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# NEWBORN SCREENING FOR RARE GENETIC DISORDERS IN INDIA: A NARRATIVE REVIEW

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## ABSTRACT
Rare genetic disorders constitute a significant yet under-recognized public health challenge in India, where high birth rates, genetic diversity, consanguinity, and limited diagnostic infrastructure contribute to delayed diagnosis and increased disease burden. Newborn screening (NBS) has emerged globally as an effective strategy for early detection and management of inherited metabolic, hematological, and genetic disorders. This narrative review evaluates the current status of newborn screening for rare genetic disorders in India, focusing on epidemiology, screening technologies, policy frameworks, ethical concerns, and future implementation strategies. A narrative review approach was adopted using recent literature, government policies, international screening frameworks, and peer-reviewed studies related to rare diseases, genomic medicine, and newborn screening programs in India and other countries. The study highlights that India continues to face major challenges including fragmented screening programs, inadequate registries, limited laboratory infrastructure, workforce shortages, and high treatment costs. Advances in tandem mass spectrometry, molecular diagnostics, genomic sequencing, and artificial intelligence are expanding the diagnostic capabilities of modern NBS systems. International models from the United States, United Kingdom, and Taiwan demonstrate the importance of integrated governance, sustainable financing, and ethical oversight in successful NBS implementation. A comprehensive national NBS framework integrating genomic medicine, rare disease registries, public health infrastructure, and sustainable financing mechanisms is essential for improving early diagnosis, reducing disability burden, and strengthening rare disease management in India.

**KEYWORDS:** Newborn screening; Rare genetic disorders; Genomic medicine; Orphan diseases; Public health policy; India

## 1. INTRODUCTION
Rare genetic disorders are a significant, but often unrecognized public health problem worldwide. While rare diseases impact a small number of people in any given area, the global impact of all rare diseases is massive—estimates are that millions of people are affected by a chronic disability, developmental abnormalities or premature death from a rare disease. It is methodologically difficult to estimate the true prevalence of rare diseases, as a result of the lack of consistency in definitions, underreporting and fragmented surveillance systems between countries (Venugopal et al., 2024). The impact of the large population size, high birth rate, and large genetic diversity is particularly deep in India. The prevalence of rare diseases in India is estimated to impact almost 96-100 million people across the country, underscoring the severity of the healthcare burden (Gupta et al., 2026). Many rare diseases appear in infancy or childhood, and result in serious neurological, metabolic or developmental disorders when not diagnosed in time. Neonatal morbidity and mortality have been heavily influenced by birth defects and inherited metabolic diseases in India, highlighting a need for improved early detection methods (Kar, 2025). Other systematic evaluation of congenital anomalies also reveals that genetic and metabolic disorders are a significant, however underdiagnosed, part of the pediatrics health care in the country (Bhide & Kar, 2018). Early diagnosis is therefore important, both for the improvement of survival rates, and also to minimise long-term disability and psychosocial burden on families. Low resource areas in India, however, are still struggling to get timely diagnoses due to poor genomic infrastructure, lack of specialists, and disease awareness about rare diseases (Angural et al., 2020). Newborn screening (NBS) is considered one of the most successful public health prevention programs for detecting genetic and metabolic disorders at an early stage. It began with the screening for the presence of the enzyme defect, phenylketonuria, in the mid-20th century and has since grown to a broad range of multi-condition screening programs that are offered globally. Dried blood spot (DBS) sampling is used in modern NBS systems, which is based on the collection of blood samples in the days following birth and subsequent biochemical and molecular analysis, with minimal invasiveness (Bouvier & Giguère, 2019). The technologies

developed have moved NBS from the detection of a single disease to multiple disease detection on a single platform, based on a population approach. New techniques like tandem mass spectrometry, molecular diagnostics and genomics are being incorporated into screening programs to enhance diagnostic accuracy and extend the spectrum of disorders that can be detected (Therrell et al., 2022). Effective NBS programs are shown to have a positive impact on the reduction of the mortality, disability and health care expenditures of people with undiagnosed genetic disorders (WHO, 2022). While strides have been made, adoption rates are not evenly distributed and in many LMICs, infrastructure challenges and lack of funding are still a barrier to broader uptake. The situation in India is very interesting for the growth of a detailed National NBS framework due to the special demographic and genetic features. The country is home to around 26 million births each year, which presents a huge opportunity for early disease detection and preventive interventions (Kapoor & Thelma, 2018). In addition, within certain communities the prevalence of certain inherited disorders is higher due to population stratification, endogamy, consanguinity, and founder mutations. At present, the implementation of NBS in India is incomplete and confined to few state-led programmes and tertiary healthcare facilities. Fragmentation of the national screening policy has led to wide variations in access to, coverage of and follow-up for screening. It is therefore often recommended that NBS should be implemented universally to ensure equitable access to health services and better health outcomes for children (Mookken, 2020). Delayed diagnosis also has a significant economic and emotional cost to families for the affected members, as treatment can be more complicated and costly when irreversible complications have occurred. The inclusion of rare/diseases programmes in wider public health programmes can increase access and reduce inequalities in access to care by socioeconomic groups (Choudhury & Chaube, 2022). Furthermore, the importance of reinforcing NBS infrastructure as a key priority in healthcare in developing countries is well recognized, where the aim is to reduce preventable childhood disability and mortality (Gaikwad et al., 2024).

