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Contents

Editorial

Use and Misuse of the *P*-Value

Alden Henderson, Chief Editor

Steven Goodman in his article entitled *Dirty Dozen: Twelve P-value Misconceptions* stated that "the *p*-value is probably the most common and the most misunderstood, misinterpreted, and occasionally miscalculated number in all biomedical research". Wasserman and a large group of statisticians went further and said that misuse of the *p*-value — a common test for judging the strength of scientific evidence — is contributing to the number of research findings that cannot be reproduced. They then took an unusual step of issuing principles to guide use of the *p*-value, which it says cannot determine whether a hypothesis is true or whether results are important.

The *p*-value is continuous value but epidemiologists often interpret it as statistically significant if it falls below 0.05 and statistically not significant if it is equal or greater than 0.05. Using these criteria, a *p*-value of 0.049 would be significant and a *p*-value of 0.051 would be not significant yet the absolute difference between the two *p*-values is only 0.002. The fault in this reasoning is that appropriate study design, sampling, bias, confounding, etc. are not considered when interpreting the *p*-value.

The "*p*" in *p*-value stands for probability and is a number between 0.0 and 1.0. The current use of *p*-values is to determine if a statistical significance exists and that the smaller the *p*-value, the more evidence you have to reject the null hypothesis. This was not what Dr. Fisher had in mind when he created the *p*-value. He chose a "value for which $p=0.05$, or 1 in 20" because "it was convenient to take this point as the limit for judging whether a deviation is to be considered significant or not. Deviations exceeding twice the standard deviation are thus formally regarded as significant." Two standard deviations include 95% of the values around the estimate. When a *p*-value approached or was below 0.05, he said more studies should be done to describe this association.

P-values are used to test hypothesis whereby H_0 is the null hypothesis and says both groups are same. H_a is the alternative hypothesis and says both groups are different. This is a simplified interpretation of *p*-value and uses a *p*-value of 0.05 to reject or fail to reject the null hypothesis. Using this interpretation yields statistically significant, though not scientifically sound, results between amount of money spent in science and suicides by hanging, $R^2=0.99$, $p=0.001$, with divorce rate and butter consumption, $R^2=0.96$, $p=0.001$, and with the number of letters in winning word in spelling bee and the number of people killed by spiders, $R^2=0.81$, $p=0.04$.

A more complicated interpretation of *p*-value considers type I and type II errors, statistical power, study design, sampling, confounding, bias, biological plausibility, etc., etc., etc. that would not report these spurious associations. Consequently, some of the *p*-values don't's are:

- Don't base your conclusions only on whether an association was "statistically significant" (i.e., $p<0.05$).

- Don't believe that an association exists just because it was statistically significant.

- Don't believe that an association is absent just because it was not statistically significant.

- Don't believe that your *p*-value gives the probability that chance alone produced the observed association or the probability that your test hypothesis is true.

- Don't conclude anything about scientific or practical importance based on statistical significance.

Some of the *p*-values dos are:

- Clearly express objectives of study.

- State whether analysis is exploratory or pre-planned.

- Put energy into careful planning, design, and execution of study.

- Be aware of size of difference between groups that are being compared.

- Understand the precision around an estimate.

- Consider related prior evidence.

Epidemiologists can also rely on the Bradford-Hill criteria for causality or MAGIC (Magnitude, Articulation, Generality, Interestingness and Credibility) to interpret *p*-values as well as confidence intervals.

In summary, epidemiological studies seek to understand the links between environment and health and provide support for evidence-based practice. Whether such links are causal can only be assessed with confidence after epidemiological noise of chance, bias and confounding are collectively considered. A $p > 0.05$ serves as a guide to further examine associations and Hill's criteria can assist in determining causation. One who is identifying association must consider chance, bias, confounders, and other supporting conditions when interpreting statistical tests. As Dr. Fisher stated when he developed *p*-values, a *p*-value close to 0.05 suggests an interesting association and that more studies should be conducted to describe this association. A single study is not sufficient to show this relationship.

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Application of Geographic Information Systems and Remote Sensing for Pesticide Exposure and Health Risk Assessment in Thailand

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Abstract

In Thailand, pesticide use has increased exponentially over the past 15 years causing critical public health concern. We used a geographic information system and applied a remote sensing method in an integrated manner on land use data to model the spatial patterns of pesticide exposure. We also used toxicological data to quantify the health effects in terms of disability-adjusted life years (DALYs) attributed to pesticide use in Thailand. We found that 56%of the total population (35,144,284 persons) had potential pesticide drift at their residences. Pesticide exposure was mostly due to glyphosate and paraquat applied to rice farms and atrazine applied to sugarcane farms, which were more widespread in the central and northeastern regions of the country. The total burden caused by pesticide use equated to 10,045 DALYs, of which more than half (52%) was due to use of paraquat. Regarding policy implications, all relevant sectors should work on reducing paraquat use in crop fields. Reduction of pesticide exposure should be placed as the top priority for making health-related pesticide management policies.

Keywords: pesticide, glyphosate, paraquat, remote sensing, GIS, Thailand

Introduction

Pesticides are commonly used to protect crops from pests and to increase agricultural productivity.[1] Pesticide use in Thailand has increased significantly over the past 10-20 years and the importation of pesticides has also shown a rising trend.[2] These rising trends are of public health concern as pesticide exposure can cause both short- and long-term adverse health consequences.[3,4] Apart from the farmers or

gardeners who apply pesticides, others living near agricultural fields which have been treated with pesticides are also at risk of exposure due to the 'pesticide drift' effect – the unintentional diffusion of pesticides and its negative effect on surrounding areas.

Remote sensing (RS) from satellite data is a useful tool for assessing pesticide exposure on a wide scale. A geographic information system (GIS) is also a commonly used tool that helps detect spatial dimensions of the determinants of interest through geo-referenced spatial databases. Evidence-based and transparent decision-making often requires spatial information to help stakeholders assess the issues of interest more comprehensively.[5] The examination of these variables in a GIS leads to a better understanding of how agricultural systems function and interact over space and time.

