Global perspectives on rare and orphan diseases: Prevalence, impact, and diagnostic challenges

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Abstract

Rare and orphan diseases affect a minor segment of the population but represent a significant global health challenge due to their diversity and the specialized care required. This study offers a comprehensive global perspective by examining the prevalence, impact, and policy responses concerning rare and orphan diseases. Utilizing a mixed-method approach, data was gathered from global health databases and interviews with healthcare professionals and policymakers. The findings underscore the gaps in current healthcare systems and highlight successful strategies implemented in various countries. The study continues with a discussion of the implications of the disease for public health policy and recommendations for future research to meet the unresolved requirements of patients with orphan and rare diseases.

Keywords: Rare diseases, Orphan diseases, Epidemiology impact, Diagnostic challenges.

1. Introduction

As stated by the World Health Organization, orphan diseases are group of illnesses with an estimated incidence of fewer than 6.5 to 10 instances per 10,000 people. Because these illnesses are incredibly rare and reported globally rarely, they have not received much public attention (1).

Orphan diseases" are ailments that are considered "neglected," meaning that there is a shortage of viable remedies due to a lack of research on diagnosis and therapy. The concepts of orphan and uncommon diseases differ, yet, in that some common diseases are nonetheless deemed orphan since they largely strike low-income countries and there may be limited financial incentives to explore them (2). Rare diseases impact around 6% of the population worldwide (3). Because of their rarity, 25% of patients have to wait 5 to 30 years for a diagnosis. Approximately 5000 to 8000 RDs have been determined around the world (4), with varying risk factors, origins, signs, remedies, and geographical distribution (5).

Despite their diverse characteristics, they all have one thing in common: they are rare, with patients confronting similar obstacles in detection, therapy, and management. Doctors in general and clinicians in local healthcare facilities may lack competence with rare diseases, resulting in a delay in detection and referred to more specialized institutes. According to a European survey, it required 5 to 30 years for nearly one-quarter of individuals with rare disorders to receive a confirmed diagnosis after experiencing early symptoms. Of these, 40% had either no diagnosis

at all or an incorrect one. Many individuals had to meet with multiple doctors before receiving their final diagnosis. The resulting delays were primarily caused by clinicians' unfamiliarity with rare disorders (6,7). Long-lasting symptoms, the advancement of the illness, lower quality of life, needless hospital stays and interventions, ineffective pharmaceutical and non-pharmacological treatment, and possibly even a higher death rate can all be consequences of a delayed diagnosis (8).

The absence of uniform statistical information across geographies and populations and the rarity of the illnesses (low prevalence) hinders clinical trial implementation and data collection in the actual world. This, in turn, impedes the development of safe and novel treatments (9). Despite significant national differences, RD treatment is still a global topic that frequently affects patients, their families, and caregivers. Patients bear a huge emotional, financial, and social burden. Patients find it difficult to navigate the healthcare system, even in industrialized nations with more developed policies, funding, and professional guidelines for rare diseases. This results in notable differences in the quality of patient care and accessibility to treatment between different socioeconomic groups and communities (10).

2. Epidemiology impact

An estimated 350-475 million people worldwide are predicted to be affected by RDs, with children making up about 50% of those affected in a 2020 World Economic Forum report. As RDs are frequently underdiagnosed, several nations only have prevalence estimates (11). Figure 1 depicts an estimated number of persons affected by Rare Diseases across different locales