In this narrative review, the status of newborn screening for rare genetic disorders in India is discussed with special reference to the epidemiological burden of the disorder, screening infrastructure, genomic advances, and policy integration. It also reviews current approaches for rare disease governance and compares the developing rare disease governance framework in India with international practices such as newborn screening and orphan disease management. Further, ethical, economic and public health concerns related to the expansion of NBS programs are explored, and future directions for establishing an integrated and equitable rare disease care system in India are discussed.

## 2. Epidemiology and Genetic Landscape of Rare Disorders in India

### 2.1 Burden of Rare Diseases in India

Rare diseases are a significant, yet poorly acknowledged healthcare problem that affects India. While accurate prevalence data are still not available due to undercoordinated surveillance and failure to maintain national registries, recent studies indicate that millions of people might be living with inherited disorders that require lifelong medical attention. Under reporting and delayed diagnosis are major issues in this because of the lack of standardized epidemiological databases. Moreover, India has a large ethnic diversity, stratification of its population and genetic variability of its population in the different geographical regions, which may affect the prevalence of diseases among these communities. It is important that the national registries are coordinated, that mechanisms for reporting diseases are strengthened, and that mechanisms for healthcare integration are improved, to better manage rare diseases and conduct epidemiological surveillance in India (Kar et al., 2024; Mishra et al., 2024). Comprehensive reviews also point out that there is a need for better genomic and public health infrastructure to deal with the rising burden of rare diseases in the future, if the planning is to take place effectively (Chaudhary & Kumar, 2025).

### 2.2 Inborn Errors of Metabolism (IEMs)

Inborn errors of metabolism (IEMs) are an important subset of inherited disorders that are frequently screened for in newborn screening programs and for which early diagnosis can dramatically influence clinical outcomes. These disorders occur due to malfunction of the metabolic pathways which may result in the build up of toxic metabolite in the system, neurological dysfunction, developmental delay and death. Newborn screening has been expanded and has enabled the detection of some disorders including, but not limited to, phenylalanine hydroxylase deficiency, methylmalonic acidemia, proximal urea cycle disorders, and arginase deficiency early in life. Epidemiological studies and systematic reviews have shown the critical role that early nutritional and therapeutic interventions play in preventing irreversible neurological complications from metabolic disorders (Therrell Jr et al., 2014). Phenylalanine hydroxylase deficiency (PAH) is also one of the most common metabolic disorders screened worldwide due to the preventable cognitive outcomes if detected early (Foreman et al., 2021). Other studies on the role of expanded metabolic panels in newborn screening programs for methylmalonic acidemia, urea cycle disorders and arginase deficiency confirm the clinical relevance of adding these tests to the newborn screening program (Almási et al., 2019; Vasquez-Loarte et al., 2020; Sawad et al., 2022).

### 2.3 Lysosomal Storage Disorders (LSDs)

Lysosomal storage disorders (LSDs) are inherited metabolic disorders that are progressive due to a deficiency of enzymes that function in the lysosomes, which are the organelles that degrade substrates inside the cells. In the

past few years, disorders like Gaucher disease, Pompe disease, Fabry disease and Hurler syndrome have come to the forefront as important candidates for newborn screening programs due to the significant impact that early treatment has on prognosis and quality of life. Molecular studies in Indian population have highlighted pathogenic variants that are specific to them and hence the need for locally validated genomic data for screening and diagnostic programs (Sheth et al., 2020).

Additionally, epidemiological studies have shown that the prevalence of Gaucher disease is influenced by factors such as ethnicity and geography, necessitating a region-specific approach to screening and planning for care.Moreover, epidemiological research has revealed considerable variation in the prevalence of Gaucher disease by country and ethnicity, highlighting the importance of region-specific screening strategies and care planning. These results all point towards the importance of incorporating LSDs into the newborn screening program for an expanded panel, especially in a genetically diverse population like India.

**2.4 Hemoglobinopathies and Sickle Cell Disease**

Hemoglobinopathies are still a public health issue in India, especially among tribal and high-risk populations, and one of the major issues is sickle cell disease (SCD), which is a hemoglobinopathy. Ethnic diversity, endogamy, and geographic isolation are the main reasons why there is regional variation in carrier frequencies. Screening for SCD in central India has been shown to identify the condition early and improve clinical surveillance and minimise the complications of SCD in early childhood (Mohanty et al., 2016). In addition, community-based antenatal screening programs for tribal communities in Tamil Nadu have also demonstrated the possibility of incorporating hemoglobinopathy screening into primary healthcare systems (Raj et al., 2022). Counselling, awareness and follow-up of parents and long-term follow-up in newborn screening are also important factors in improving patient outcome as seen from the Indian experience (Colah et al., 2018). Besides, significant ethnic differences have been demonstrated in the prevalence of congenital endocrine and haematological disorders in global meta-analyses, emphasizing the need for population-specific screening strategies (Navarro-Zambrana & Sheets, 2023). Table1 summarizes the priority rare genetic disorders which are thought to be relevant for wider newborn screening in India, the methods of screening them and the clinical importance of these disorders.