This study aims to quantify the magnitude and geographical distribution of disease burden in terms of disability-adjusted life years (DALYs) attributable to pesticide exposure through application of GIS and RS.[6]

Methods

We used a GIS and RS of land use data in an integrated manner to model the spatial patterns of pesticide exposure and applied an exposure-based approach based on toxicological data to quantify the human health effects in terms of DALYs attributed to pesticide use in Thailand during 2017. The 'Global Burden of Disease Risk Assessment Framework' was employed as a conceptual framework for this study (Figure 1). The framework highlighted two components: (i) exposure and effect size estimation, and (ii) health impact indicators assessment.[7]

Exposure and Effect Size Estimation

Exposure and effect size estimation was conducted through a GIS-based exposure model. The model describes interactions between pesticide drift distance and populations living near the crop fields. The estimation was divided into subcomponents as follows.

Pesticide-Use Data

Concerning pesticide selection, we selected the most frequently used pesticides in Thailand, namely, atrazine, glyphosate, paraquat and chlorpyrifos, based on the import quantity ranking.[8] Pesticide use data was published in the report from the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) between 2009 and 2014.[9,10] Noting that the FAO/WHO report did not include local pesticide use, we therefore assumed that the total pesticide use was twice the amount reported by the FAO/WHO. This assumption was supported by a prior study by Lamers et al.[11]
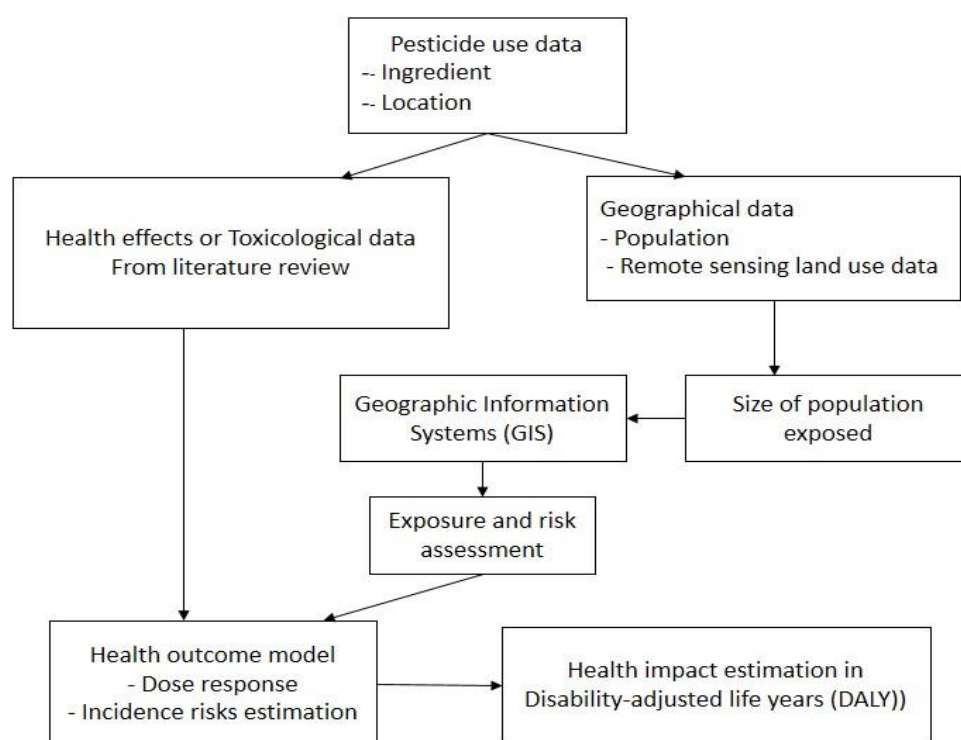

Figure 1. Conceptual framework of this study

Crops Data

We obtained the Moderate Resolution Imaging Spectroradiometer satellite crops data processed from the Geo-Informatics and Space Technology Development Agency in 2014. The analysis was limited to four types of crops: rice, cane, cassava and corn.[12] The ground data between January 2014 and December 2014, the most recent annual data available, were provided in the form of Geographical Positioning System reference data points.

Population-Weighted Pesticide Exposure Model

We modelled the population-weighted pesticide exposure in residential areas and crop fields using RS land use data and pesticide drift distance. We created a pesticide exposure map by applying the pesticide fate and the fraction loss in the environment and in crops.[13] Population data and the pesticide exposure model were combined together to estimate the population at risk of pesticide drift. The population data was obtained from the US grid population dataset, generated in 2000 by the Socioeconomic Data and Applications Center, Columbia University.[14] The population data were arranged in grids of size 30 arc-second (approximately 1 km at the equator).

We assumed no dynamic population movement around the residential areas because we had no information on farmers' activities at their place of residences or in the fields. Based on the literature review, any person living within a buffer distance of 110 meters from the centroid of a grid in which a pesticide was applied were assumed to be exposed to that pesticide (so-called, pesticide drift).[15,16] 110 meters was used to differentiate exposure from non-exposure based on previous studies by Fritz et al and Longley et al.[17,18]

Health Impact Estimation

We used risk and regulatory hazard-based toxicological effect indicators to estimate the pesticide health damage factors (HDFs) in terms of DALYs.[19] HDFs are the estimates of toxicological impacts that are attributable to the emission of pesticides into the environment over time and space.[19,20] The HDFs consisted of two factors: (i) the intake fraction: the fraction of a release taken by the population taking into account the fate of chemical exposure , and (ii) the effect factor: the incidence of chronic toxicological effect per unit intake by the population (in this study, focusing on cancers).[19] The equation for HDF is described as: HDFs = IF × β × D where IF is the intake fraction of the mass of pesticide (in kg)

released into the environment of a population grid, β is the dose-response slope factor (also known as ED50 – the median effective dose) and D is the burden of disease (DALYs/incidence). More than 99.9% of pesticides applied for pest control application remained contaminated in the residence and environment outside field application, and another study reported that application of indoor-released chemical in residences produced approximately 10^{-3} to 10^{-1} of intake.[13,21] We therefore assumed that fraction of 1% of pesticide residue in population-weight pesticide exposure entered the human.

