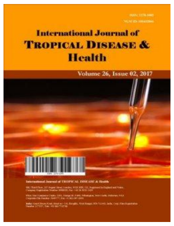

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Estimated Burden of Premature Death and Morbidity from Low Birth Weight Infants in Thailand

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Authors' contributions

This work was carried out in collaboration between all authors. Authors EEA and KB designed the study and wrote the protocol. Authors EEA and NM performed the statistical analysis and managed the analyses of the study. Authors EEA and KB interpreted the study's results. Author EEA managed the literature searches and wrote the first draft of the manuscript. Authors EEA and KB edited and revised the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Aims: The aim of this study was to estimate the burden of premature death and morbidity consequences due to infants born with a low birth weight (LBW).

Study Design: This study was a secondary data analysis and part of the study of the burden of diseases and injuries in the Thai population in 2014.

Methodology: Data were collected from national public health statistics, a vital registration database, and the morbidity burden from the LBW consequences was analysed according to the Global Burden of Disease (GBD) study 2000. The burden was estimated by the disability-adjusted life years (DALYs). DALYs are the combination of two components: years of life lost (YLL) and years lived with disability (YLD).

Results: Among the registered live births in 2014, 10.4% were born with a birth weight less than or equal to 2500 g accounting for 180,853 healthy lives lost. The number of deaths resulting from LBW was 2.4 per 1000 live births for both genders, and LBW was the leading cause of death in children under five years of age. Cerebral palsy and mild permanent disabilities were the highest attributed

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morbidity burden among children with a disability. The estimated burden of LBW attributed to 16.1% of the total DALYs loss from the burden of all causes among children under five years old.
Conclusion: LBW remains a burden in Thailand. Premature death was the primary driver for the total DALYs loss. The current study revealed the need to develop appropriate interventions for the developmental delay and children with a disability, as well as to conduct a long-term follow-up study concerning infants born with LBW.

Keywords: Low birth weight; premature death; years of life lost; year lived with disability; disability-adjusted life year; Thailand.

1. INTRODUCTION

Newborn weight is one of the indicators of the maternal health and nutrition status [1,2,3] and is important for infants' survival, growth and health risk [4,5,6]. Low birth weight (LBW) has been defined by the World Health Organisation (WHO) as weight at birth less than 2500 grams (g) or about 5.5 pounds [7]. Infants born with a LBW are at a higher risk of dying, especially in their first year than infants with a normal birth weight [8]. While trying to achieve one of the targets of a Sustainable Development Goal (SDGs) [9] by reducing child mortality, significant reduction in the prevalence of LBW has made an important contribution.

Moreover, many related studies have documented that a LBW affects the infant's physical growth and intellectual development process. Although children with a LBW were reported to be free from severe disabilities during early childhood, other problems were observed including neurological development and growth sequelae that still persisted until young adulthood [10,11]. Children born with a LBW also risked developing a lower IQ and having cognitive disabilities, which negatively affected their performance at school and their job opportunities as adults [10,12,13]. Additionally, LBW infants who survive may have an increased risk of diseases in later life [14,15].

Globally, more than 20 million babies are born with a LBW each year, or approximately 16% of all live births. More than 95% of all LBW babies are born in developing countries [7]. However, a large variation exists in the prevalence of LBW across regions, especially in low and middle income countries. Asia has the highest LBW rate in the world at 18.3%, and this is especially highest in South-Central Asia at 27% [16].

The incidence of infants born with a LBW remains a public health problem in many countries including Thailand [8,17,18,19]. In the 1980s, the proportion of LBWs in total live births was about 12% in Thailand, but this declined throughout 1990-2000 (about 8-9%) with little annual variation [20]. The Multiple Indicator Cluster Survey (MICS) 2015-2016 reported that 9.4% of the live births within the last two years weighed below 2,500 g at birth [21].

According to the Global Burden of Disease (GBD) study 2004, LBW contributed to more than 44.3 million healthy lives lost globally [22]. As the developmental delays worsen in the early childhood period and continue throughout life, society, community, caregivers and parents should be equipped to accommodate disabled children's needs. [11]. Moreover, significant health and developmental impacts due to LBW can impose huge costs on society [23,24]. Estimating the burden of LBW by disability-adjusted life years (DALYs) is important for not only to implement appropriate developmental and educational programmes by identifying disability consequences, but also to consider intervention prioritisation and evaluation on the efficacy of the interventions to reduce the overall burden.

