. Despite this, it is anticipated that the present rate of R&D will not be capable of producing drugs for the majority of rare diseases in the next years. This worldwide rare disease challenge would need unprecedented, large-scale worldwide collaboration across geographically dispersed government and non-government entities, as well as R&D departments of various pharmaceutical corporations [25,26]. Since family members frequently have to stop working outside the home to take care of their sick family member, rare diseases pose a serious threat to population health and, if left untreated, are likely to result in significant social and economic losses that affect more than just the individual. On the other hand, patients who got treatment are less likely to need further expensive procedures like pain management and surgery. Additionally, because the cost of therapy is costly, most families cannot afford to pay for the treatment of rare diseases without government aid. This has catastrophic effects on families in terms of both mental and financial stress [25]. This has prompted parents of children with rare diseases whose treatment expenses were not covered by insurance or otherwise compensated to file an appeal in court, seeking that the government provide the pharmaceuticals free of charge so that the therapy can continue. The Ministry of Health & Family Welfare was ordered to develop a national policy on the treatment of rare illnesses by the High Court of Delhi in W.P. (C) Nos. 4444/2016,

7730/2016, and 7729/2013. This policy was to includes he The V. K. Paul Committee Report and Sub-committee on rare diseases in India.

The V. K. Paul Committee Report [27]

The V. K. Paul Committee Report was released in February 2021 by the Ministry of Health and Family Welfare in India. The report was prepared by a committee headed by Dr. V. K. Paul, member (health) of the NITI Aayog, with the aim of developing a national policy for rare diseases in India. The report highlighted the lack of a comprehensive policy for rare diseases in India and recommended the creation of a national policy to address this issue. The report also recommended the establishment of a national registry for rare diseases to collect data on the prevalence of these diseases in India. Other recommendations made in the report include the creation of a network of centres of excellence for rare diseases, the development of a framework for clinical trials of drugs for rare diseases, and the provision of financial support for the treatment of rare diseases. The report also emphasized the need for collaboration between various stakeholders, including patients, healthcare providers, industry, and the government, to ensure the effective implementation of the recommendations. The V.K. Paul Committee Report aims to improve the diagnosis, treatment, and management of rare diseases in India and to provide support to patients and families affected by these conditions.

Sub-committee on rare diseases in India [27]

The Sub-committee on rare diseases in India under Prof. I. C. Verma was constituted by the Ministry of Health and Family Welfare, Government of India, in 2013. The sub-committee was set up to study the issues related to rare diseases in India and make recommendations for the development of a national policy on rare diseases.

Prof. I.C. Verma, who was the former director of the All India Institute of Medical Sciences (AIIMS), was appointed as the chairperson of the sub-committee. The other members of the sub-committee included representatives from various government departments, medical institutions, patient organizations, and industry associations. The sub-committee conducted a comprehensive study of the prevalence, diagnosis, treatment, and management of rare diseases in India. It also reviewed the existing policies, regulations, and programs related to rare diseases in other nations and given recommendations for adaption to the Indian setting. Based on its findings, the sub-committee submitted a report to the Ministry of Health and Family Welfare in 2015, it advocated a national policy for rare illnesses in India. The policy intended to ensure adequate access to diagnosis, therapy, and care for people suffering from rare illnesses, as well as to encourage research and development in this field. The recommendations of the sub-committee formed the basis for the the Ministry of Health and Family Welfare established a National Policy for Rare Diseases in 2021. The policy provides a framework for the avoidance, management, and treatment of rare diseases in India, with the goal of improving patients' and their families' quality of life.

Common rare diseases, Alice in Wonderland Syndrome (AIWS) and Chronic Pulmonary Aspergillosis (CPA) are briefly described below:

Alice in Wonderland Syndrome (AIWS)

Alice in Wonderland syndrome is a rare neurological condition that affects perception, causing distortions in the sense of space, time, and size. The syndrome is named after Lewis Carroll's Alice's Adventures in Wonderland, where Alice often experiences size distortions and other sensory changes. It is also named as 'Todd Syndrome' as British psychiatrist John Todd introduced the term in 1955.

Occurrence:

The syndrome is most commonly observed in children and adolescents but can occur at any age. AIWS has been associated with pathogen infections such as the Epstein-Barr virus [28]. It is most often associated with migraines, epilepsy, and other neurological disorders.

Symptoms:

The most common symptoms of the syndrome include [29]:

a) Alterations in the perception of the size of objects or body parts. b) Distorted visual images that can appear larger or smaller than they are. c) Time distortions, where time appears to be either slowed down or sped up. d) Auditory hallucinations, where sounds may be distorted or seem very loud. 'Alice in Wonderland' Syndrome also includes migraines, epilepsy, and many other neuropsychiatric disorders. Research scientist, Coleman and Lippmann, have made significant contributions to the description of AIWS. In AIWS instances, a comprehensive study revealed 42 visual symptoms, 16 aesthetic symptoms, and additional symptoms. These symptoms were depicted as sensory distortions rather than hallucinations [30].