Dose-Response Slope Factor (β or ED50)

Since pesticide dose-response slope factor for human toxicity is not available in most substances (including the four pesticides selected in this study), we therefore estimated this factor based on animal-based dose-response data. We then calculated the dose-response slope factor from a chronic lifetime dose of pesticide affecting 50% of the animal population (ED50). ED50 is the chronic dose-rate which would induce cancers in 50% of the tested animals at the end of the standard lifespan.[22] The formula for estimating ED50 is as follows.

$$\beta_i(ED50) = cfED50 \times \frac{NOEL_{i,s} \times cfNOEL \times BW \times LT \times 365 \text{ days}}{cf_s \times cf_{time}}$$

where cfED50 = 0.5 equating the human response level corresponding to ED50; NOEL = non-observed level effects (varying by species and substances), cfNOEL = 9 equating NOEL-to-ED50 extrapolation factor, BW = 70 kg/person denoting an average body weight; LT = 70 years denoting an average human lifetime; cf_s = correction factor for the interspecies difference; and cf_{time} represents difference in exposure time.

Burden of Disease Data (D)

The burden of disease was described as DALYs/incidence and categorized into two groups (cancerous versus non-cancerous effects). We relied on burden of disease data obtained from the International Health Policy Program, Thailand, in 2009 and reviewed the literature on selected health outcomes of both cancerous and non-cancerous effects.[23] The relevant diseases were mentioned in a study by Huijbregts et al in 2005.[24]

Model Analysis: Correlation between Estimated Pesticide Exposure and Patient Volume

We determined the association between pesticide exposure and the number of pesticide poisoning cases
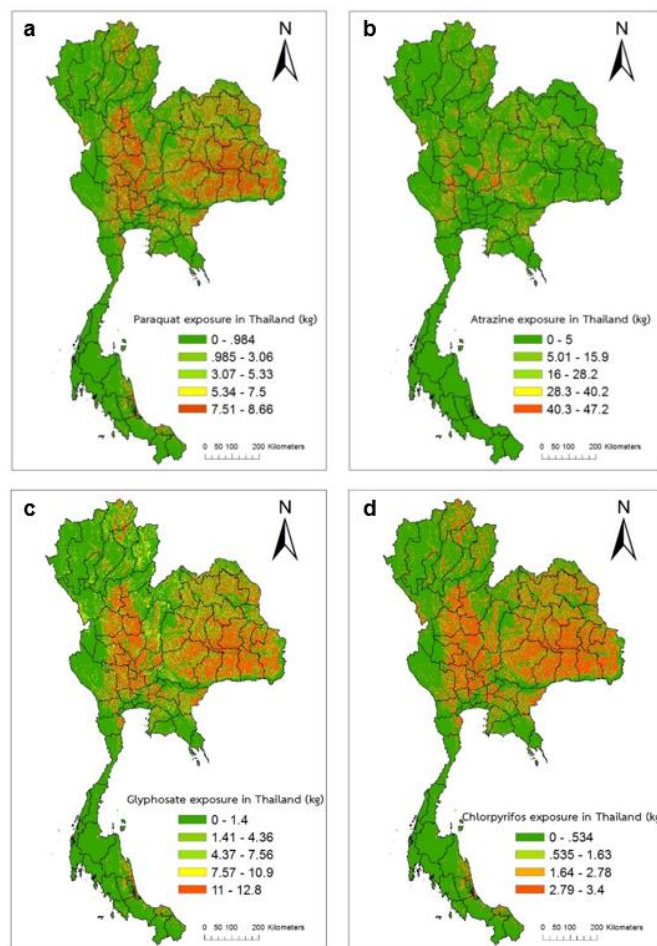
**Figure 2. Exposure distribution of four selected pesticides in Thailand:
paraquat (a); atrazine (b); glyphosate (c); chlorpyrifos (d)**

reported in 2017, defined as any patient with an ICD-10 code of T60 (toxic effect of pesticides) using Pearson's correlation coefficient (r-value). This data was obtained from the National Health Security Office and analysis was done at the provincial level. Statistical significance was set at 0.01 and all *p*-values were two-tailed.

Results

Exposure Model

Using the population grid centers, 56.0% of the total population (n=339,448 grids) or 35,144,284 persons had crops planted within 100 meters of their place of residence. The spatial distribution of exposure to the four selected pesticides is presented in Figure 2. The spatial pattern of exposure for all four pesticides were relatively similar. Residents in the central and northeastern region had a higher level of pesticide exposure than those in other regions. The maximal exposure per population grid level for atrazine, glyphosate, paraquat and chlorpyrifos was approximately 47.2, 12.8, 8.7 and 3.4 kg, respectively.

Table 1. Crop-specific level of exposure to different pesticides in Thailand, 2014

Crop	Area (rai[†])	Exposed area (rai[†]) (%)	Population exposed (persons)	Pesticide exposure (1,000 kg)			
				Paraquat	Atrazine	Glyphosate	Chlorpyrifos
Sugarcane	10,530,927	715,382.1 (6.8)	5,159,457	260.9	1,424.4	384.9	102.6
Cassava	8,975,865	469,121.7 (5.2)	3,290,604	171.1	934.1	252.4	67.3
Corn	7,292,697	461,681.3 (6.3)	1,943,210	168.4	919.2	178.0	66.2
Rice	76,927,017	3,438,122.1 (4.5)	24,751,014	1,254.2	-	1,849.8	493.3
Total	103,726,506	5,084,307.1 (4.9)	35,144,284	1,854.8	3,277.6	2,665.1	729.4

Note: Dose response relationship for paraquat, atrazine, glyphosate and chlorpyrifos equated 0.104, 0.037, 0.013 and 0.031, respectively (unit = life-time incidence/kg intake). †1 rai = 1,600 m²