**Table 1.** Priority Rare Genetic Disorders for Expanded Newborn Screening in India

| **Disorder** | **Public Health Relevance in India** | **Primary Screening Technique** | **Early Intervention Benefit** | **Key Reference** |
|---|---|---|---|---|
| Congenital Hypothyroidism | Major preventable cause of intellectual disability | TSH assay (DBS) | Prevents neurodevelopmental delay | Verma et al. (2020) |
| Congenital Adrenal Hyperplasia | Life-threatening neonatal endocrine disorder | 17-OHP assay | Prevents adrenal crisis | Verma et al. (2020) |
| Phenylketonuria (PKU) | Severe neurological impairment if untreated | MS/MS | Prevents cognitive disability | Foreman et al. (2021) |
| Methylmalonic Acidemia | High metabolic mortality risk | MS/MS | Reduces neurological complications | Almási et al. (2019) |
| Pompe Disease | Progressive neuromuscular disorder | Enzyme assay | Improves survival with ERT | Sheth et al. (2020) |
| Gaucher Disease | Significant lysosomal storage disorder burden | Enzyme/molecular testing | Enables early enzyme therapy | Castillon et al. (2022) |
| Sickle Cell Disease | Highly prevalent in tribal populations | HPLC | Reduces childhood morbidity | Colah et al. (2018) |
| G6PD Deficiency | Common cause of neonatal hemolysis | Enzyme assay | Prevents kernicterus | Verma et al. (2020) |

**2.5 Emerging Role of Genomic Epidemiology**

The revolution in genomic epidemiology has revolutionised the diagnosis and management of rare genetic disorders in India. Recent advances in commonly used technologies like whole-exome sequencing (WES) and

whole genome sequencing (WGS) have greatly aided in the identification of pathogenic variants linked to inherited diseases. Next-generation sequencing methods have been shown to be useful for detecting novel disease-causing mutations, as part of expanded carrier screening in North Indian populations (Singh et al., 2020). Further, genomic research efforts in India have underscored the need for the creation of population-specific genomic databases for better variant interpretation and precision medicine approaches (Sivasubbu & Scaria, 2019). Newborn genome sequencing may also be integrated into public health screening programs in the future, supported by increasing international expert opinion, due to its ability to broaden the spectrum of diagnosable disorders and its potential for personalized treatment for rare diseases (Gold et al., 2023).

## 3. Scientific Foundations of Newborn Screening

### 3.1 Principles of Effective NBS Programs

Effective newborn screening (NBS) programs are guided by the "Wilson and Jungner" screening principles: to detect serious conditions in which treatment is available, at an early stage. For inclusion in screening panels, clinical validity, diagnostic accuracy and therapeutic benefit must be met. For disorders for which the therapeutic window is narrow, early intervention is especially crucial because the delay treatment could result in irreversible neurological injury or death. Ethical monitoring, equitable access, quality assurance and follow-up systems are also key components of modern screening frameworks for long-term systems (Cornel et al., 2021; WHO, 2022).

### 3.2 Technologies Used in Modern NBS

Newborn screening programs have seen great advances in technology in terms of scope and efficiency. Multiple metabolic disorders can be detected simultaneously using tandem mass spectrometry (MS/MS) and hemoglobinopathy screening is usually performed using high-performance liquid chromatography (HPLC). Biochemical and molecular diagnostics platforms have proven to be effective when combined in neonatal screening programs to support improving healthcare in India (Verma et al., 2020). The introduction of new technologies in molecular diagnosis, such as allele-specific PCR, AI-assisted interpretation systems, and other innovations, continues to improve the diagnostic sensitivity, automation, and genetic screening capabilities of molecular diagnostics (Mahmud & Enni, 2025). Table 2 provides a summary of the major technologies employed in current newborn screening programs and their applications, advantages and disadvantages.

