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Health System Barriers to Thalassemia Care in Cambodia: A Regional Comparison

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ABSTRACT

Thalassemia is a genetic disease that raises public health concerns around the world, particularly in the Southeast Asia region. However, this disease remains a significant but under-recognized challenge in Cambodia. This study aims to explore the institutional gaps that shape the treatment of thalassemia in Cambodia. This study focuses on the structural factors that contribute to the concerning state of the disease in Cambodia and compares them with regional peers to identify system disparities. This literature review analyzes the influence of health infrastructure, finance, and policy on the approach to healthcare for thalassemia patients and discusses its position in the general state of the health care system. The search databases used in this literature review were PubMed, Google Scholar, WHO Publications, official Ministry of Health and non-governmental organizations reports. A total of 36 articles were included in this research paper. The findings suggest that Cambodia has limited health infrastructure and policy contributes to delayed detection and inconsistent treatment. In addition, primary care has particularly weak platforms and feeble financing mechanisms. Moreover, policy and governance gaps play a crucial role in reducing the sustainability of services. The results in this study may be beneficial in understanding the disease status in Cambodia. The purpose of this study is engaging in academic discussion of the healthcare theoretical framework and reasoning behind its worrying conditions.

INTRODUCTION

Overview of Thalassemia

Thalassemia is a group of inherited blood disorders characterized by abnormal hemoglobin production [1]. It is caused by genetic mutations affecting globin protein synthesis. Thalassemia follows an autosomal recessive pattern [8]. Individuals with one defective gene are asymptomatic heterozygous carriers, whereas individuals with mutations affecting multiple genes may develop moderate to severe transfusion-dependent form (homozygous) [8]. It can manifest primarily as α- or β-thalassemia, depending on which globin gene is affected. There are four α-globin genes on chromosome 16 and two β-globin genes on chromosome 11 [8]. The severity of α-thalassemia depends on the number of gene deletions (from one to four), while β-thalassemia is characterized by reduced (β^+) to no (β^0) β-globin production [1, 8].

Presentation and Diagnosis

Thalassemia may cause patients to present symptoms like jaundice, hepatosplenomegaly, skeletal deformities, growth retardation, and chronic anemia [2, 3, 4]. Patients may also run risk of heart failure and cognitive impairment [6].

Thalassemia is diagnosed through blood tests and genetic studies [2, 3, 4]. The iron studies test is a set of laboratory measurements designed to assess the amount of iron in the body, how it is stored, and how well it is transported [5]. Complete blood count and iron studies are used to help rule out iron deficiency anemia. To confirm diagnosis, molecular genetic testing is used to identify specific gene mutations or deletions, while high-performance liquid chromatography (HPLC) is used to measure hemoglobin types. Genetic Hb disorders complicate the assessment of iron deficiency because typical biomarkers (e.g. ferritin, sTfR) are confounded [19].

Prognosis

Pathophysiological mechanisms lead to complications of iron overload involving numerous organs. These complications significantly affect patient quality of life, and survival is dependent on health care [8]. Moreover, the necessity of lifelong treatment imposes significant financial burdens on patients and healthcare systems. The prognosis of transfusion-dependent thalassemia has substantially improved patient life expectancy due to standardized transfusion protocols and iron monitoring programs. However, complications from iron overload remain the leading cause of mortality [3, 8].

Treatments and Preventions

Patients with this blood condition are recommended to receive regular treatments, such as blood transfusions, iron chelation therapy, folic acid supplementation, and splenectomy [1]. Blood transfusions help patients alleviate anemia by providing healthy red blood cells with normal hemoglobin levels. For iron chelation therapy, medications, such as deferoxamine, deferiprone, and deferasirox, help prevent iron accumulation in the vital organs of patients undergoing chronic blood transfusions [1]. Folic acid supplementation improves energy levels and reduces symptoms of fatigue. Splenectomy is the removal of the enlarged spleen on severe thalassemia patients due to chronic hemolysis and ineffective erythropoiesis. While emerging treatments, such as gene therapy and fetal hemoglobin induction, show promising results, the only known curative treatment for this disease is bone marrow transplantation, also known as hematopoietic stem cell transplantation [1]. This treatment involves replacing a patient's defective bone marrow with healthy donor stem cells capable of normal hemoglobin production.

