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ORIGINAL RESEARCH

Impacts and Economic Burden of Pompe Disease on Patients and Families in Thailand: A Mixed Method Study

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Purpose: This study aimed to explore the impacts and economic burden experienced by patients and families affected by Pompe disease in Thailand.

Patients and Methods: A mixed-methods analysis was employed. To estimate the direct medical cost, databases and/or medical records of the seven rare disease (RD) centers in Thailand from 2010 to 2021 were reviewed. Structured interviews were also conducted to examine direct non-medical and indirect costs. The economic burden was presented in 2024 US dollars (USD) value (1 USD = 35.29 THB). In-depth interviews were conducted with four patients and two caregivers to explore the impacts of this disease.

Results: Frequently reported symptoms included fatigue, muscle weakness, and difficulty breathing during sleep. These symptoms had significant and profound impacts on patients' functioning, family and social roles, self-esteem, emotion, and financial status. Frequent visits to the RD centers, along with the referral process, were reported as a substantial burden to the patients and families. The mean annual direct medical cost per patient, excluding the cost of enzyme replacement therapy, ranged between 2,505 and 14,042 USD from the provider's perspective and 1,484 USD from the patient's perspective. Direct non-medical costs were highly significant, with the annual cost of informal care of 1,878–1,992 USD per patient. Around 43% of the patients reported requiring informal care. On average, each patient required 2.6 ± 3.5 hours of informal care per day.

Conclusion: Our findings revealed substantial impacts of Pompe disease on individuals' physical, social, emotional, and functional capacities as a result of its symptoms. Coordinated care, where patients can be treated by clinicians at local hospitals who operate in close liaison with specialists from the RD centers, is warranted. Psychosocial, welfare, and transportation supports are clearly justified to alleviate the burden and improve the quality of life of the patients.

Keywords: Pompe disease, economic, burden, cost, IOPD, LOPD

Introduction

Pompe disease, also known as glycogen storage disease type II or acid maltase deficiency, is a rare genetic disorder caused by a deficiency of the lysosomal enzyme acid alpha-glucosidase (GAA). This deficiency leads to the accumulation of glycogen in the tissues, especially cardiac, skeletal, and respiratory muscle.[1–3] Based on age of onset, organ

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involvement, and rate of progression, Pompe disease is classified into two main types: infantile-onset Pompe disease (IOPD), and late-onset Pompe disease (LOPD).[4,5]

IOPD presents during the first year of life with symptoms of hypertrophic cardiomyopathy, hypotonia, generalized muscle weakness, and hepatomegaly.[4] Cardiac involvement is also considered a prominent presentation of IOPD.[5,6] Without specific treatment, classic IOPD patients usually die from cardiorespiratory failure within the first year of life.[4,5] Conversely, LOPD typically presents in childhood or adulthood with proximal weakness beginning in the thigh (pelvic-girdle) muscles and slowly spreading to other skeletal muscles, with axial and diaphragmatic predominance leading to ventilatory insufficiency and generalized weakness by the second or third decade, and many patients become wheelchair- or ventilator-dependent.[4,7] A recent systematic review revealed that Pompe disease leads to profound negative impacts on humanistic outcomes (e.g., health-related quality of life, activities of daily living, and caregiver quality of life).[8] Nevertheless, the previous review was limited to studies published up to 2016, with the vast majority conducted in Western countries. Only two studies originated from Asia (specifically Japan[9] and Turkey[10]). Given the evolution of healthcare systems, advancements in treatment options, and changing patient expectations over time, earlier findings may no longer accurately represent current patient experiences and perceptions. Moreover, quality of life is a complex and multidimensional construct that is deeply shaped by cultural and contextual influences. As such, existing studies may not sufficiently capture this variability, thereby reducing the generalizability and applicability of their findings to other populations, particularly those in Asia.

Given that Pompe disease is a progressive disorder that affects many organ systems, patients will require lifelong and regular assessment by a multidisciplinary team, including neurologists, pulmonologists, cardiologists, geneticists, physiotherapists, occupational therapists, speech therapists, and dieticians. Nowadays, enzyme replacement therapy (ERT) with recombinant human acid alpha-glucosidase (rhGAA), marketed as myozyme®, is considered the only specific treatment for patients with Pompe disease.[11] However, ERT is very costly and time consuming as it requires intravenous infusion every two weeks.