**Table 2.** Technologies Used in Modern Newborn Screening Programs

| Technology | Principle/Application | Disorders Commonly Detected | Major Advantages | Key Limitations |
|---|---|---|---|---|
| Tandem Mass Spectrometry (MS/MS) | Simultaneous metabolic profiling from dried blood spots | Amino acid disorders, fatty acid oxidation disorders, organic acidemias | High-throughput multiplex screening | High equipment and operational cost |
| High-Performance Liquid Chromatography (HPLC) | Separation and quantification of hemoglobin variants | Sickle cell disease and other hemoglobinopathies | Reliable and widely used screening method | Limited detection of non-hematological disorders |
| Allele-Specific PCR (AS-PCR) | Detection of targeted pathogenic genetic variants | Monogenic inherited disorders | Rapid and highly specific analysis | Limited mutation coverage |
| Whole-Exome Sequencing (WES) | Sequencing of coding regions of the genome | Rare Mendelian disorders | Broad mutation detection capability | Complex interpretation of variants |
| Whole-Genome Sequencing (WGS) | Comprehensive genome-wide sequencing | Rare genetic and genomic disorders | Highest diagnostic coverage | High cost and ethical concerns |
| AI-Assisted Genomic Interpretation | Automated computational analysis of genomic data | Variant prioritization and genomic screening support | Improved analytical speed and efficiency | Requires robust genomic databases and validation |

### 3.3 Biomarkers and Disease Prioritization

The selection of disorders included in newborn screening panels is related to the prevalence, clinical severity, reliability of the biomarkers, availability of treatment and cost-effectiveness of the screening program. To decrease diagnostic errors and increase screening accuracy, biomarkers should be highly sensitive and specific. For IEMs, the emergence of early dietary and pharmacological treatments that prevent severe neurological complications,

and decrease healthcare costs, continues to make these a primary target (Therrell Jr et al., 2014). Some recent Indian research has documented problems with coverage of disease, quality control in the lab and standardization of screening, emphasizing the need for evidence-based prioritisation strategies in national screening programs (Patel et al, 2024).

### 3.4 Transition from Biochemical to Genomic Screening

It is now recognised that newborn screening is transitioning from biochemical testing to genomic testing such as whole genome sequencing or whole exome sequencing. A genomic screen can more accurately diagnose a condition and uncover a wider range of rare disease than traditional tests. Precision medicine and early treatment have been shown to be promising applications of first-line genome sequencing, as evidenced by studies (Wigby et al., 2024). The problems with genomic NBS, however, include incidental findings, variant interpretation, and ethical governance. Genomic integration—experiences from Australia and elsewhere—is brought to the fore by the preparation, public engagement and data privacy issues. A progression from traditional biochemical assays to more advanced assays using AI and genomic platforms is illustrated in Figure 1.


**Figure 1.** Evolution of Newborn Screening Technologies

The above graph indicates the progression of technologies for newborn screening from traditional biochemical tests to modern technologies such as genomics and artificial intelligence (AI), which are much more accurate and allow a wider range of diagnoses.

## 4. Current Status of Newborn Screening in India

### 4.1 Evolution of NBS Initiatives in India

The first NBS programs in India started with the help of pilot projects under the guidance of the Indian Council of Medical Research (ICMR), concentrating primarily on congenital hypothyroidism and hereditary metabolic diseases. These initial experiments proved the practicality and importance of such programs in India's healthcare system (Mathur, 2014). Later, screening programs conducted by states and other institutions grew to encompass other hereditary illnesses. Although significant advances have been made, a widespread program has not yet been achieved due to infrastructural, economic, and political problems in achieving equity in healthcare access throughout India (Mookken et al., 2024).

### 4.2 State-Level Screening Models

Knowledge of the health care needs and availability of health care facilities to the local population has led to the emergence of local models in some Indian states with respect to newborn screening. In Chandigarh, Goa and Kerala screening programmes have focused on the identification of congenital disorders such as congenital hypothyroidism, congenital adrenal hyperplasia, glucose-6-phosphate dehydrogenase deficiency and hemoglobinopathy. This type of programs has been found to be feasible for implementation in health care services across different regions and highlighted the gaps that exist between different states on laboratory support, care follow-up and disease coverage (Verma et al., 2020). The screening journey with sickle cell disease also identified the need for local solutions to achieve healthy outcomes for children (Colah et al., 2018).

### 4.3 UMMID and NIDAN Kendras

To promote the diagnosis and management of inherited diseases with genomic technologies, genetic counselling and prenatal diagnostic services, the Department of Biotechnology (DBT) initiated UMMID. NIDAN Kendras set up as a part of this initiative intend to make advanced genetic testing facilities more accessible in India (Department of Biotechnology [DBT], 2019). These centres have played an important role in implementing molecular diagnostics and reproductive counselling in the management of rare diseases. Further, experiences from tertiary genetic centres highlight the growing importance of prenatal diagnosis and genomic evaluation in identifying inherited disorders and shaping clinical management strategies for the future (Sheth et al., 2025).

### 4.4 National Registries and Data Infrastructure

India is still facing challenging issues with the development of comprehensive national registries and centralized surveillance systems for the rare diseases. The importance of supporting integrated databases to enhance epidemiological monitoring, healthcare planning and resource allocation for newborn screening programs is highlighted in current policy discussions (Gupta et al., 2026). Patient organisations and patient advocacy groups have also played a role in raising awareness, assisting in the creation of patient registries and improving patient policy involvement within the rare disease ecosystem (Choudhury & Saberwal, 2019). But problems with data sharing, interoperability and sustainability remain to be overcome.