Figure 3. Estimated yearly incidence of cancer by type of pesticide
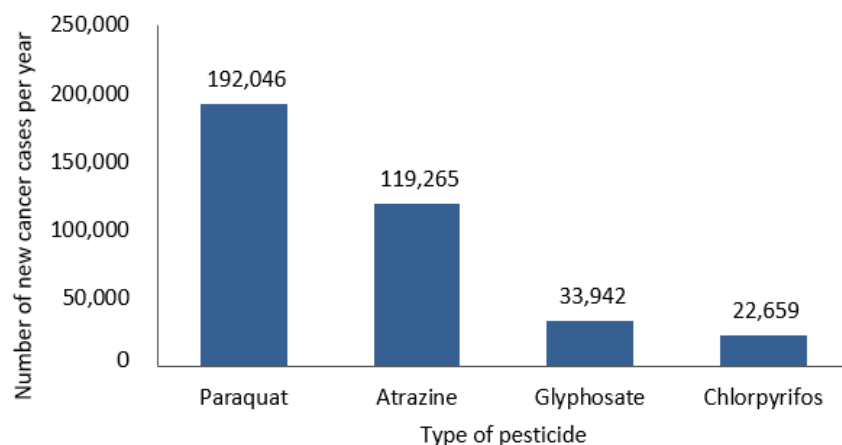
The level of exposure for various crops based on our model is summarized in Table 1. The majority of pesticide exposure was attributable to glyphosate and paraquat applied to rice farms and atrazine applied to sugarcane farms. Among the four pesticides, atrazine contributed the greatest level of exposure (3.3 million kg) followed by glyphosate (2.7 million kg).

Health Impact Estimation

Figure 3 shows the estimated yearly number of new cancer cases, including carcinoma, sarcoma, leukemia, lymphoma and myeloma, attributed to each of the four pesticides. Paraquat was responsible for the greatest number of cases (192,046) followed by atrazine (119,265) and glyphosate (33,942).

The incidence/100,000 population exposed by province is shown in Figure 4. A similar pattern for each pesticide was apparent; the Northern and Central regions had higher cancer incidences. Paraquat and atrazine accounted for the highest incidence rates in these regions compared to the other pesticides.

DALYs lost attributable to the four pesticides are demonstrated in Table 2. The total burden of disease
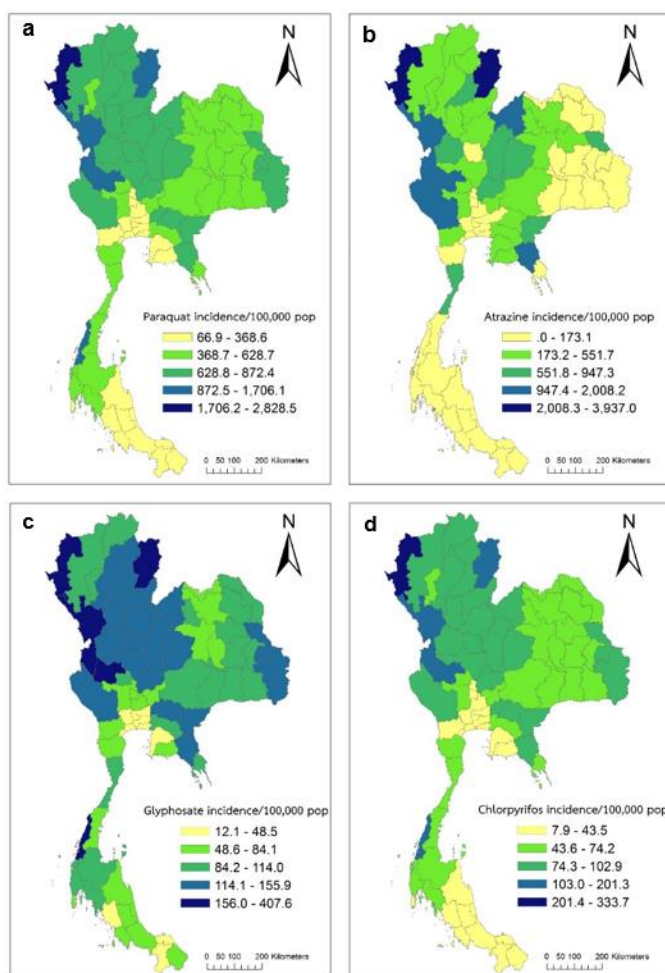

Figure 4. Incidence of relevant cancers per 100,000 population exposed by type of pesticide and province, Thailand, 2014: paraquat (a); atrazine (b); glyphosate (c); chlorpyrifos (d)

caused by all four pesticides accounted for 10,044.7 DALYs. Over half (51.6%) of the burden was due to paraquat exposure (5,185.2 DALYs).

Table 2 Estimated DALYs by type of pesticide.

Pesticide	DALYs (%)
Paraquat	5,185.2 (51.6)
Atrazine	3,220.2 (32.1)
Glyphosate	983.3 (9.8)
Chlorpyrifos	656.0 (6.5)
Total	10,044.7 (100.0)

Table 3 summarizes the correlations between pesticide exposure and pesticide toxicity. All correlations were highly significant, ranging from 0.421 to 0.691.

Discussion

This study presented the geographic health impact from exposure to four commonly used pesticides in Thailand. Results showed that about 56% of the Thai population (about 35 million people) were exposed to pesticides in 2017. About 70% of the exposed population live within 100 meters of rice farms treated with pesticides, of which glyphosate and paraquat were the main ones. Paraquat caused the greatest health impact (about 5,185 DALYs lost) among the four pesticides of interest.

The highest residual pesticide was atrazin with almost three million kilograms used, representing 38.4% of total atrazine imports in Thailand. The amount of residue depended, to a certain extent, on the amount of agricultural land used. Atrazine exposure per population grid in the US was about 2-7 times higher than in our study.[25] This difference might be due to application of pesticide aerial spraying in the US, a method which leads to a more effective distance of pesticide drift.