According to WHO-TIF guidelines, thalassemia prevention focuses on reducing the incidence of severe birth cases [7, 3]. A comprehensive prevention strategy involves genetic counseling, premarital screening, and structured clinical management. As outlined by the World Health Organization (WHO) and the Thalassemia International Federation (TIF), disease management should integrate early screening, regular clinical follow-up, patient education, and psychosocial support to improve survival and quality of life [7,

3]. Strong governance and policy framework, such as the establishment of national registries and integrating screening into the primary care system, are needed to further strengthen the prevention effort [3].

Trends in Disease Burden

Thalassemia poses a significant public health concern, notably in regions such as the Mediterranean, Middle East, South Asia, and Southeast Asia, where carrier frequencies may range from 5% to over 30% [8]. Thalassemia prevalence in Europe and North America, however, is substantially lower. In most Western European countries and the United States, β-thalassemia major occurs in 1 in 100,000 live births. Carrier frequencies in Northern Europe are generally below 2% [1, 8]. In high-income countries such as the United States, national newborn screening programs, centralized hemoglobinopathy registries, routine molecular diagnostics, and comprehensive transfusion services have significantly improved survival outcomes [8]. Multidisciplinary thalassemia centers also provide constant monitoring for complications [1]. In contrast, Southeast Asia bears a disproportionately high burden due to substantial carrier pools for α-thalassaemia, β-thalassaemia, and Hb E, as well as limited healthcare infrastructure [9]. In addition, lower- to middle-income countries such as Thailand, Laos, and Vietnam have implemented national prevention and control programs that involve premarital and prenatal screening, which have significantly reduced the incidence of severe thalassemia at birth [10]. However, mortality and morbidity still remain high in much of the region due to uneven access to diagnosis and treatment, gaps in public awareness, and variability in national health priorities [11].

The prevalence of thalassemia in Cambodia is among the highest in Southeast Asia and has exhibited a concerning situation with the highest disease burden in 2021, due to lower to middle-level health expenditure (Health Expenditure per Capita, current USD) [12]. Cambodia's total health expenditure represents 1.4% of Gross Domestic Product (GDP), reflecting limited fiscal space for specialized chronic disease management [7]. This calls for the development of national policies for the prevention and control of thalassemia. According to a 2019 report, the estimated hemoglobinopathy carriers are approximately 40% (ranging from 30% to 50%) in a general population of 16 million, and 2240 annual births of β-thalassemia major [13]. There is an overall prevalence of 40.9% and 39.6% in β- and α-thalassemia respectively. The Ministry of Health (MoH) developed national guidelines for the clinical management of patients with thalassemia in 2011. However, public health strategies and prevention are minimal, reflecting broader systematic challenges in resource allocation and laboratory capacity [7]. This often results in late diagnosis, typically when symptoms become severe, and routine screening is rare. Despite the high prevalence of the region, Cambodia has an under-researched setting, namely preliminary studies on the prevalence of hemoglobinopathies. Moreover, there is limited epidemiological data and the disease burden is evidently higher than in any other Southeast Asian country [9]. Consequently, this raises important questions about the responsiveness of the healthcare system. The author hypothesized that Cambodia's health infrastructure has directly or indirectly affected access to quality thalassemia treatment compared to Southeast Asian countries. This research paper aims to explore the influence of Cambodia's health infrastructure, finance, and policy on the thalassemia care program and its position within the overall state of the healthcare system.