History and treatment:

The condition was initially characterised by British psychiatrist John Todd in 1955, when he noticed that some of his migraine patients were suffering strange visual abnormalities. Currently, there is no specific

treatment for the syndrome, but symptoms can be alleviated with anti-migraine medications or other medications for symptomatic relief. Rarely AIWS-like conditions are under studied and can lead to significant challenges to provide accurate medical care as providers may not have sufficient insight epidemiology and pathophysiology of such diseases.

Statistical information related to Alice in Wonderland Syndrome [31,32].

Alice in Wonderland Syndrome (AIWS) is a rare disorder, and there is limited numerical data available on its prevalence and incidence.

- Studies suggest that between 5% and 10% of the general population experiences at least one AIWS episode in their lifetime.
- AIWS is more common in children, but it can occur in adults as well.
- AIWS has been found to be associated with migraines, epilepsy, and infectious diseases such as mononucleosis and Lyme disease.
- According to a study published in the national and international standard database, the frequency of AIWS episodes in patients with epilepsy was found higher compared to the general population.
- Another study suggested that AIWS symptoms may be more severe in patients with temporal lobe epilepsy.
- There is no known cure for AIWS, but it typically resolves on its own within a few minutes to hours. However, some medications and behavioural strategies have been found to be helpful in managing the symptoms.

Current scenario:

Alice in Wonderland syndrome is a rare condition and often goes undiagnosed. Many people who experience these symptoms may not realize that they have a condition and may not seek medical attention. More research is needed to understand the causes and develop better treatments for the syndrome. The purpose of learning AIWS is to Strengthen the global knowledge base on this condition and the relevant factors that can drive it better clinical care [33]. Another purpose of studying AIWS is to study comorbidities. Still in the age of precision Health sciences investigating complex biopsychosocial issues related to neuropsychiatry Conditions facilitate the effective integration of advanced analytical techniques for accurate results Diagnosis and treatment. It aims not only to advance scientific knowledge in this field, but also to advance medical practice.

Chronic Pulmonary Aspergillosis

Chronic Pulmonary Aspergillosis (CPA) is a rare fungal infection of the lungs caused by Aspergillus species. It is estimated to affect less than 1% of the general population, and most commonly occurs in individuals with underlying lung disease such as tuberculosis, bronchiectasis, or chronic obstructive pulmonary disease (COPD). The symptoms of CPA can vary depending on the severity of the infection and may include cough, chest pain, weight loss, fatigue, and shortness of breath [34]. The diagnosis of CPA can be challenging as it often requires a combination of clinical and radiological findings, as well as laboratory testing such as sputum culture and serology. Treatment of CPA typically involves long-term antifungal therapy with drugs such as itraconazole or voriconazole. In some cases, surgical interventions may be necessary to remove infected lung tissue or to limit further damage to the lungs.

CPA as Rare

Overall, while CPA is a rare disease, it can have significant consequences for patients with underlying lung disease and may lead to chronic lung impairment and reduced quality of life. Therefore, early diagnosis and appropriate management are critical for improving patient outcomes. Chronic pulmonary aspergillosis (CPA) is a long-term fungal infection of the lungs caused by the Aspergillus species. It affects people who have a weakened immune system, pre-existing lung disease, or prolonged exposure to Aspergillus spores. CPA is a severe condition that can lead to permanent lung damage, respiratory failure, and death. CPA occurs in individuals with underlying lung diseases such as tuberculosis, chronic obstructive pulmonary disease (COPD), asthma, bronchiectasis, cystic fibrosis, or those who have undergone lung surgery or transplantation. It is also prevalent in people with weakened immune systems due to HIV, cancer chemotherapy, or long-term use of corticosteroids [35,36].

History and current scenario of CPA

The history of CPA dates back to the early 20th century when it was known as 'Aspergilloma' or 'fungus ball' due to the formation of a large fungal mass in the lung cavities. Initially, surgery was the only treatment option for CPA. However, with the advent of antifungal drugs such as itraconazole, voriconazole, and amphotericin B, medical treatment has become the mainstay of therapy [37,38]. Despite advances in medical treatment, CPA remains a challenging condition to manage. The prolonged course of treatment, the

requirement for long-term antifungal therapy, and the risk of drug-related side effects present significant challenges to clinicians.
In the current scenario, CPA continues to be a significant respiratory health issue, particularly in developing countries. The lack of awareness, delayed diagnosis, and limited access to antifungal drugs contribute to the high morbidity and mortality rates associated with CPA. However, early diagnosis, prompt treatment, and ongoing monitoring can improve outcomes for people with CPA.

CONCLUSION

A huge percentage of practising doctors had never met even one patient with a rare condition throughout their entire professional career, and the majority of health workers had never seen people with rare diseases. The two factors, diagnosis and awareness are the most crucial behind this. Here, we made an effort to evaluate the fundamental information on rare diseases in India and worldwide. The outcomes act as an overview for thorough comprehension. In order to develop a focused and fruitful national health care policy for rare diseases, much more work must be done to assess the severity of the issues. Even while there are still difficulties unique to researching rare illnesses, there has never been a better time to make major contributions to cutting-edge research, establish rewarding careers in academia, and most importantly improve the lives of those who are affected by rare diseases and who carers of patients of rare diseases.

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