Another study in the US, which applied RS land use data with a buffer distance of 500 meters, reported a pesticide exposure level of about 0.05 kg/rai in agricultural areas.[26] This is approximately one sixth of the estimate reported in our study (0.3 kg/rai). This difference might be explained by differences in the definition of exposed group and in data source. To improve the accuracy of estimated pesticide exposure among the exposed group, the residential mobility should be taken into account. For example, Rull & Ritz simulated a random selection of population controls and applied a zonal exposure model on pesticide use reports in California which contained more in-depth details compared to our study.[26]

For health impact estimation, we selected health outcomes that can be associated with pesticide exposure based on burden of disease data in the Thai population in 2009. Long term pesticide exposure is linked with the development of many diseases, such as Parkinson's disease, respiratory diseases and depression.[27-29] Pesticide exposure is also found to be related to cancer risks, including non-Hodgkin's lymphoma and leukaemia.[30] With respect to previous studies, the use of an average disease-specific health is a good alternative given the lack of critical-effect information.[30,31] However, Huijbregts et al reported that as pesticide can cause multiple diseases, the estimation on health impact should use the disease with the highest DALY to account for the damage factor.[30]

From a methodological point of view, our study had both strengths and limitations. The application of GIS and RS on land use data at a national level meant that our results could partly represent the situation of pesticide use nationwide. Another advantage of using RS data was that it allowed the analysis to delve into the local scale without requiring

Table 3 Pearson's correlation analysis between pesticide exposure and pesticide toxicity

Pesticide	Admission diagnosis*	Pesticide exposure (10^6 kg)	Pesticide toxicity (total number)	Pearson correlation	P-value
Paraquat	T60.3	1.85	1,904	0.575	<0.001
	T60all		4,159	0.516	<0.001
Atrazine	T60.3	3.28	1,904	0.691	<0.001
	T60all		4,159	0.421	<0.001
Glyphosate	T60.3	2.65	1,904	0.550	<0.001
	T60all		4,159	0.506	<0.001
Chlorpyrifos	T60.0	0.73	1,904	0.575	<0.001
	T60all		4,159	0.516	<0.001

*Note: * based on the International Statistical Classification of Diseases and Related Health Problems version 10; T60.0 = organophosphate and carbamate insecticides, T60.3 = herbicides and fungicides, T60all = all types of pesticides.*

expensive or time-consuming activities. However, there remained some limitations in this study. First, this study relied on available pesticide application fate and the FAO/WHO report on food residues.[9,10] The actual pesticide used might be much more than that reported by the FAO/WHO.[32] Second, measurement errors may have occurred in terms of the resolution of RS land use data and intake assumption. The pesticide drift distance in this study was based on a local study and a recommendation from the US Environmental Protection Agency.[9,10,15,16] The pesticide drift might spread up from 500 meters to 1 kilometer, depending on the spraying tools. Pesticide spraying data along with its residue detection at field scale are essential to improve the estimation of pesticide application in Thailand. For intake fraction, Bennett et al reported that an intake fraction to exposed population of 10^{-5} to 10^{-7} could be applied as for every kilogram of pollutant released into the environment; but for pesticides with a longer environmental lifetime, the intake fraction might be higher.[33] In addition, we used population grid data from 2000.[34] Updated data is now available that includes demographic characteristics such as age and sex. Application of this new information may improve estimation, especially in vulnerable populations such as children and the elderly. Third, we did not apply a full-scale simulation of the pesticide fate and transport from farmers' pesticide spraying along the food-chain. A related pesticide assessment in aquatic ecosystems would improve the exposure model. Finally, we did not include various neighborhood crops or horticultural areas, such as fruit orchards, rubber tree plantations, and oil palms in this analysis. Some of these crops were reported to have pesticide residue.[35-37] Accounting for these neighborhood crops will help improve the accuracy of health burden estimation in the future.

Conclusions and Recommendations

Our results can be beneficial to researchers and local stakeholders to understand the situation of pesticide exposure and its ecological risks in Thailand. We clearly demonstrated that all four pesticides used in economic crops were associated with risk of cancers in the Thai population. The greatest health gain can thus be realized by reducing pesticide exposure, especially for paraquat and atrazine. This should be the top priority in all health-related agricultural and environmental management plans. In addition, our results can help policy makers design and prioritize pesticide reduction strategies pinpointing the pattern of pesticide use in certain areas based on the GIS and RS data. The database can also help researchers conduct further epidemiological studies related to other chronic diseases such as neurological disorders and birth defects at provincial or national levels. Spatial maps of pesticide exposure and health impact could be used to alert local populations and policy planners to potential contamination of the ecological systems in their residential areas due to pesticide use.

Suggested Citation

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Epidemiological Trends of Malaria in Eastern Shan State, Myanmar 2000-2016

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Abstract

Malaria is a priority communicable disease in Eastern Shan State (ESS) of Myanmar. This study aimed to describe the malaria situation, epidemiology and treatment services in ESS during 2000-2016. Data from township malaria monthly reports in ESS during 2000-2016 were analyzed by time, place, person, species and treatment services. Malaria morbidity, mortality and case-fatality rate decreased from 25.0 to 3.7 per 1,000 population, 15.0 to 0.2 per 100,000 population and 4.6% to 1.3%, respectively, during 2000-2016. The male to female ratio was 3:2 and those over 15 years old constituted 60% of all cases. The number of cases declined by 88% and 99% among those younger than 5 years of age and pregnant women, respectively. During 2011-2016, the case detection rate increased from 2% to 12%, and 94% of blood examinations used a rapid diagnostic test. *Plasmodium vivax* (63%) was the most prevalent parasite species, followed by *Plasmodium falciparum* (33%) while mixed parasites accounted for 4% of all infections. Non-government-controlled areas contributed more than 80% of cases between 2013 and 2016. Remarkable reductions in malaria morbidity and mortality in ESS followed improvements in early detection, appropriate treatment and effective vector control. However, the overwhelming contribution on caseload in non-government-controlled areas remain a challenge for the elimination of malaria in Myanmar.

Keywords: malaria, morbidity, mortality, annual blood examination rate, Eastern Shan State, Myanmar

Introduction

In 2015, there were an estimated 212 million cases of malaria and 429,000 malaria-related deaths globally. In the South-East Asia Region, about 1.4 billion people were at risk of malaria, with 237 million at high risk in 2015.[1] Malaria in Myanmar contributed approximately two-thirds of both morbidity and mortality in the Greater Mekong Subregion during 2013.[1] As a result, the National Malaria Control Programme (NMCP) was developed in coordination with both international and local agencies, including the World Health Organization to reduce the incidence of malaria to less than one case per 1,000 population in all states/regions by 2020 by scaling up malaria control interventions.[2]