METHODS

PRISMA guidelines were used to report the results presented in *Table 1*, which consists of peer-reviewed articles from PubMed, and additional gray literature from national health reports, WHO and World Bank databases, and non-governmental organizations (NGOs).

The search databases used in this paper were PubMed, Web of Science, Scopus, Cochrane Library, Google Scholar, and scientific journals (MDPI Journal, British Journal of Haematology, Hemoglobin, BMC Public Health). Additional grey literature sources from WHO publications, national health ministries (Cambodia, Vietnam, Malaysia, Thailand), and recognized NGOs websites (Thalassemia International Federation (TIF), World Bank Health System, Integrated Quality Laboratory Services). All search results went through a screening process that aimed to identify relevant literature on thalassemia such as diagnosis, treatments, and prevalence. The potential studies were independently reviewed to be included in this literature review. The inclusion criteria were: (1) studies were published in English; (2) peer-reviewed studies and regional comparative publications containing qualitative data relevant to Cambodia and Southeast Asia; (3) studies on thalassemia or hemoglobinopathies, (4) health system and clinical guidelines; (5) regional and national reports; (5) health system and economic aspects across Southeast Asia. The search strategy was set for the 1990-2025 timeline, "Cambodia", "Thalassemia" OR "Hemoglobinopathies", "prevalence", “epidemiology” OR “molecular epidemiology”, "treatment" OR “clinical management", “screening”, “guidelines”, “Cambodia” OR “Vietnam” OR “Thailand”, AND "Southeast Asia". The exclusion criteria were non-medical sources, opinion pieces without data, studies outside the scope, and duplicates. Extracted data were summarized with identifiable patterns including authors’ names, publication year, country, sample size, healthcare practices and policies, prevalence rate, screening methods, treatment and data gaps across some countries in Southeast Asia. A total of 730 articles were identified in this research topic. But approximately 671 were duplicates, out of scope of the topic, not in English, and technical. The study selection and review process are illustrated in *Figure 1***.**