While clinical manifestations, pathophysiology, genetic characteristics of Pompe disease, as well as efficacy of ERT, are frequently studied, there is a paucity of literature on the impacts and economic burden that Pompe disease imposes on patients, families, and the healthcare system. Understanding these issues is critical in the development of suitable health service interventions, social support, and policies that fulfill the needs of these affected individuals. Also, it is useful for designing specific patient-reported outcome (PRO) measures for Pompe disease. Despite the scarcity of studies, a recent systematic review[12] indicated that Pompe disease imposed a significant economic burden on patients, families, the healthcare system, and society. Studies examining economic burden of Pompe disease in middle-income countries were even scarce.[13–15] Moreover, all studies[13,16–19] but two[14,15] examining the economic burden of Pompe disease were conducted over a decade ago. Due to the changes in medical service patterns, including medical technology over time, cost estimates from the previous studies may not accurately reflect the current economic burden, indicating the need to conduct further studies.

Thailand is a middle-income country, located in the Southeast Asia region. Since 2002, Universal Health Coverage (UHC) has been implemented so that Thai citizens can access essential health services without financial risk. As of 2022, alglucosidase alfa for Pompe disease is not on the reimbursement list due to its high cost. As part of a larger study aimed to provide evidence to support policy decision making on benefits package development for patients with Pompe disease under the Thai UHC Scheme, this study examined the impacts and economic burden faced by providers, patients, and families affected by Pompe disease in Thailand.

Materials and Methods

Our study employed a mixed method analysis, incorporating both qualitative and quantitative data collection and analysis techniques. Research participants were patients and their caregivers who were followed up at 7 rare disease (RD) centers throughout Thailand, namely, Ramathibodi Hospital, Siriraj Hospital, King Chulalongkorn Memorial Hospital, Phramongkutklao Hospital, Thammasat University Hospital, Srinagarind Hospital, and Queen Sirikit National Institute of Child Health, during 1 January 2011 to 1 July 2021.

Estimating Economic Burden

Economic burden was estimated in terms of annual cost per patient from both patient and healthcare provider perspectives. Cost components included direct medical costs (eg, cost of medical services such as pharmaceutical, diagnosis, laboratory, medical device, etc.), direct non-medical costs (ie, traveling, meal, accommodation, informal care, and time loss of caregivers), and indirect cost (ie, time loss of patients). All costs were reported in 2024 USD value, and presented for the 1st, 2nd, and 3rd year after diagnosis of Pompe disease.

Direct Medical Costs

Data on service utilization and healthcare service costs excluding ERT of patients with Pompe disease at the RD centers, except Queen Sirikit National Institute of Child Health, were used to estimate annual direct medical costs from healthcare provider perspective. Data retrieval process was conducted during January 2022 to March 2022 after the approval of ethical review boards. Charges for all medical services were converted to costs using cost-to-charge ratio of 1.63.[20]

Direct Non-Medical Costs and Indirect Costs

Direct non-medical costs and indirect costs were derived from the interview of the participants who met the following criteria: 1) having a confirmed diagnosis of Pompe disease or having a family member diagnosed with Pompe disease; 2) aged ≥ 18 years; 3) have ever received or have family members who received treatment for Pompe disease at 1 of the 7 RD centers during 2011 to 2021; 4) being able to provide information on treatment-related expenses of the patients; and 5) providing a written informed consent. Of note, the diagnosis of Pompe disease was confirmed by biochemical (leukocyte enzyme) analysis plus molecular (mutation) testing. All diagnosed cases were symptomatic at presentation; none were identified through newborn screening or asymptomatic siblings of the affected individuals.