Eastern Shan State (ESS) is situated in the most eastern part of Myanmar and consists of ten townships, eight sub-townships, 71 wards, 147 village tracts and 2,063 villages with a population of approximately 800,000. According to area micro-stratification of ESS in 2015, about 53% and 28% of the population lived in malaria risk areas and probable risk areas, respectively. Because of the high proportion of the population at risk of infection,

community-based malaria control interventions were developed and have been implemented since 2007 in ESS to increase accessibility of quality diagnosis and effective treatment, especially in remote areas.[3] For example, microscopy has been used for malaria diagnosis in health centers where microscopes are available and malaria rapid diagnostic tests (RDTs) have been used in all healthcare settings ranging from health centers to the community level. The basic reporting units are village health volunteers (VHVs) and basic health staffs. All examined cases are recorded in carbonless case registers and reported monthly.[4]

Eastern Shan State has experienced many malaria epidemics. One major epidemic occurred during 2001 in which an estimated 10,000 persons were affected with 1,066 reported deaths in 23 villages.[3] In addition, because ESS contains many so called "special regions" (politically unstable areas), non-government controlled areas, and extremely hard-to-reach areas, it is classified as a high risk malaria area.[3,5] Consequently, the extent of malaria and treatment service coverage is largely unknown. The objective of this study was to describe the malaria epidemiology and coverage of treatment services in ESS during 2000-2016 in the presence of malaria intervention activities.

Methods

We conducted a descriptive study on malaria in ESS during 2000-2016.

Data Sources and Data Collection

We reviewed aggregated data on malaria cases and deaths during 2000 – 2016 from the Vector Borne Disease Control (VBDC) programme at the state level. The data included monthly reports, carbonless registers from townships, State VBDC annual reports and reports from international non-governmental organizations (INGOs) and non-governmental organizations (NGOs). However, malaria data of time, place, person and type of species were not available before 2011. Data on case detection and management by type of service are available only after 2012.

Operational Definition

A confirmed malaria case was defined as a patient whose blood film was positive by microscopy or rapid diagnostic test (RDT). There were two types of

reported malaria cases: outpatients (OP): those who had uncomplicated malaria, and inpatients (IP): those who had severe malaria, were hospitalized and had a high risk of death.[4]

The OP malaria case definition varied from year to year depending on the type of blood test performed. In the past, the NMCP diagnosed patients with positive blood films as "confirmed malaria cases" and "clinically suspected cases" based on clinical symptoms. In 2006, the NMCP introduced, to some health centers, RDT which could detect only *P. falciparum* species. Since 2011, the NMCP has been distributing (through the State VBDC) bivalent RDTs, which can diagnose *P. falciparum* and *P. vivax* malaria and, therefore, all malaria cases were regarded as confirmed cases.[4]

Data Analysis

We analyzed data between 2000 and 2016 for morbidity and mortality rates, OP and IP malaria cases and deaths by time and township. We also described the distribution of cases by type of service (i.e. health facility, village health volunteer and NGO/INGO), gender age and species from 2011-2016 because data prior to this period were not available. We calculated the annual blood examination rate (ABER) and annual parasite incidence (API) and used ArcGis 10.1 software for mapping.

Descriptive statistics including frequency, rates and proportions were computed. We calculated malaria morbidity rates per 1,000 and malaria mortality rates per 100,000. We calculated ABER from the number of patients examined by microscopy or RDT per 100 population and API rate per 1,000 population at-risk.[6]

Results

Malaria Morbidity and Mortality Rates, 2000-2016

Figure 1 shows the trends of malaria morbidity (per 1,000 population) and mortality rates (per 100,000 population) in Eastern Shan State between 2000 and 2016. The morbidity and mortality rates gradually declined between 2000 and 2009 and then remained fairly steady over the next 7 years. In 2000, the malaria morbidity rate was 25 per 1,000 and the mortality rate was 15 per 100,000 population. In 2016, the malaria morbidity rate was 3.7 per 1,000 and the mortality rate was 0.2 per 100,000. The highest morbidity rate (29.4/1,000) and mortality rate (19.4/100,000) were reported in 2001.
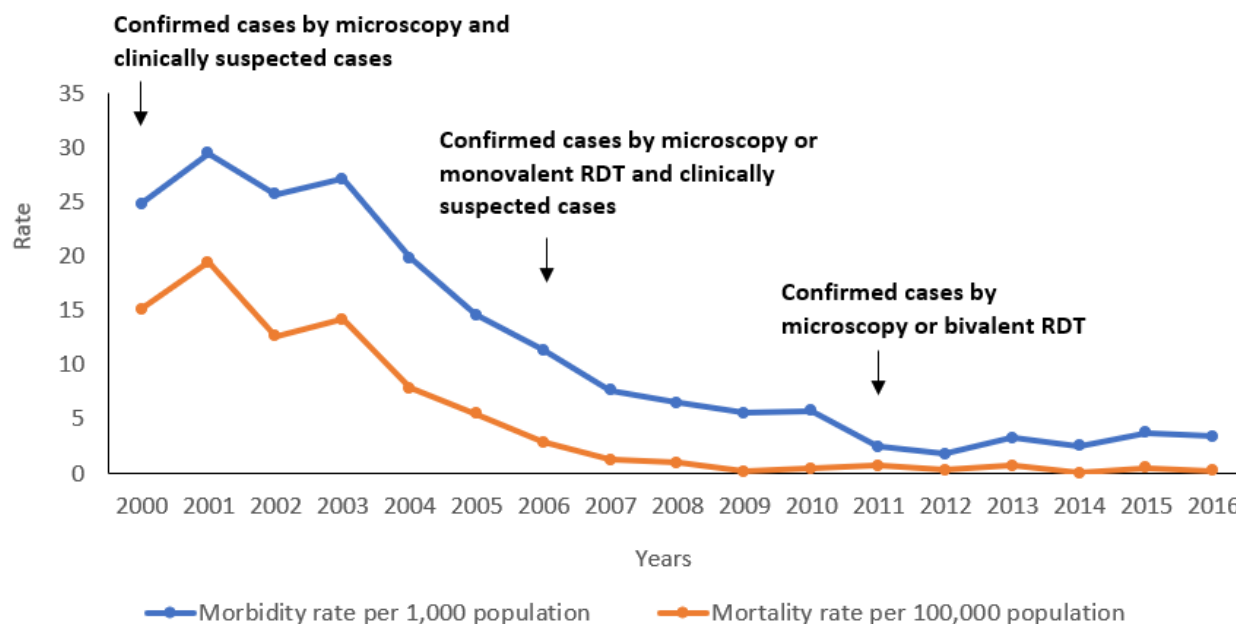
Figure 1. Trends of malaria morbidity rate (per 1,000 population) and mortality rate (per 100,000 population) in Eastern Shan State, Myanmar, 2000-2016.