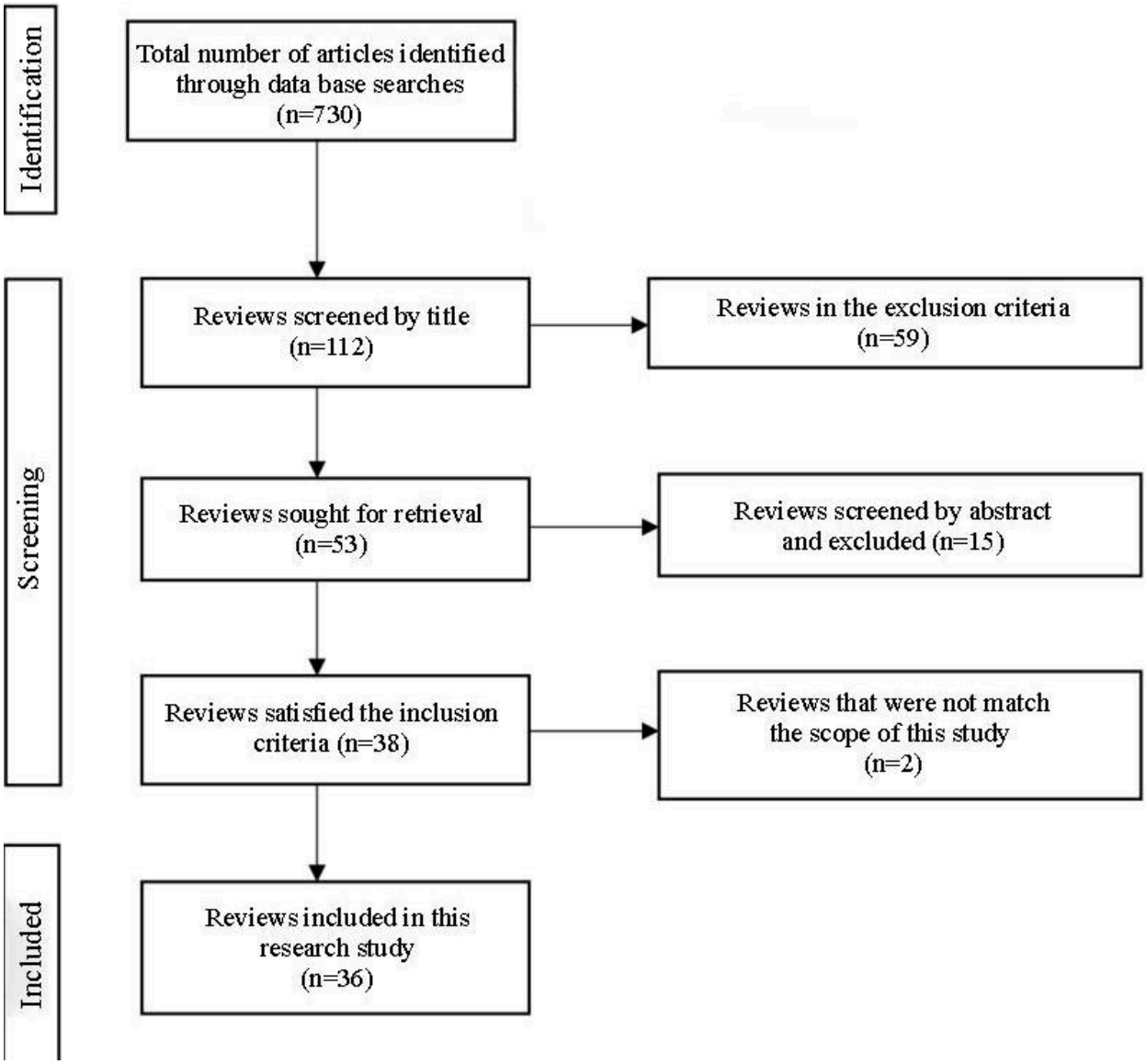

Figure 1. Flow diagram of literature review

RESULTS

Given that effective clinical management requires early diagnosis, continuous transfusion access, iron chelation therapy, and screening programs, the national health system plays a crucial role in determining patient outcomes.

Cambodia's Health Infrastructure and Thalassemia Care

Cambodia has undergone post-conflict reforms in rebuilding service delivery since the 1990s [7]. The public sector is organized in a tiered system that includes national hospitals, provincial hospitals, referral hospitals, and health centers under the responsibility of the MoH. A 2010 study shows rapid growth of the private sector with 57% of people first going to private providers and only about 29% sought care in the public sector [7]. Primary services are underutilized, and the regulation of the private sector is limited. The lack of regulatory oversight leads to variability in service quality and fragmented referral pathways, which is problematic for chronic conditions that require coordinated care such as thalassemia [14, 16, 22]. Moreover, a recent analysis shows varying capacity and inefficiency in terms of resource allocation, distance, and low service quality [14]. There are also shortages of qualified professionals and an uneven distribution of services throughout the country [15]. Government health funding is at 1.4% of GDP and is heavily dependent on foreign donors financing about 50% of the total fund [7]. Out-of-pocket payments account for 61% of total health expenditure [7]. One of the main aims of Cambodia's health reform is to achieve universal health coverage by comprising demand- based financing mechanisms, such as the Health Equity Fund for the poor, voucher schemes, voluntary community-based or private health insurance, and the National Social Security Fund for formal sector workers. However, their coverage remains limited and has direct implications for access, resulting in delay or forgoing of needed service. In rural areas especially, issues such as geographic disparity, socio-economic inequities and limited health literacy further complicate the perception of quality and utilization problems [16]. Cambodia's health spending remains oriented to infectious disease control, maternal and primary care [17]. Laboratory projects and genetic services are dependent on project funding from donors and government budgets, rather than domestic recurring budgets. The Cambodian program reports describe strong needs for clinician and counseling training, which implies service gaps in the workforce [18].