### 4.5 Urban-Rural and Socioeconomic Disparities

The gap between urban and rural areas in terms of newborn screening access is still large in India. Low-resource areas generally have limited access to healthcare experts, geneticists, and diagnostic services, leading to delayed diagnoses and inadequate follow-up care (Angural et al., 2020). A large scale newborn screening program is also limited by advanced laboratory facilities that are not available in many rural public hospitals. Other factors contributing to coverage gaps for neonatal screening include limited budgets and lack of awareness and inequitable access to health care. The results underscore the critical need to invest in infrastructure development and access to equitable health care in order to facilitate universal newborn screening in India (Gaikwad et al., 2024).

## 5. Regulatory and Policy Framework Governing Rare Diseases in India

### 5.1 New Drugs and Clinical Trials Rules (NDCTR) 2019

India has an important regulatory pathway for Orphan drugs with the introduction of the New Drugs and Clinical Trials Rules (NDCTR) 2019. According to these guidelines, any drug which is used in not more than five lakh people in the country is called an orphan drug. Certain features of the framework confer regulatory advantages such as clinical trial fee waivers, speedier review processes and in certain cases, the ability to waive local clinical trial requirements. The framework, however, does not include any significant market exclusivity, tax benefits or a dedicated ecosystem for orphan drug development (CDSCO, 2019).

### 5.2 National Policy for Rare Diseases (NPRD) 2021

National Policy for Rare Diseases (NPRD) 2021 is the frame policy of the Central Government of India related to the management of rare diseases. It categorizes rare diseases by different types of treatment, the length of treatment and its cost. The policy also includes a financial support criterion for eligible patients and specifies the Centres of Excellence (CoEs) for diagnosis, treatment and care coordination. There are challenges in implementation, especially in terms of long term funding, equitable access and integration with treatment pathways (MoHFW, 2021)

### 5.3 Financing Challenges in Rare Disease Care

High treatment costs for enzyme replacement therapies and other treatments that require long-term use of orphan drugs are a significant influence on the delivery of rare disease care in India. For many families, their access to therapy still relies on the ability to afford it, and they have to shell out a lot of cash if they want it, or may have to wait or stop using it altogether. Orphan drug availability in India has been found to have a consistent lack of access, affordability, and sustainable supply mechanisms (Naik et al., 2023). Additional policy reviews suggest that rare disease programs need more robust financing mechanisms, public procurement and reimbursement policies for meaningful access to diagnosis through newborn screening, and to ensure meaningful access to treatment, as a result of the newborn screening diagnosis (Mishra et al., 2024).

### 5.4 Judicial Interventions and the Right to Health

Rare disease policy debates have been influenced by judicial interventions particularly when patients have been seeking access to the life-saving, but unaffordable, therapies. The access to treatment and the state's duty to safeguard a vulnerable patient with rare disorder has constitutional implications that have been brought to the fore in litigation. But, court access is not an appropriate replacement for a systematic public health plan. Rare disease care can be integrated into public health programmes, such as National Health Mission, to deliver more equitable and scalable care in the long term (Choudhury & Chaube, 2022). This integration can work for short term solution but not as a long-term plan.

### 5.5 Need for a Dedicated Rare Disease and Orphan Drug Act

India's rare disease policy is not integrated across the various parts of the drug administration, public health policy, genetic services, and reimbursement system. Newborn screening, disease registration, orphan drug incentives, genetic counselling and treatment financing can all be included in a single statutory framework in a dedicated Rare Disease and Orphan Drug Act. Guidance for genetic screening in India has been laid down, and focuses on having structured screening, counselling, and follow-up systems in place for the management of inherited disorders (Phadke et al., 2017). There is also global public health guidance for the implementation of comprehensive newborn screening systems that are tied to diagnosis, treatment, quality assurance and access (WHO, 2022).

**Table 3.** Major Regulatory and Policy Frameworks Governing Rare Diseases in India

| Framework/Policy | Year | Major Focus | Key Limitation | Key Reference |
|---|---|---|---|---|
| New Drugs and Clinical Trials Rules (NDCTR) | 2019 | Orphan drug regulation and accelerated approval pathways | Limited innovation incentives and market exclusivity | CDSCO (2019) |
| National Policy for Rare Diseases (NPRD) | 2021 | Rare disease classification and financial assistance | Funding and implementation challenges | MoHFW (2021) |
| UMMID Initiative | 2019 | Genetic diagnosis, counselling, and research support | Limited nationwide accessibility | DBT (2019) |
| National Health Mission-linked Rare Disease Integration | Ongoing | Integration of rare disease care into public health systems | Infrastructure and workforce limitations | Choudhury & Chaube (2022) |

## 6. International Perspectives on Newborn Screening and Rare Disease Governance

### 6.1 United States: Integrated Screening and Orphan Drug Incentives

The United States has one of the best models of newborn screening governance in the form of the Recommended Uniform Screening Panel (RUSP) that governs the newborn screening programs in the state and facilitates disease selection uniformity. The US model is based on screening expansion being associated with treatments, clinical usefulness, and public health benefit (Therrell et al., 2022). The [new] recommendations for newborn screening for CF, which are particular to the condition, further illustrate the impact of evidence-based consensus to improve the accuracy of screening, follow-up and long-term management (McGarry et al., 2025).