The objective of this study was to estimate the burden of LBW in Thailand in 2014 by combining the number of premature deaths and long-term consequences.

2. METHODOLOGY

2.1 Study Design

This study was a secondary data analysis, and part of the study of the problem of the burden of disease and injury estimation concerning the Thai population in 2014. The burden due to infants born with a LBW was estimated by means of DALYs, a health gap measured by combining the years of life lost (YLL) due to premature death and years lived with disability (YLD) due to specific nonfatal conditions. One DALY refers to one lost year of "healthy" life.

2.2 Data Sources and Disease Consequences

The information of the infants' weight at birth was collected from the Thailand Public Health Statistics 2014 report [25], as this was the most reliable and available data at the national level. The national civil registration system (vital registration system) was used to estimate the mortality burden. The coverage for the under-reported infant deaths was adjusted with the infant mortality rate (IMR) from the Population Change Survey (SPC) 2005-2006.

In this study, LBW was classified into (1) very low birth weight (VLBW, ≤ 1500g), and (2) LBW (1501-2500 g). Survivors among LBW infants was estimated based on VLBW or birth weight of 1501-2500 g according to the literature review [8, 17,18,19], with 80% and 98.3%, respectively. Among surviving infants, 25% of VLBW, and 5% of LBW (1501-2500g) had disability consequences, as defined by Shibuya and Murray's study [26], and five major disability conditions were considered according to the Global Burden of Disease (GBD) study 2000 [27].

The proportion of disability consequences among the total number of disabled infants was obtained from Shibuya and Murray's (1996) study [26] for epilepsy (4.2%), hearing loss (2.8%), and vision loss (4.8%). Mental retardation (intellectual disability) due to LBW was concluded from the overall estimates of mental retardation from the Burden of Disease and Injuries Thailand study 2014, with the distribution of mild (62%), moderate (22%), severe (11%) and profound (5%) levels. In addition, 60% of the total incidents of cerebral palsy (CP) cases (at 2.25 per 1000 live births) was attributed to LBW, which was similar to the findings of an Australian study [28]. Rather than these five major consequences, the rest of the disabled proportion of LBW infants was categorised as other mild permanent disabilities attributed by LBW. Standard reviews of local data sources were referred to and discussed with external experts to derive the best estimate of disabling sequelae due to LBW.

2.3 Data Analysis

The total number of DALYs was analysed based on the GBD study 2000 [27] by combining the following two components:

$$DALYs = YLL + YLD$$

A detailed description can be found in the study of Murray and Lopez (1996) [29]. YLL was calculated using:

$$YLL = \Sigma dx^{*}ex$$

Where ex is the expected life at age x based on the standard life expectancy and derived from the Coale and Demeny West Model 26 life table; dx represents the number of deaths at age x (number of deaths by LBW). YLD was calculated using:

$$YLD = I^{*}DW^{*}L$$

Where I is the number of incident cases in the reference period, DW represents the disability weight, and L is the average length of disability until remission or death measured in years.

Disability weight (DW) indicates the valuation of a health state, scale from zero (perfect health) to one (worst possible). The DW for all causes and consequences were referred from the Dutch Weight [30]. The burden estimation of mental disorders was used as a reference for the duration of the disability from the differing levels of mental retardation due to a LBW. Durations for the other sequelae were assumed to be less than the normal life expectancy at birth and were projected using the DisMod Programme [31] with twice the background mortality rate [32] without remission.

3. RESULTS AND DISCUSSION

3.1 Distribution of LBW among Live Births

In Thailand, 711,805 live births were registered in 2014. Among them, 74,345 newborns (10.4% of the total live births) were born with a birth weight less than or equal to 2500g with 9.6% being male and 11.4% being female live births. Among all LBW infants, there were 0.8% with a birth weight ≤ 1500 g and 9.7% with a birth weight 1501-2500 g (Table 1). According to the statistics, a higher proportion of LBW among live births was observed in mothers aged ≤15years (20.3%), 45-49 years (18.5%), and ≥50 years (22.2%) compared with other age groups. Among all LBW infants, 21.7% were born from adolescent mothers (aged < 20 years).