Multiple studies have shown that Cambodia has a high prevalence of thalassemia carriers. The underlying burden is concerning; however, the full clinical burden remains uncertain. The current carrier rate of gene mutation is 62.7% for α- and β-thalassemia combined in 1631 individuals [20]. A study suggests that the burden of severe thalassemia might be lower in the Siem Reap region [21]. In a study of 260 children, 51.5% were found to have some variant of the hemoglobinopathies gene. Most abnormalities were heterozygous and may have mild disease, but the risk of severe disease remains if both parents are carriers. In addition, a national micronutrient and hemoglobin disorder survey revealed a very high burden of hemoglobinopathies among children and women of reproductive age [22]. This study suggests that hemoglobinopathies contribute strongly to Cambodia's anemia burden, around 26.7% of children and 28.4% of women are common carriers of heterozygous Hb E. It was concluded that thalassemia carrier states are a major, under-recognized public health problem, and that prevention strategies, such as screening and genetic counseling, should be prioritized alongside nutritional programs.

The diagnosis process utilizes the Capillary Minicap Analyzer by Hb electrophoresis, while genotyping is not available [13]. Treatments such as packed red blood cell (PRC) blood transfusions are available at referral hospitals. However, oral iron chelators such as deferiprone and deferasirox are not included on the essential medicine list and are only available through private pharmaceutical companies. Splenectomy is carried out in some hospitals in Phnom Penh and the provinces. The distribution of transfusion centers and specialist thalassemia clinics is highly limited. There are also no notable policies for prevention

control, genetic counseling, or the National Registry of patients. Public awareness of thalassemia is low; however, health-education interventions have shown promising results [23]. A quasi-experimental study was conducted in Phnom Penh, Cambodia, with 241 adults (aged 18-40) from four surrounding communities divided into intervention and control groups. The intervention group (124) received structured health education, while the control group (117) were given the same information after the study. The pre and post-tests measured knowledge, attitudes, and willingness to be screened. Notably, after receiving structured health education on severe thalassemia, the scores of the intervention group jumped and 84.8% of the group expressed willingness to have blood screening, compared to 55.6% in the control group. This study concluded that community-based educational intervention significantly improved both intent and actual screening uptake and can be a feasible first step for thalassemia prevention in Cambodia [23].

Regional Comparison Overview

Table 1. Comparison of thalassemia-relevant indicators: Cambodia vs Vietnam

Indicator	Cambodia	Vietnam
Health system & UHC performance	Lower UHC index (58 out of 100); high out-of-pocket spending; system developing with external support.	Higher UHC index (68 out of 100) and broader insurance coverage; stronger public capacity.
Blood-transfusion infrastructure	PRCs are available at most provincial hospitals; the national blood system strengthened via external programs (new regional blood centers have been established).	National hematology centers and outpatient clinics; more mature blood services.
Availability of iron chelation	Oral chelators are limited to private channels; affordability is an issue.	Available in referral centers; growing access in local practices and economic burden.
Specialized services & monitoring	Limited but improving: monitoring and comprehensive care is concentrated at major hospitals.	Established referral centers and outpatient clinics providing more consistent monitoring and follow-up.
Affordability & financial protection	High out-of-pocket spending; substantial financial burden for lifelong treatment.	Greater insurance coverage reduces but does not eliminate financial burden.

Source: WHO and World Bank health system indicators; PubMed reports on thalassemia in Cambodia and Vietnam; national blood service assessments and program reports [24][13][25][26][27].