For direct non-medical costs, the unit costs of meals, transportation, and accommodation were based on actual expenses derived from the interview. On the other hand, the number of resources used per year (ie, number of visits, number of admissions, and length of hospitalization) was determined based on the review of hospital databases. All out-of-pocket expenses for treatments related to Pompe disease that were incurred outside hospitals were also asked to estimate direct medical costs from the patient's perspective. Human capital approach was employed to estimate informal care cost and indirect cost of the patient. Details of the analyses were as follows:[20]

Annual cost of informal care = Number of hours lost due to caregiving per day * productivity cost per hour * number of days lost due to caregiving per week * 52 weeks per year

Productivity cost per week = Gross National Income (GNI) per capita in 2021/52 weeks per year

Productivity cost per hour = Productivity cost per week/48 hours per week

Annual indirect cost = Percentage of time loss of the patient due to the disease per year * GNI per capita in 2021

To calculate the informal care and indirect cost, the GNI per capita of Thailand in 2021 (ie, 6,988 USD or 232,176 Thai baht (THB)) was adopted.[21] Notably, the indirect cost was only calculated for patients whose ages were between 18 and 60 years old.

Impacts of Pompe Disease

The impacts of Pompe disease were examined from the in-depth-interview of the participants who met the following criteria: 1) having the diagnosis of Pompe disease or having a family caregiver of patients diagnosed with Pompe disease; 2) patients aged ≥7 years or caregivers aged ≥18 years; 3) have ever received or have family members who received treatment for Pompe disease at 1 of the 7 RD centers during 2011 to 2021; and 4) providing a written informed consent. Exclusion criteria were having cognitive impairment or declining to provide written informed consent.

Data Collection

Interviews were conducted via online platforms, ie, Line, Zoom, or Webex application. Eligible participants were recruited from Genetic Lysosomal Storage Disorder (LSD) Foundation and the RD centers. Based on the medical record review by geneticists, nurses from the RD centers contacted the potential participants by telephone. They provided details

about the study and requested permission for the research team to make further contact. Upon participants' agreement, the researcher team proceeded to contact potential participants by phone, explained the study, invited them to participate in the study, and arranged the date and mode of interview based on the participant's convenience. Recruitment advertisement was also distributed via the Genetic LSD Foundation. Individuals who were interested in participating in the study could contact the research team via phone or email.

All potential participants received a participant information sheet and consent form via postal mail before the interview. Participants were allowed to discuss and asked questions to the researcher before they agreed to participate. Written informed consent and/or assent, which included approval for the publication of anonymized data, was obtained from all patients, parents, or legal guardians before the interview. The interviews were conducted between December 2021 and January 2022 after ethical approval was granted. Each in-depth interview section lasted approximately 30 minutes and was audio-recorded with participants' consent.

A structured questionnaire was employed to collect the following data: direct medical costs, direct non-medical costs, and indirect costs. During the interview, information on travel costs, meal costs, and time loss were gathered. To explore the burden of Pompe disease, interviews using semi-structured questionnaires were conducted. During the interview, participants were asked to describe their treatment experiences and the impacts of Pompe disease on several aspects such as physical health, psycho-social well-being, and financial situations.

This study was approved by the Central Research Ethics Committee (CREC) (COA-CREC078/2021), and Queen Sirikit Institute for Child Health (REC. 145/2564). The approval was endorsed by the institutional review boards of all participating hospitals.

Data Analysis

All costs were reported in terms of mean, standard deviation (SD), median, and interquartile range (IQR). The total economic burden was derived from the summation of direct medical, direct non-medical, and indirect costs and was presented as annual costs per patient. All costs were calculated from the patient and healthcare provider perspectives without the cost of ERT. Costs were estimated in the 2021 THB value and, later, converted to the value in 2024 USD using the consumer price index and exchange rate (1 USD = 35.29 THB).[22,23]

For qualitative data, audio-recording data were transcribed verbatim for thematic analysis. Transcripts were read and re-read multiple times by 3 researchers (SY, MT, CL) to identify codes and potential themes through color coding of the transcripts. Themes were reviewed and refined with the codes.