### 6.2 United Kingdom: The Shift Toward Genomic Newborn Screening

The United Kingdom is making strides towards implementing a genomic model of newborn screening via the Newborn Genomes Programme. The UK model has a different focus, with screening systems based primarily on clinical actionability and early diagnosis, and having long-term genomic utility. There are important ethical considerations regarding consent, incidental findings, storage of genomic information, and future applications of genomic information (UK National Screening Committee, 2024). Additional considerations from expert perspectives about the implementation of newborn genome sequencing underscore the importance of moving forward with a balanced approach that safeguards families and enhances diagnostics (Gold et al., 2023).

### 6.3 Taiwan as a Strategic Model for India

The case study in Taiwan is a very relevant one for India due to the way newborn screening, recognition of rare diseases, designation as orphan drugs, and reimbursement are coordinated in a coordinated legal and health insurance system. The Rare Disease and Orphan Drug Act has improved patient access to diagnosis and treatment, and lowered financial barriers to access (Hsiang et al., 2022). The quick orphan drug recognition and registration system in Taiwan is another example of streamlined access to rare disease drugs (TFDA, 2023).

### 6.4 Comparative Lessons for India

Practical experience abroad has demonstrated the need for a coordinated approach in the implementation of newborn screening systems which include sustainable financing, ethical control, access to treatment, laboratory infrastructure, and governance. Comparative evidence indicates that the transition to the genetic and genomic approach to screening is taking place in countries and the implementation process needs to be tailored to the country's resources and public health priorities (Bouvier & Giguère, 2019). But lessons learnt from the genomic area screening systems also indicate that India needs a phased approach which ensures affordability, equity, clinical actionability, and long-term planning of care for rare diseases. Figure 2 summarises comparative international approaches and some of the main policy lessons that are pertinent to strengthening newborn screening and rare disease governance in India.

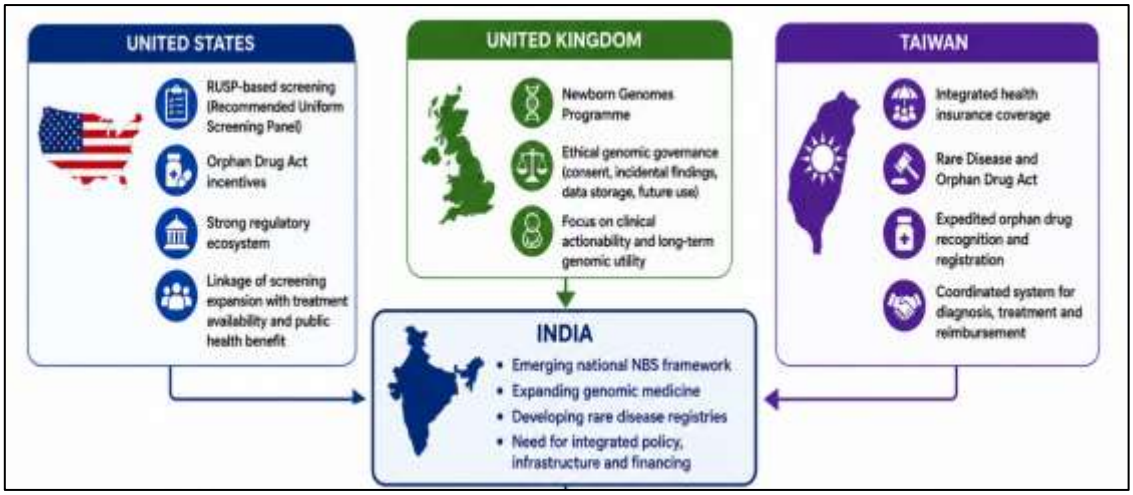


**Figure 2.** International Models of Newborn Screening Relevant to India

The figure shows the differences in the way countries have been implementing NBSC, genomic medicine, financing and regulatory frameworks in the governance of rare diseases. The international experiences offer valuable policies lessons for India as it works to create a sustainable, equitable, genomics-based newborn screening system.

## 7. Ethical, Legal, and Social Implications (ELSI) of Newborn Screening

### 7.1 Informed Consent in Neonatal Screening

Often, the debate about newborn screening is whether or not screening should be mandated or offered as an option. There are advantages to obligatory measures in terms of coverage and early detection but issues of parental choice and consent are raised. Screening in the context of genomic testing and retention of data for future use makes consent more complicated. Another factor affecting trust in screening systems is public perceptions of what they'll do with samples of dried blood spots. Studies on the context of genomic screening highlight the significance of clear consent processes and communication with families regarding future applications of genetic data (Belaramani et al., 2023).