Countries across the Southeast Asia region have adopted distinct approaches in the management of thalassemia. For example, Thailand has implemented a comprehensive national screening and subsidy program, which involves integrating population-based carrier screening and parental diagnosis into primary healthcare and the Universal Health Coverage (UHC) system. This ensures equal access and sustainability while emphasizing prevention of severe cases [28, 29]. Moreover, as shown in *Table 1*, Vietnam is concentrating on advanced molecular testing, treatment services, and specialized care in tertiary and regional hospitals. These hospital-based networks and diagnostic integration allow for high-quality care and capacity-building, despite coverage remaining urban-centered [30, 31]. In contrast, Malaysia has integrated a national thalassemia effort by establishing a multi-component program that pairs screening with genetic counseling, public education, prenatal diagnosis services, and a National Thalassemia Registry [32, 33, 34]. Recent MoH guidelines and clinical practices further reinforce the integration of genetic counseling into screening venues and antenatal care pathways [34]. There are key programs such as population screening with on-site or referral genetic counseling, antenatal screening and prenatal diagnosis for at-risk couples, and registry monitoring service planning and burden estimates [32, 33, 34]. However, Indonesia faces substantial practical barriers to scalable newborn and carrier screening due to inconsistent screening coverage and referral pathways. Evidence showed that decentralized healthcare places service decision-making at district levels, resulting in heterogeneity in capacity, staff training, and resource allocation [35, 36].

DISCUSSION

This study has demonstrated that Cambodia's limited health care and policy support directly hinder thalassemia treatment. Despite having one of the highest prevalence in Southeast Asia, Cambodia has substantial barriers in thalassemia diagnosis and long-term treatment; having a particularly weak primary care platforms and financing mechanisms. Low epidemiology data prevent efficient targeting of molecular tests, making it harder for policymakers to prioritize planning and delay investment. The results are open to many interpretations, however there are recognizable patterns in maldistribution, service delivery, intermittent supplies, late diagnosis, and high financial burden. The absence of genotyping capacity and reliance on Hb electrophoresis limit diagnostic precision. Additionally, given that 57% of patients seek care in the private sector, unregulated healthcare providers may lead to inconsistent treatment.

According to these findings, government health expenditure at 1.4% GDP and out-of-pocket payments accounting for 61% of total health expenditure demonstrate structural financial constraints that limit sustainable thalassemia service. Due to limited public financing and competing health priorities, critical supports such as facility upgrades, laboratory capacity, and essential medicines procurement are restricted. Moreover, insufficient numbers of trained diagnostic professionals lower the quality of thalassemia care and service. Especially in rural areas, where infrastructure and clinic capacity are weaker with even lower quality care and fewer points of service. This increases the patient's burden and reduces timely access.

There are no notable prevention control programs available. However, there are few screening programs, but they are often organized in community-based outreach programs and many cases go undetected. This shows that the screening and detection system are still limited and uncertain. Based on the results, the national financial schemes proved to be inadequate with restricted social protection for low-income patients. Direct and indirect costs such as transport, user fees, low income, and high out-of-pocket payment further discourage patients from clinical follow-up. These financial barriers serve as an incentive to avoid care and discontinue treatment. Furthermore, policy and governance gaps play a crucial role in reducing the sustainability of services in thalassemia care. Evidence shows limited strategic planning initiative and its dependence on project-based donor funding significantly reduced the scaling of service. While there are national guidelines in place, implementation is still unsteady.

Advanced healthcare settings, such as those in the United States, are favorable for transfusion-dependent patients, resulting in a higher life expectancy. Whereas in Cambodia, limited infrastructure and financing constrain the implementation of comparable system [8, 1, 13]. These epidemiological disparities justify the difference in resource allocations.

Together, these factors create intersecting barriers explaining the overall poorer outcomes observed in Cambodia relative to regional peers. The findings clearly suggest a health system fragility; creating barriers in accessibility, affordability, availability, and acceptability. The cause of thalassemia high disease burden is rooted in complex building blocks of the health system rather than an isolated program failure itself. As a result, Cambodia's limitations create specific disadvantages compared to countries in the region with stronger infrastructure and primary care. However, there are emerging studies being done to assist in the establishment of prevention and control programs [20]. From a general point of view, Cambodia should focus on improving its central infrastructure framework and strengthening health policies and financing. Nevertheless, particularly in Siem Reap, it has been argued that thalassemia does not necessarily represent a major health burden [21].