Results

Of the 14 patients identified from the database and/or medical record review, seven patients were alive during the study period (IOPD n = 3; LOPD n = 4). One patient could not be reached, while six patients were invited to participate in the study. Finally, telephone interviews were conducted among individuals with Pompe disease (n = 3) and the family caregivers (n = 3). Characteristics of the patients are displayed in Table 1. Patients' ages ranged from 2 to 64 years. For patients with LOPD (n = 4), the age at diagnosis varied between 14 to 60 years. One patient with IOPD received a prenatal diagnosis as his elder siblings were affected by Pompe disease. All six patients were currently receiving ERT.

Impacts of Pompe Disease

All patients experienced muscle weakness, particularly in their legs, as well as fatigue. Three LOPD patients and one IOPD reported experiencing difficulty breathing during sleep. As a result, four of them required ventilatory support during sleep. Importantly, these symptoms led to several impacts across various domains, including physical, role function, family, social, work/school, emotional, and financial, as shown in Figure 1.

Regarding physical impacts, muscle weakness substantially limited walking and mobility ability as well as the ability to climb stairs, and rise from the sitting or squatting position, resulting in difficulty in performing daily activities and traveling. Additionally, these symptoms constrained role functioning, including the ability to fulfill responsibilities as a spouse and parent. One LOPD patient got divorced from her husband due to the symptoms of the disease, which caused

Table 1 General Characteristics of Patients

Code	Current age of Patients as of 2022 (Year)	Gender	Age at Diagnosis (Years)	Phenotypes	Ability for Self-Care	Employment/ School Status	Caregiver	Age at Onset of Disability
P1*	6	F	At birth	IOPD	Yes, but a bit slow	Attending school	Parent	4
P2*	2	M	At birth	IOPD	NA	NA	Parent	1
P3	41	F	35	LOPD	Yes	No	Parent	32
P4*	64	M	60	LOPD	Yes	Retired	Son/spouse	60
P5	24	M	14	LOPD	Yes	No	Parent	14
P6	31	F	20	LOPD	Yes	No	Parent	30

Notes: * interview was conducted on family caregivers.
Abbreviation: NA, Not applicable.

fatigue and rendered her unable to engage in outside activities with her husband. Sorrowfully, one LOPD patient reported that she was unable to play with her child or provide care for her child due to her muscle weakness and fatigue.

Pompe disease not only affects patients but also their family members. All patients depend heavily on family support, and half of the caregivers (n = 3) reported having to adjust their daily activities or even quit their occupations to provide care for patients. All 2 IOPD patients were accompanied by their parents from the time of diagnosis through the initiation of treatment. Likewise, two out of 3 LOPD patients were accompanied by family members since the initiation of treatment. Subsequently, many caregivers reported that they were unable to join any social events as they needed to take care of the patients. Similarly, the patients themselves reported social deprivation due to muscle weakness.