Note: RDT: rapid diagnostic test.

Proportion of Malaria among All Hospital Cases and Deaths, 2000-2016

In 2000, there were 11,810 reported outpatient (OP) and 1,801 inpatient (IP) malaria cases. Only 83 malaria deaths were reported. The highest peak of OP and IP cases occurred in 2003 (16,102 and 2,144 cases, respectively). Between 2000 and 2016, there was a 75% reduction in OP malaria cases, a 92% reduction in IP cases and a 98% reduction in malaria deaths. The proportion of malaria cases among total patients decreased among both OP and IP cases. In 2000, there were 80,567 out-patients, of whom 11,801 (14.6%) were malaria cases while of the 253,443 out-patients in 2016, only 2,917 (1.2%) were malaria cases. A decrease in the proportion of IP malaria cases was similarly observed. In 2000, there were 330 deaths from all causes in hospitals of which 83 (25.2%) were from malaria. In 2016, of 126 deaths in hospitals, only 2 (1.6%) were malaria-related. The overall malaria case fatality rate (CFR) reduced during 2000-2016.

Malaria Morbidity and Mortality Rates by Township

Figure 2 shows the malaria morbidity (2a) and mortality (2b) rates in Eastern Shan State according to township in 2000, 2005, 2010, and 2016. The morbidity and mortality rates declined in all townships during 2000-2016. In 2000, Mong Tong Township had the highest malaria morbidity and mortality rates (56.4/1,000 and 52.8/100,000, respectively) while Mong Yaung township had the lowest morbidity rate (12.4/1,000). In 2016, there was a 78% reduction in morbidity rate and a 96% reduction in mortality rate in Mong Tong Township compared to 2000. The lowest morbidity rate in 2016 among all townships was in Mong Lar (0.1/1,000).

Coverage of Case Detection and Annual Blood Examination Rate by Township

Figure 3 shows the annual blood examination rates (ABER) in Eastern Shan State according to township in 2000, 2005, 2010 and 2016. In 2000, all the townships reported an ABER of less than 5.0% except for Mong Hsat Township which had an ABER of 10.6%. Case detection rates increased over the years from 2000 to 2016. In 2016, all townships reported an ABER of more than 5.0% and Mong Yang township had the highest rate of 29.4%.

Distribution of Malaria Cases by Month

Malaria cases occurred throughout the year but were highest during the rainy season (June to August). However, in 2015 and 2016, there were two peaks: one in the rainy season and the other in the early winter months. Each year, the majority of reported cases were male (60%).

From 2011 to 2016, malaria was reported among all age groups, but those aged 15 years and above constituted 60% of all cases. Figure 4 shows the trends in malaria incidence among children aged less than 5 years and pregnant women in Eastern Shan State during 2000-2016. The incidence of malaria

among children aged under 5-years and pregnant women decreased from 2000 to 2016. There were 2,385 malaria cases among children aged less than 5 years in 2000 and this number decreased to 385 in 2016. Although the incidence of malaria in children aged under 5 years declined by approximately 88.4% over this period, the proportion of malaria cases in this age group to all cases remained at 11%. For pregnant women, there were 663 malaria cases in 2000 and only 6 cases in 2016 (99.5% reduction).

Malaria Diagnosis and Species Distribution

A total of 251,931 cases were examined during 2011 to 2016 by both microscopy and RDT to identify confirmed malaria cases. Among all cases examined, most (94%) were detected by RDT and only 6% were diagnosed by microscopy. *Plasmodium vivax*,

Plasmodium falciparum and mixed infections accounted for 63%, 33% and 4% of confirmed cases.