3.2 Healthy Life Loss from Premature Death Due to LBW

Death due to LBW attributed to more than 40% among all causes of deaths from perinatal conditions (International Classification of Diseases (ICD-10 code) P00-P96) [33] under one year with more than half among males and one third among females. The mortality rate due to LBW was 2.4 per 1000 live births in total with 3.4 among males (1,264 deaths) and 1.4 among females (473 deaths) in this analysis. YLLs due to premature death are presented in Table 2. In total 140,055 years were lost from premature death with a higher distribution among males (72.2%) than females (27.8%).

3.3 Healthy Life Lost Due to Morbidity Consequences from LBW

The number of infants for all disability outcomes due to LBW was 4,513 in total (2,166 males and 2,347 females). Overall, YLD due to LBW totalled 40,799 years. Nearly one half of the morbidity burden was attributed to mild permanent disabilities (48.5%) followed by cerebral palsy without an intellectual disability (25.9%). Severe hearing loss, moderate vision loss and mild intellectual disability contributed to nearly 6% of the total YLD, individually. Only 5% of the total YLD contributed to moderate, severe and profound intellectual disabilities (mental retardation) due to LBW. A higher morbidity burden was found among females than among males; thus, a relatively high incidence of LBW infants was observed in the female group. The estimated numbers of infants with a disability and YLD accounted for all disability sequelae of LBW (Table 3).

3.4 Distribution of DALYs Loss by LBW in the Total DALYs of under Five-year-old Children

The total DALYs due to infants born with LBW was 180,853 years accounting for 66.1% among males and 33.9% among females. YLLs due to LBW contributed to 77.4% of the total DALYs and the remaining 22.6% was attributed to YLDs. A higher DALYs attribution by LBW among under five-year-old children DALYs loss was found in males (19.4%) than in females (12.1%). Nearly 20% of the total YLL and 10.5% of the total YLD among infants under five years old was contributed to the LBW burden (Table 4).

Table 1. Distribution of infants with LBW by category

	Male		Female		Both	
	Number	% in total LBs	Number	% in total LBs	Number	% in total LBs
Total live births (LBs)	366,649	100.0	345,156	100.0	711,805	100.0
VLBW ≤ 1500g	2,924	0.8	2,765	0.8	5,689	0.8
LBW 1501-2500g	32,165	8.8	36,491	10.6	68,656	9.7
Total LBWs	35,089	9.6	39,256	11.4	74,345	10.4

VLBW: Very low birth weight; LBW: Low birth weight

Table 2. Premature death due to LBW, the proportion in all-cause of deaths from perinatal condition, and year life lost by gender

	Number of deaths		Mortality rate per 1,000 live births		% of LBW in all-cause of perinatal conditions	YLL
	LBW	All-cause of perinatal conditions *	LBW	All-cause of perinatal conditions		
Male	1,264	2,460	3.4	6.7	51.4	101,059
Female	473	1,509	1.4	4.4	31.3	38,996
Total	1,737	3,969	2.4	5.8	43.8	140,055

**Number of deaths from all-cause of perinatal conditions (ICD-10 code P00-P96) were referred from the Burden of Diseases and Injuries Thailand study 2014 [34]. YLL: Year life lost*

Table 3. Total number of newborns with disabilities and YLD counts due to LBW by sex

Sequelae	DW	Duration (Years)		Total number of cases		YLD		Total YLDs of both (% of the grand total)
		M	F	M	F	M	F	
Intellectual disability								
Mild	0.290	61.9	68.0	69	54	1,231	1,062	2,296 (5.6)
Moderate	0.430	49.9	54.8	24	19	514	444	958 (2.4)
Severe	0.820	43.9	48.2	12	9	432	372	804 (2.0)
Profound	0.760	30.7	33.7	5	4	123	106	229 (0.6)
Cerebral palsy (without intellectual disability)	0.170	59.9	69.0	453	508	4,611	5,955	10,566 (25.9)
Epilepsy	0.110	59.9	69.0	91	99	599	748	1,347 (3.3)
Severe hearing loss (congenital or early acquired)	0.230	59.9	69.0	78	84	1,074	1,340	2,414 (5.9)
Moderate vision loss	0.170	59.9	69.0	104	113	1,058	1,320	2,378 (5.8)
Others Mild permanent disability	0.110	59.9	69.0	1,330	1,457	8,760	11,049	19,809 (48.5)
Grand Total				2,166	2,347	18,403	22,396	40,799 (100)