### 7.2 Data Privacy and Genetic Information Protection

With the expansion of the genomic newborn screening program, issues regarding long-term storage of genomic data and issues of genetic data governance and confidentiality have been raised. The large-scale sequencing programs generate highly sensitive data which could impact on not only newborns but also family members. Future re-analysis of stored genomic data, data ownership, unauthorised access and potential for discrimination are ethical issues. As of now, there is strong evidence that patient privacy protection and secure data management systems are needed to ensure that the vast potential of genomic screening technologies for clinical and research applications can be realized.

### 7.3 Equity and Justice in Rare Disease Care

Equity in newborn screening and rare disease services is an important moral challenge, particularly at a rural level and in marginalised communities. Diagnosis and treatment of these is often delayed due to poor health care facilities, lack of skills in health workers, and socio-economic differences. Ethical issues also emerge with respect to the allocation of scarce health-care resources for the use of costly drugs for rare diseases. Balanced healthcare policies, which ensure universal access, affordability and involvement of marginalized groups in national screening programs are, therefore, essential to ensure justice in rare disease care.

### 7.4 Psychosocial Impact on Families

Families of affected individuals may experience psychosocial impacts following the results of newborn screening and genetic diagnosis such as anxiety, uncertainty, emotional distress, and stigma. Psychological stress is common in families in the process of confirmatory testing and in long-term management of the disease. Poor public understanding of genetic disorders also can increase discrimination and stigmatisation of individuals affected by them, in many contexts. Previous research on rare disease stigma highlights the need for culturally appropriate communication approaches, counselling support and community education to alleviate the psychological burden and enhance family coping strategies (Baynam et al., 2024).

### 7.5 Ethical Challenges in Genomic NBS

In addition to the usual ethical issues arising from biochemical screening, there are other issues unique to genomic newborn screening. Incidental findings that are not related to childhood disease, such as information on carrier status and/or information about disorders that appear in adulthood, may be discovered through whole-exome and

whole genome sequencing. These revelations suggest clinical significance and psychological repercussions, as well as possible future autonomy issues. Genomic technologies have also been expanded to include carrier screening studies which often reveal the unexpected presence of pathogenic variants with unclear implications for the family and health care providers (Singh et al., 2020). The complexities underscore the need for meticulous ethical principles that guide the use of the genome in interpretation, disclosure and follow-up.

## 8. Economic and Health System Implications of National NBS

### 8.1 Cost-Effectiveness of Early Detection

Newborn screening is an effective way to reduce long term health care expenses by preventing the long-term consequences of untreated genetic disorders and serious issues. Early treatment reduces cost of hospitalizations, developmental outcomes, and the economic burden on families and health systems. The experience gained from screening in India has shown that early detection of inherited disorder can help in better management of the disease in the long run and in minimizing the preventable morbidity (Mathur, 2014). Moreover, detailed assessment of rare diseases also shows that investment in programmes of early screening is cost effective when compared to the long-term cost of chronic care of disability caused by delayed diagnosis (Chaudhary & Kumar, 2025).

### 8.2 Public Health Impact of Nationwide Screening

Newborn screening programs may significantly impact the public health for reducing infant mortality, the incidence of neurological impairment, and quality adjusted life years (QALYs). The additional screening systems also bolster preventative health care as they allow the early clinical intervention before disease progression. A recent study has pointed towards the need for a comprehensive national newborn screening strategy to enhance the health of the pediatric population in India, and decrease inequities in access to diagnosis and treatment (Mookken et al., 2024). These programmes also help to enhance long-term surveillance and health system planning for rare diseases.

### 8.3 Pharmaceutical and Biotechnology Opportunities

With the expansion of newborn screening programs, there are considerable opportunities for indigenous orphan drug development and biotechnology innovation. Rare diseases could lead to greater research, manufacturing, and targeted treatments in the country for inherited diseases. The genetic studies of the Indian population have identified population-specific pathogenic variants which could aid in the development of locally relevant therapeutic strategies and precision medicine approaches for a range of lysosomal storage disorders (Sheth et al., 2020). Furthermore, the prevalence of rare disorders, including GD, is a growing need for specialized orphan treatments and investment in biotechnology across the globe (Castillon et al., 2022).

### 8.4 Integration with Ayushman Bharat and Universal Health Coverage

Incorporation of newborn screening within Ayushman Bharat or universal health coverage systems can enhance the primary healthcare delivery and provide equal access to genetic services. The integration of newborn screening into current maternal and child health services may enable early identification, referral, and follow-up newborn treatment coordination at multiple-levels of health services. Policy alignment of rare disease management and national healthcare policies might also minimize out-of-pocket costs and promote continuity of care for impacted families. Enhancement of primary healthcare infrastructure is thus still crucial to ensure sustainability of the newborn screening program across India (Choudhury & Chaube, 2022). Figure 3 shows the key economic, clinical, and health system impacts of a nationwide newborn screening program.