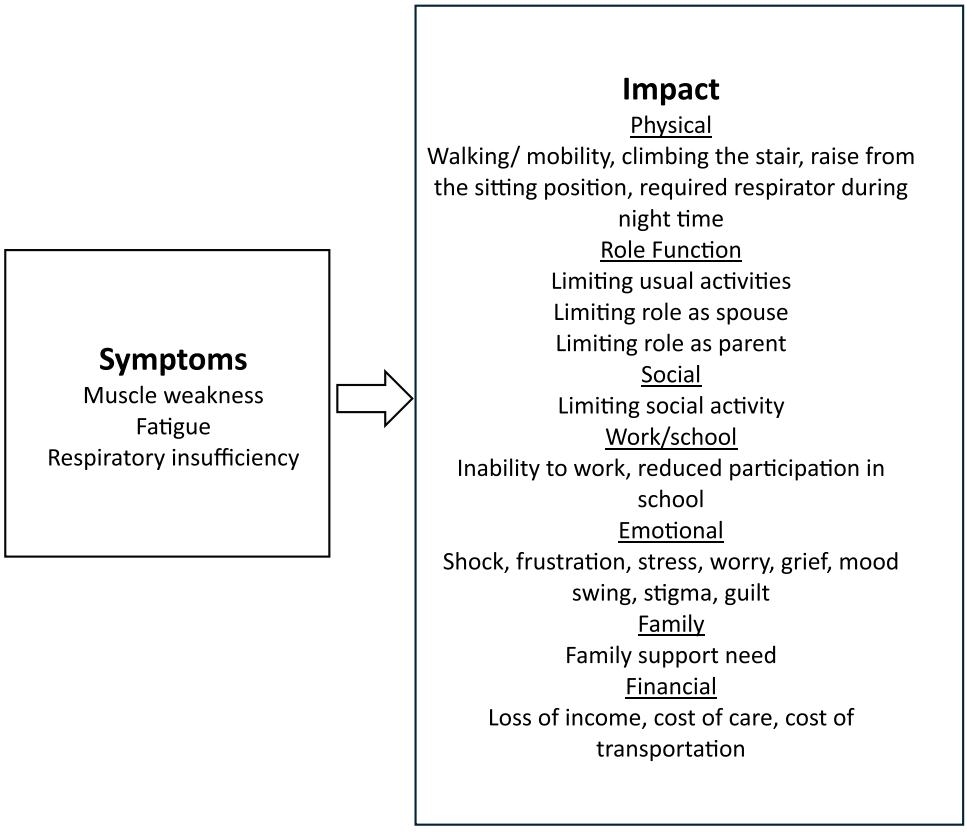

Figure 1 Symptoms and impacts of Pompe disease.

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With regard to emotional impact, Pompe disease imposed a significant psychological burden on both patients and their families. After receiving a diagnosis of Pompe disease, patients or family caregivers felt stressed, anxious, frustrated, and shocked. One LOPD patient, who is a single parent, expressed concerns about the future in the context of how her child would be if something happened to her. The other two young adults with LOPD expressed concerns about their future well-being if their parents, who were their caregivers, passed away. Similarly, caregivers of IOPD patients expressed concerns about the conditions of their children in the future. One LOPD patient reported having mood swings, irritability, and upset due to her stress over her chronic illness. One LOPD adult patient, who is a single parent, expressed the feeling of guilt that she and her daughter had to rely on her parents' income. One LOPD patient experienced social stigma as she had to register for a disabled identification card to get direct access to medical treatment at the RD center without the need for a referral. One IOPD patient regularly misses school for doctor appointments.

In terms of financial effect, all three working-age LOPD patients were currently unemployed due to muscle weakness and fatigue. Among them, two individuals who used to work had to quit their jobs due to the progression of the disease. To take care of her child who was affected with IOPD, one mother had to resign from her job, resulting in the reduction of family income. One family had to take a loan to cover the expenses of providing care for the patient. Furthermore, treatments for Pompe disease imposed a significant economic burden on the patients and families as patients required lifelong and regular visits to the RD center for symptom monitoring and ERT infusion. This resulted in substantial transportation costs and time costs/burdens. In addition, the patients also had to pay for many treatment-related equipment such as Bilevel positive airway pressure (BiPAP), immunosuppressant, wheelchair, etc.

Treatment Experiences

Frequent visits to RD centers for ERT treatment and monitoring were reported by the patients or families. Due to high transportation costs, one patient decided to stop ERT despite receiving it at no cost (ie, donation). Three patients reported being referred to the RD centers, which located in province differences from where they resided. The process of referral from their primary health care center to the RD centers is time-consuming and burdensome. Several patients expressed their preferences to receive treatment at local hospitals under the collaboration between geneticists at the RD centers and the local doctors.

Economic Burden of Pompe Disease

As shown in Table 2, the mean ± SD of annual direct medical costs excluding ERT per patient from the healthcare provider perspective at the 1st, 2nd, and 3rd year+ after diagnosis were estimated at 14,042 ± 5,514 USD, 3,681 ± 1,241

Table 2 Annual Costs Associated with Pompe Disease from Healthcare Provider and Patient Perspectives (Value in 2024 USD/Person)

	Year 1 (USD)*				Year 2 (USD)*				Year 3+ (USD)*			
	Mean	**SD**	**Median**	**IQR**	**Mean**	**SD**	**Median**	**IQR**	**Mean**	**SD**	**Median**	**IQR**
***Healthcare provider perspective* (n = *10*)**												
Direct medical costs												
OPD	453	255	415	283	554	409	527	543	358	344	194	415
IPD	13,589	16,409	7,543	15,452	3,127	3,665	1,087	1,096	2,148	2,362	2,148	418
Total costs (healthcare provider perspective)	**14,042**	**5,514**	**–**	**–**	**3,681**	**1,241**	**–**	**–**	**2,505**	**804**	**–**	**–**
***Patient perspective* (n = *6*)**												
Direct medical costs	Mean = 1,484 SD = 1,462 Median = 1,291 IQR = 2,061											

(*Continued*)

Table 2 (Continued).