DW: Disability weight; M: Male; F: Female; YLD: Year lived with disability

Table 4. YLD, YLL, and DALYs account for LBW and its contribution in under five-year-old children's total burden

	Total burden of all-causes in <five year olds* in years			Burden of LBW in years (% of the burden from LBW in the total burden of all-causes among < Five Year Olds)		
	YLL	**YLD**	**DALYs**	**YLL**	**YLD**	**DALYs**
Male	409,247	207,811	617,058	101,059 (24.7)	18,403 (8.9)	119,462 (19.4)
Female	327,481	180,858	508,339	38,996 (11.9)	22,396 (12.4)	61,391 (12.1)
Total	736,728	388,669	1,125,397	140,055 (19.0)	40,799 (10.5)	180,853 (16.1)

** Total burden of YLL, YLD and DALYs of under five-year-old children were referred from the Burden of Diseases and Injuries Thailand study 2014 [34].*
YLL: Year life lost; YLD: Year lived with disability; DALYs: Disability adjusted life years

In 2014, 10.4% of LBWs accounted for 180,853 years of DALYs lost. The total DALYs lost was due to a LBW in males that was nearly twice the amount when compared with that of in females. From the study's analysis, DALYs lost due to LBW contributed to about 16.1% of the total number in under five-year-old children and 11.1% in under 15-year-olds for males and females in 2014 [34]. Compared with 1999 when the LBW burden in both males and females under 15 years old were ranked first [35], in 2014, the LBW burden among females was ranked second whereas there was no change in the ranking for males. That decrease in the ranking of the burden among females might be due to the increased survival rate of infants with LBW in females (46.2% of the total deaths by LBW attributed to females in 1999 compared to only 27.2% in 2014).

From the aspect of the mortality burden, premature death was primarily driven to the overall DALYs loss due to LBW. More than 40% of the total number of deaths from all perinatal conditions (under ICD-10 code P00-P96) could be attributed to LBW. According to the Burden of Diseases and Injuries Thailand study in 2014, the infant mortality rate from all perinatal conditions (under ICD-10 code P00-P96) was 5.8 per 1000 live births, and it was higher than the national public health statistics report (2014) where the infant mortality rate was 3.3 per 1000 live births [25]. The study of Lumbiganon et al. mentioned that Thai perinatal and infant mortality rates obtained from official reports was lower when compared with other sources due to the failure to register as many people who did not recognise the importance of valid health statistics, and so failed to report the infant deaths when the birth had not yet been registered [36]. Different mortality rates from LBW by gender was observed in this study, and males were found to have a higher rate than females. Similarly, Stevenson et al. reported that males were more likely to die than females of those born with a LBW [37]. The mortality rate from LBW by geographical area was not examined separately in this analysis, but the Southern region of Thailand had the highest overall infant mortality rate than other regions according to the national public health statistics [25] and highest proportion of infants born with LBW among live births in the last two years according to the MICS (2015-2016) report [21]. This was due to the lowest coverage of maternal and child health (MCH) in that region compared with other regions although the overall coverage of MCH at the national level was more than 95% [38].

Regarding the morbidity burden, the nonfatal adverse health outcomes due to LBW concerning the short term (during hospitalisation) and long term were presented in many studies. However, the current estimation followed the GBD study 2000, and the estimation did not include the short-term burden during hospitalisation; such as, asphyxia, respiratory infections, necrotising enterocolitis, intraventricular haemorrhage, and moderate or severe bronchopulmonary dysplasia [17,18,19]. Additionally, Hintz et al.'s study on neurodevelopmental outcomes reported observable differences between males and females, but this was not consistently in favour of females [39]. Therefore, the authors considered the same proportion of the morbidity outcomes between males and females. Moreover, there has been different risks of morbidity and impaired growth depending on the categories of the birth weight [40]. As the proportion of the VLBW was less than 1% in the total number of live births, the burden of consequences was not analysed separately on the birth weight categories. Nonetheless, regarding the original source of the proportion of disability consequences, Shibuya and Murray estimated the proportion of disabilities for all infants with LBW based on the relative proportion of the total number of LBW cases for each birth weight category to obtain the total proportion of disabilities [26].