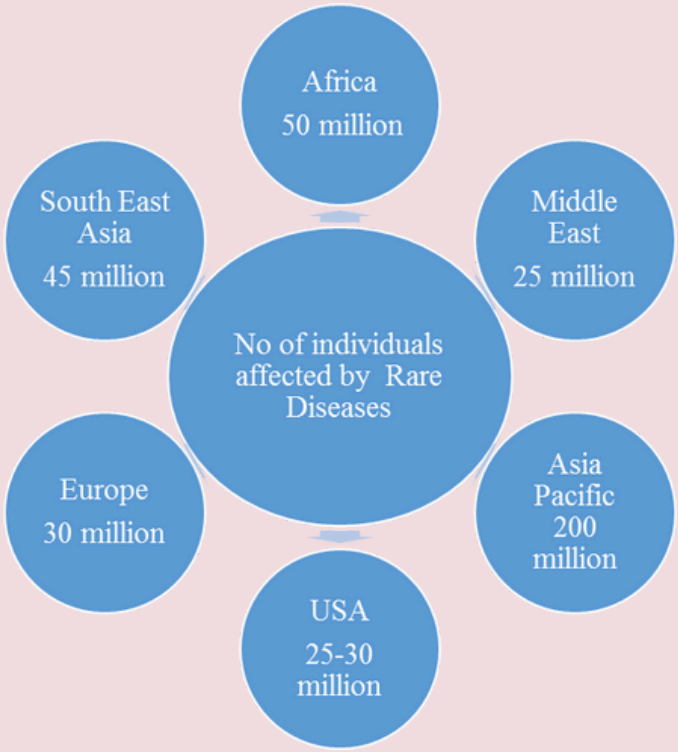

Figure 1. Number of individuals affected by rare diseases

3. Causes

3.1 Genetic mutations

Many rare and orphan diseases have a genetic basis, meaning they are result of mutations in the sequence of DNA. These mutations may be inherited from one or both parents (autosomal recessive, autosomal dominant) or occur spontaneously during embryonic development. Examples include Huntington's disease, cystic fibrosis, and Duchenne muscular dystrophy (12).

3.2 Environmental factors

Some rare diseases are influenced by environmental factors such as exposure to toxins, infectious agents, or certain drugs. Environmental triggers may interact with genetic predispositions to cause or exacerbate disease. For example, certain forms of cancer, autoimmune diseases, and metabolic disorders may have environmental components (13).

3.3 Immune dysregulation

Disorders characterized by dysregulated immune responses can lead to rare and orphan diseases. This category includes autoimmune disorders, which occur when the immune system targets the body's own tissues. Examples include systemic lupus erythematosus (SLE), multiple sclerosis (MS), and autoimmune hepatitis (14).

3.4 Metabolic abnormalities

Rare diseases may arise from abnormalities in metabolic pathways, leading to the accumulation or deficiency of certain substances within the body. Inborn metabolic errors, such as, maple syrup urine disease, phenylketonuria and Gaucher disease, can result in major health consequences (1

3.5 Structural abnormalities

Structural abnormalities in organs or tissues can give rise to rare diseases. These abnormalities may be present from birth (congenital) or develop later in life. Examples include congenital heart defects, craniofacial anomalies, and skeletal dysplasia (16).

3.6 Unknown causes

In some cases, the exact cause of a rare or orphan disease may be unknown or not well understood. Genetics and molecular biology advancement contributed to the identification of causative factors for many rare diseases, but there are still conditions for which the underlying mechanisms remain elusive (17).

4. Diagnostic challenges

People with orphan and rare diseases face numerous obstacles as a result of delayed or erroneous diagnosis, care, and treatments. Rapid diagnosis has become more important due to the exchange of genetic test results, new genetic sequencing techniques, and programs like Undiagnosed Disorders Network International (UDNI) and Undiagnosed Diseases Network (UDN) program that focus on undiagnosed disorders (18-21).

Genetic testing, including sequencing of whole genome and exome, has become a crucial diagnostic tool for identifying the genes linked to the onset of orphan diseases because it has been shown that defects in the mechanisms that repair single- and double-stranded DNA breaks are the cause of orphan diseases. Genetic counselling is critical in identifying and maintaining the good quality of life of people with rare disorders (22,23). DNA-powered applications are currently available to evaluate unprocessed DNA information from various sequences of genomes and genetic testing. In addition to figuring out how small molecules can be used to study genes that are responsible for the cure of rare or orphan disease, chemical genetics is becoming more and more popular these days. It can be used to uncover the molecular mechanism behind the neurological disorders development that are rarely reported, like ALS, DMD, SMA, and FAP (24).

5. Conclusion

Rare and orphan diseases collectively present a significant challenge to global health systems, primarily owing to their low prevalence and the lack of comprehensive treatment options. This article has explored the multifaceted impact of these diseases, highlighting the burden they place on affected individuals, healthcare systems, and societies worldwide. Despite the challenges, our analysis reveals progressive strides in specialized care and policy development aimed at addressing the needs of patients suffering from these conditions. To facilitate ongoing improvement, international collaboration must extend research, share expertise, and harmonize efforts in diagnostic processes, treatment protocols, and patient support mechanisms. Looking to the future, increased investment in medical research and policy innovation holds the key to unlocking better health outcomes for those affected by rare and orphan diseases. It is only through persistent effort and dedication to understanding and combating these conditions that we can hope to alleviate their impact and foster a more inclusive and responsive global health environment.

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Rare Diseases in India

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