		Year 1 (USD)*				Year 2 (USD)*				Year 3+ (USD)*			
		Mean	**SD**	**Median**	**IQR**	**Mean**	**SD**	**Median**	**IQR**	**Mean**	**SD**	**Median**	**IQR**
Direct non-medical costs													
OPD	Travel	663	459	473	663	985	816	852	568	1,184	1,211	947	1,752
	Food	108	75	77	108	160	133	139	92	192	197	154	285
	Accommodation	31	43	–	78	68	103	–	104	21	28	–	52
IPD	Travel	358	282	504	252	773	143	773	101	756	166	756	118
	Food	81	64	115	57	176	32	176	23	172	38	172	27
	Accommodation	155	122	218	109	334	62	334	44	326	72	326	51
Informal care costs Caretaker		1,878	3,008	148	2,840	1,954	2,954	386	2,874	1,992	3,008	341	3,170
Formal care costs		Mean = 305 SD = 7,468											
Total direct non-medical costs		**3,580**	**3,012**	**2,649**	**3,728**	**4,754**	**3,106**	**4,471**	**3,829**	**4,954**	**3,247**	**4,800**	**4,320**
Indirect costs		Mean = 3,546 SD = 3,884 Median = 3,546 IQR = 7,092											
Total costs (patient perspective)		**8,610**	**2,672**	**8,796**	**3,747**	**9,784**	**2,635**	**9,620**	**2,807**	**9,983**	**2,146**	**10,457**	**2,426**

Note: *1 USD = 35.29 THB.

USD, and 2,505 ± 804 USD, respectively. From the patients' perspective, the mean ± SD of total costs per patient were estimated at 8,610 ± 2,672 USD, 9,784 ± 2,635 USD, and 9,983 ± 2,146 THB at the 1st, 2nd, and 3rd year+ after diagnosis, respectively. It should be noted that the costs incurred by patients ranged from 38% of the total costs in the first year to 73% and 80% of the total costs during the second and third years of diagnosis, respectively. From the patients' perspective, direct non-medical costs accounted for 42%–50% of the total cost, while indirect costs accounted for 36%–41% of the total cost. It was found that all of the IOPD cases required informal care, while 25% of the LOPD cases required informal care. On average, each patient required 2.6 ± 3.5 hours of informal care per day. Average annual informal care ranged between 1,878 and 1,992 USD per patient, representing around 40–52% of total direct non-medical costs.

Discussion

Our study is the first to focus specifically on the impacts and economic burden of Pompe disease in Thailand. Our study revealed that muscle weakness (especially in the legs and knees) and fatigue were the most frequent symptoms described by the patients, followed by difficulty breathing while sleeping. These findings were in line with other previous studies.[24,25] Additionally, these symptoms substantially affected walking ability, reducing the ability to travel and independence. They also interfered with patients' roles as spouses or parents and limited their abilities to fully participate in paid labor. Many family caregivers reported the need to modify their daily activities, including having to quit from jobs to provide care for patients. This was in agreement with the earlier studies,[16,26] which reported that provision of informal care resulted in a significant burden to the caregivers of patients with Pompe disease.

As found in the previous studies,[8,27,28] living with Pompe disease caused profound emotional impacts on patients and families. Our study found that patients experienced negative emotions, including worry or anxiety, stress, mood swings, grief, being afraid of uncertainties for future life, and a sense of guilt throughout the journey of the disease starting from the onset of the disease, the diagnosis, and day-to-day challenges of living with the condition. Therefore, attempts should be made to improve access to professional psychological support, increase awareness of the emotional challenges of

living with Pompe disease among healthcare professionals, and frequently assess mental health and wellbeing[27] to improve the mental health of patients and families living with Pompe disease.