The disability outcomes may vary with the study's characteristics. According to the hypothesis of this current study, estimating disabilities; such as, hearing loss, vision loss, CP, epilepsy and intellectual disabilities comprised about 3%, 5%, 21.3%, 4.2% and 4.3% of the total number of children with disabilities, respectively. Yet, one Thai cohort study of an 18 to 24 months follow-up concerning growth and developmental outcomes among 30 infants with VLBW reported that 3.3% presented hearing abnormalities and 16.7% presented vision loss of all VLBW cases [19]. One reason for the differences in the proportion of disabilities between the two studies was that this study was hospital based and focused only on VLBW outcomes while the current study estimated the number of disabilities from the overall number of the LBW cases. An evidence-based review study of Cole reported that the disabilities outcomes varied, which depended on the birth weight with the proportion of disabilities. These are as follows: 7-17% of the ELBW infants and 7-10% of the VLBW infants had cerebral palsy, 12-50% had a neurologic disability, 5-21% were blind, and 8-11% were deaf [40]. Another study that predicted disabilities resulting from preterm births in Bangladesh indicated that 35.2% presented intellectual disabilities, 3.4% exhibited a hearing loss, and 7.9% presented vision defects [41]. Depending on the variation in the study designs, the sample characteristics: preterm (gestational age) or/and LBW, LBW categories and outcome measurements criteria, analysis and comparison of the results among studies was sometimes difficult.

Many related studies revealed that the risk and chance of adverse health outcomes were inversely related to not only birth weight, but also the gestational age at birth, and both of these factors were highly correlated with an interdependent risk to health [40,42]. Because of that reason, in recent years, many studies have preferred to use the gestational age as the major marker to measure the prematurity to predict adverse health outcomes [10,13,40,42]. Although birth weight is not a perfect measure as it might be disproportionately large or small for the gestational age, the current study used birth weight because almost all infants (98.9%) were weighed at birth [21], and this could avoid discrepancies when assessing the gestational age [12]. The Global Burden of Disease Report 2010 estimated that DALYs due to preterm birth (short gestational age) in East-Southeast Asia and the Pacific contributed to about 10% of the worldwide total burden [43].

Improving the maternal nutritional status, preventing risk factors during pregnancy, and reducing adolescent pregnancies would be a great benefit in reducing the number of infants born with LBW and preterm babies. A higher rate of LBWs among infants born from mothers aged <15 years and over 45 years old than other age groups suggested considering the quality and coverage of antenatal care services including early assessment of at-risk and high risk pregnancies to all target groups [44] while trying to achieve the third target of “six global nutrition targets for 2025” comprising a 30% reduction of LBW prevalence by 2025 according to the World Health Assembly [16] and to reduce child mortality. Moreover, building a good network of communication between medical personnel and LBW infants would be crucial for early detection and interventions, and provide appropriate care and better follow-up to reduce the negative health impact in childhood and later in adulthood [11,19]. Thus, special education and school programming interventions are required for children with a low IQ and impaired functions [11].

Some limitations occurred in the current study’s estimation; such as, uncertainty regarding the vital registration for the cause of death data, information gap of the population-based cohort study concerning neurodevelopmental consequences, and underestimated burden as the current results did not cover the short-term burden during hospitalisation and did not consider the determinants of a short gestational age from adverse health outcomes.

Even though the study had certain limitations, it would be helpful in establishing research and clinical service priorities, as well as be useful in providing information support on policy approaches to help children with developmental delays and disabilities.

4. CONCLUSION

LBW is the leading cause of burden among males and is ranked second among females under five years old. Premature death was found to be the key driver of the total DALYs due to LBW, and cerebral palsy (without an intellectual disability) and mild permanent disabilities contributed the most to the morbidity burden. From this study, clinicians and researchers are urged to address the healthcare needs for long-term morbidity from LBW and the gestational age as well. Moreover, this study encouraged the researchers to explore further investigations to identify the consequent burden of LBW according to preterm birth and/or intrauterine growth restriction, as well as to obtain more precise results for policymakers to consider. Early detection, screening and adequate curative healthcare alongside behavioural, social, and special educational interventions are needed to be implemented appropriately to reduce the burden. The information from this study would be helpful to develop and implement effective and appropriate maternal and child health policies and allocate resources in health systems.

CONSENT

It is not applicable.

ETHICAL APPROVAL

This study did not require ethical approval, as it was a secondary data analysis and literature review.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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