Regional Context

In a regional context, the challenges of Cambodia stand out tremendously. Neighboring countries such as Vietnam, Malaysia, and Thailand have stronger policy frameworks, a more developed health system, and wider screening programs that help in earlier diagnosis and treatment. Data briefly mentioned in *Table 1* shows the differences in national health financing, governance, and infrastructure. These insights highlight how these factors directly shape patients' outcomes. However, to improve equitable care for individuals with thalassemia, it is crucial to strengthen Cambodia's health system through policy implementation, resource allocation, and workforce planning.

Recommendations for Thalassemia Needs

With respect to thalassemia treatment, it is clear that Cambodia is in urgent need for a national registry, policy on thalassemia prevention and control, new low-cost detection methods, screening programs, support for blood transfusion centers, and the availability of iron chelators on the list of essential

medicines [13]. Moreover, laboratory facilities are also needed and would be cost-effective for detecting thalassemia among Cambodian couples [23]. Nevertheless, we should not overlook the importance of the epidemiological data on thalassemia for more effective planning of prevention and control program [20].

Limitations

There are a number of limitations that should be addressed in this literature review. Firstly, only data from a few selected Southeast Asian countries were included in the review, therefore only a few types of thalassemia prevalence rates were specifically mentioned. There is missing data in economic burden studies, for example the direct estimate costing in house-hold level and system-level. While there were some prevalence cases reported in various papers, this paper does not specifically cover socioeconomic status and up-to-date quantitative data analysis in national prevalence or screening coverage. This study targeted urban and rural areas in Cambodia and Southeast Asia, and did not include ethnic stratification because the majority of studies included in this review population-based studies only. Clinical cohort studies tracking treatment adherence, clinical outcome, and long-term mortality and morbidity were not included due to limited studies with robust data.

Future Directions

For future reference, policy and evaluation studies should be performed exclusively to analyze governance barriers to sustained program financing. Moreover, intervention from the MoH in performance assessment could reinforce positive intervention and service acceptability. Surveillance of prevalence by region should also be done to strengthen routine data tracking in both private and public sectors as well as regional and remote areas. Future studies should aim to generate actionable insights to improve thalassemia control.

CONCLUSION

This is the first literature review that has evaluated the effects of the health system on thalassemia treatment in Cambodia. Most of the results follow a literature review framework and are accessible through online databases, such as PubMed and NGOs websites. Thalassemia is a genetic disease that poses a public health concern globally, especially in the Southeast Asia region. Among those countries, Cambodia has a significantly higher disease burden and prevalence than its neighbors. These gaps in the literature review led this research paper to explore and discuss the responsiveness of the Cambodian health system and its effects on thalassemia management. The findings suggest that Cambodia's limited health infrastructure and policy significantly hinder access to thalassemia treatment and diagnosis; which warrants the high disease burden of thalassemia. Patients might have restricted access to continuous care mainly due to financial barriers and rural inequities. Moreover, delayed detection and irregular treatment impose a substantial burden and display insufficiency in the overall healthcare system. Evidently, Cambodia's limitations are more apparent compared to other Southeast Asian countries with stronger programs and better health systems.

This research has a scarcity of comprehensive data and limited availability of prevalence estimates for Cambodia, Vietnam, and Malaysia. Many selected studies relied on small scale sample or regional comparative studies' data, resulting in imprecise estimates. I believe that more studies are needed to produce accurate data and evaluate the effectiveness of existing interventions.

This study is for educational purposes; hoping to shine some light on the basis of thalassemia concerning status in Cambodia. The reports in this study may be beneficial for anyone looking to understand the disease status in Cambodia and the reasoning behind its worrying conditions.

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