Among the three out of six patients, who were referred to RC centers in different provinces, the median travel distance was 369 kilometers, with an estimated median travel time of 4 hours 45 minutes. For patients with Pompe disease, who experienced fatigue, frequent visits to RD centers, which are usually located far away from home along with the referral process to the RD centers led to a substantial burden for the patients and caregivers and could result into non-adherence for medical appointments. Therefore, the development of shared care arrangements and protocols where patients can be treated with clinicians at local hospitals who operate in close liaison with the Pompe disease specialist from the RD center should be developed to lessen the burden and improve treatment adherence.[29] Furthermore, coordinated care in which care is provided as a one-stop service at one setting, where patients can access a range of services during one hospital visit[30] should be developed and delivered to patients with Pompe disease to reduce the time and financial burden of frequent visits to the hospital.

Consistent with previous studies,[12–16,19] Pompe disease imposes a significant economic burden on patients, families, health systems, and society. Our study indicated that the total annual economic burden ranged between 12,488 USD and 22,652 USD per patient. It was found that direct medical cost, direct non-medical cost, and indirect cost represented 32%–69%, 16%–40%, and 16%–28% of the total costs, respectively. It should be noted that our estimates of total annual cost per patient were substantially higher than that of the recent estimates in Shanghai, China, in 2019 which found that the mean (SD) total economic burden of patients with four lysosomal storage diseases (LSD) (ie, Pompe, Fabry, and Mucopolysaccharidoses) not receiving ERT was 58,352 CNY (2019 value) or 17,414 USD (2024 value).[14] Of this amount, 60.5%, 37.5%, and 2% were attributable to direct medical costs, indirect costs, and direct non-medical costs, respectively.[14] This difference could be due to many factors, such as differences in patient characteristics as well as healthcare services provided to the patients in different settings, and unit cost. While the previous study[14] reported that the mean outpatient visit for each patient was 0.5 per person per year and the mean hospitalization days were 3.5 days, the mean number of annual OPD visits per patient in our study was about 8–9 visits, while the mean number of hospitalization days was approximately 17–30 days. It should be noted that all patients in our study have been receiving ERT, while in the previous study,[14] none of the patients received ERT. Therefore, a higher number of outpatient visits and lengths of stay were observed in our study. Also, it should be noted that the previous study[14] relied on self-reporting to estimate all types of costs, while our study employed medical records and/or database review to estimate direct medical costs (provider perspective), numbers of hospital visits, and length of stay. Compared to another study conducted in a middle-income country,[15] which reported annual direct non-medical costs per person ranging from 1,997 USD (2024) for adult PD patient to 11,268 USD (2024) for pediatric PD patient, our findings—showing the median direct non-medical cost of 4,754 USD—appeared similar but slightly lower, given that we estimated the costs from 2 IOPD and 4 LOPD patients.

Our findings indicated that direct medical costs excluded cost of ERT represented 15%–17% of the total cost from the patients' perspective. This is probably because almost all essential medical treatments were already in the benefits package under the UHC. Nevertheless, the cost incurred by patients in terms of direct non-medical costs was still high, ranging from 3,580 USD to 4,954 USD. This could endanger the ability of households to maintain their standard of living.

Consistent with the previous study,[16] our study found that informal care represented the largest part of the direct non-medical costs. In line with that of the previous study,[16] which found that around three-fourths of patients with Pompe disease received informal care with an average of 18 hours per week, 43% of patients in our study required informal care with an average of 2.6 ± 3.5 hours per day or approximately 18 hours per week.

While transportation costs accounted for 28.5%–39.2% of direct non-medical costs in our study, they accounted for only 2.8% of the direct non-medical costs in the previous studies.[16] Consistent with the findings from our interview, transportation to RD centers, which are located in major cities, led to a substantial economic burden for the patients, especially when several patients or caregivers did not participate in paid labor work. Therefore, financial aid to support transportation and meal costs related to hospital visits is highly warranted.