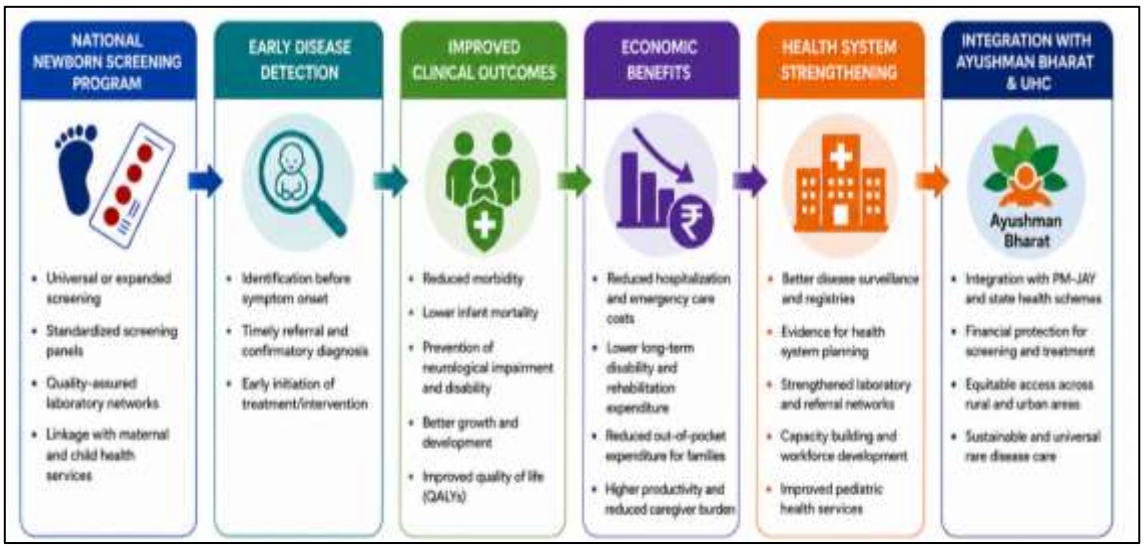


**Figure 3.** Economic and Health System Impact of National Newborn Screening Programs

The figure illustrates that a newborn screening program with integration can not only optimize early detection and clinical results, but also bring economic savings, strengthen the healthcare system, and enhance access to care of rare diseases in an equitable manner in the long run. All these benefits contribute towards building the foundation of a more sustainable and inclusive public health system in India.

**9. Future Directions in Newborn Screening in India**

India's policy on neonatal screening needs to be a gradual shift towards a mandatory national newborn screening (NBS) programme with a agreed minimum screening panel to screen common high-priority genetic and metabolic disorders. Enhancement of screening services can be facilitated through increased public health infrastructure, better referral systems, and a national roll-out plan. The possibilities of genomic technologies, AI, and digital health tools for the future of integration and precision diagnostics are immense.

Disease registries and centralized monitoring of rare diseases will be vital to epidemiological surveillance, health care planning, and enhancing the research. Investment in human resources in the form of training geneticists, lab technicians and genetic counsellors and improving the diagnostic facilities in government hospitals and non-governmental hospitals is also required in India.

Long-term program sustainability will require an effective policy framework that combines newborn screening and orphan drug policies with sustainable funding and public–private partnerships. India's journey towards creating an equitable and comprehensive NBS ecosystem could be further accelerated by the help of international cooperation, genomic research partnerships, and technology transfer.

**10. CONCLUSION**

Newborn screening (NBS) has been shown to be a valuable public health intervention for early detection and treatment of rare genetic disorders, particularly in a high-burden and highly diverse population such as India. This review highlights the fact that rare diseases have an important clinical, economic and social burden and that many of these diseases involve infants and children. Results clearly show that early diagnosis by NBS helps to curtail morbidity, mortality, lifelong disability and health care cost, when diagnosed early, therapeutic interventions can be achieved. The review also demonstrates that India has been taking incremental steps with pilot projects, State level initiatives, UMMID, NIDAN Kendras and the progressive policy frameworks like the National Policy for Rare Diseases (NPRD) 2021. The fragmentation of implementation, however, is caused by the lack of infrastructure, lack of staffing, lack of funding and unequal health service provision in various regions. Advancements in molecular diagnostics, genomic sequencing, tandem mass spectrometry, and the use of AI for interpretation have expanded the scope and specificity of these modern NBS programs, which could be incorporated into public health systems, resulting in genomic medicine. The experience in the United States, the United Kingdom and Taiwan indicates that the successful development of NBS systems must be managed, funded, monitored and managed. When expanding in the future, informed consent, genomic privacy, incidental findings, and issues of equity will also have to be addressed with great care, however. It is concluded that a holistic and cohesive national NBS system could significantly enhance the management of rare diseases, the health of children and promote precision medicine programs in India.

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