Concerning productivity loss, while a previous study[16] found that 40% of LOPD patients quit their job due to disease and that 20% had to reduce work hours, we found that all working LOPD patients were unable to participate in paid-labor work, while 50% of caregivers of IOPD patients had to quit the job resulted in the annual productivity loss of approximately 3,546 USD per patient. Therefore, welfare support for unemployed caregivers should be considered to alleviate such economic burden on the family.

Given the limited evidence on the impact of Pompe disease in the middle-income countries, our study contributes to the growing body of literature by providing additional real-world data on economic impact of Pompe disease from Thailand. However, we acknowledge that economic burden is influenced not only by national income level but also by contextual factors such as healthcare system organization and insurance coverage. These variations may constrain the applicability of our findings to other country settings. Although our study does not contribute to novel findings regarding clinical symptoms beyond those documented in prior research, it enhances understanding of the challenges related to health service delivery encountered by patients with Pompe disease in Thailand. Specifically, we highlight issues related to health care access, such as referral process to RD centers as well as the high travel costs and physical burden associated with accessing care. These findings underscore the need to improve the organization and accessibility of care pathways for Pompe disease within the country. This may offer valuable guidance for improving care delivery models in similar contexts.

There were some limitations in this study. First, due to its rarity, only 6 patients or caregivers participated in the interviews. Direct medical costs were also estimated from only 10 patients. Due to the small sample size, uncertainty around the cost estimates existed. Nevertheless, it should be noted that this represented almost all patients identified from the RD centers throughout the country. Although there might be a chance of missing information from Pompe patients who did not receive treatment at RD centers. However, the chance is quite small as almost all patients with rare diseases were referred to an RD center. Secondly, symptoms reported relied exclusively on self-reported health data. While deemed appropriate to address the experiences and burden of individual patients, the inclusion of clinical information from medical record review might further provide useful information. Lastly, it should be noted that the cost reported here might be underestimated as direct medical costs were based on actual care received, not the standard of care patients should receive, and the cost of premature mortality was not included in the analysis. In addition, the cost of ERT was not included in this study. Despite these limitations, this study represents the actual situation and the first attempt to explore treatment experience and the impact of Pompe disease as well as economic burden in Thailand, a middle-income country with UHC.

Conclusion

The study highlights substantial impacts faced by patients with Pompe disease and their caregivers in Thailand in various aspects, including physical health, role functioning, financial strain, and emotional well-being. These impacts were attributable to muscle weakness, fatigue, and respiratory insufficiency. Furthermore, Pompe disease poses a tremendous economic burden to society and patients. In terms of patients' experiences, patients reported the burden due to frequent visits to RD centers, along with the burdensome referral process to coordinate care. Co-ordinate care plan in which care is provided as a one-stop service at one setting, where patients can access a range of services during one hospital visit, and a shared care arrangement where patients can be treated with clinicians at local hospitals who operate in close liaison with the Pompe specialist from the RD centers. In addition, psychosocial, welfare and transportation support should be provided to lessen the burden and improve treatment adherence.

Abbreviations

CREC, Central Research Ethics Committee; ERT, Enzyme Replacement Therapy; GAA, Acid alpha-glucosidase; GNI, Gross National Income; IOPD, Infantile-Onset Pompe; IQR, Interquartile Range; LSD, Lysosomal Storage Disorder; LOPD, Late-Onset Pompe; rHGAA, Recombinant human acid alpha-glucosidase; THB, Thai Baht; UHC, Universal Health Coverage; USD, US Dollar.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical Approval and Consent to Participate

Informed consent/assent, which included publication of anonymized responses was obtained from all the participants/legally acceptable representatives before the interview. This study was approved by the Central Research Ethics Committee (CREC) (COA-CREC078/2021) and the Institutional Review Board of Queen Sirikit Institute for Child Health (REC 145/2564). The approval was endorsed by the institutional review boards of all participating hospitals.

Consent for Publication

Consent for publication was obtained from all patients and legally acceptable representatives.

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Author Contributions

All authors made a significant contribution to the work report, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas, took part in drafting, revising, or critically reviewing the article, gave final approval of the version to be published, agreed on the journal to which the article has been submitted, and agreed to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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