Malaria Case Management

Malaria case management was done not only in public health facilities but also in communities by village health volunteers (VHVs) trained by the NMCP. In addition, both national and international NGOs also conducted case management through mobile and fixed clinics. Data from VHVs and NGOs were not available during 2012 to 2014; although those services did implement malaria case detection services. In 2015, 70.7% of cases were treated at a public health facility, while 19.6% were treated by VHVs and 9.8% by NGOs. The proportion of cases treated by VHVs and NGOs implementing partners were22.9% and 12.4%, respectively, in 2016.
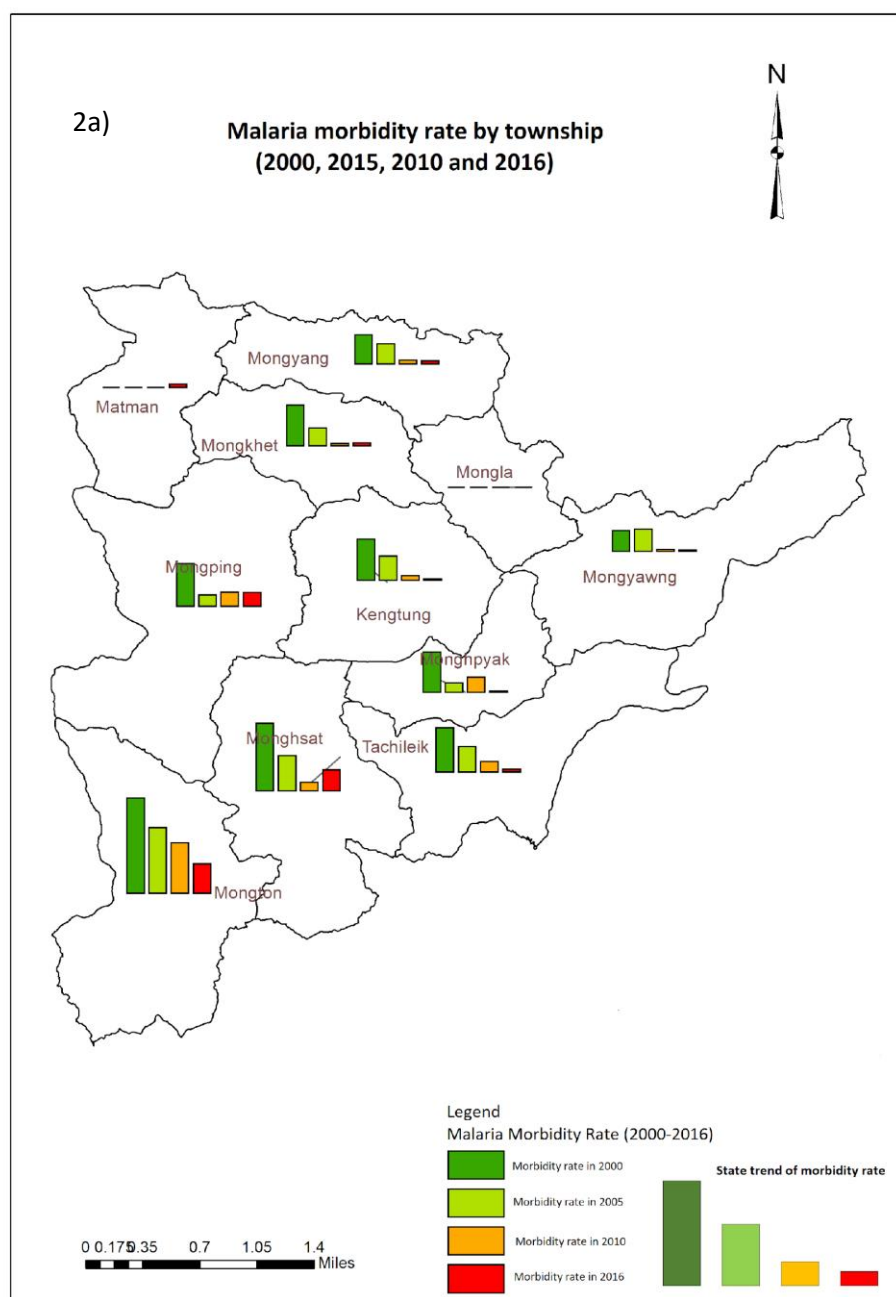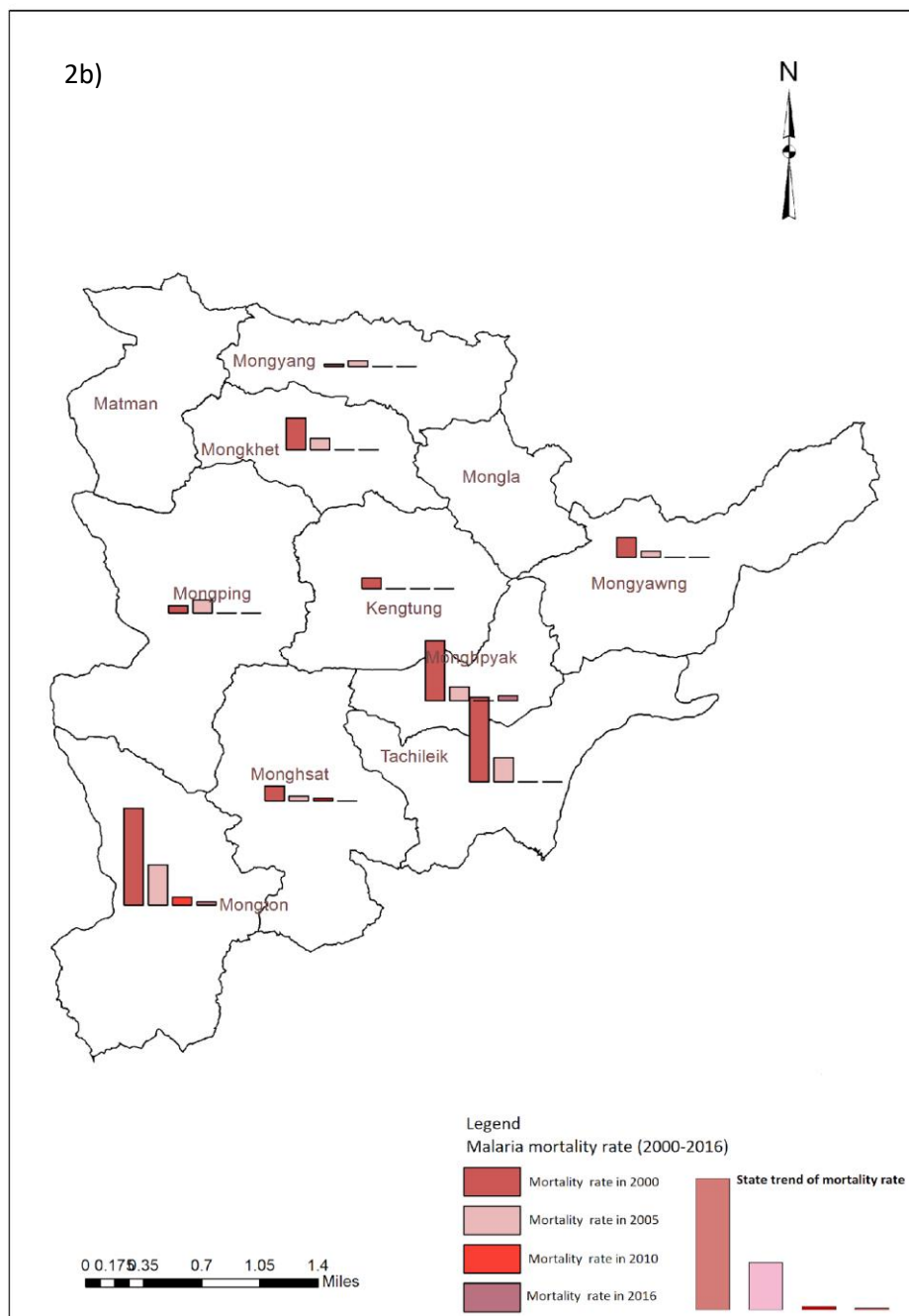

Figure 2. Malaria morbidity and mortality rates in Eastern Shan State, Myanmar according to township, 2000, 2005, 2010, and 2016 (1)

Figure 2. Malaria morbidity and mortality rates in Eastern Shan State, Myanmar according to township, 2000, 2005, 2010, and 2016 (2)
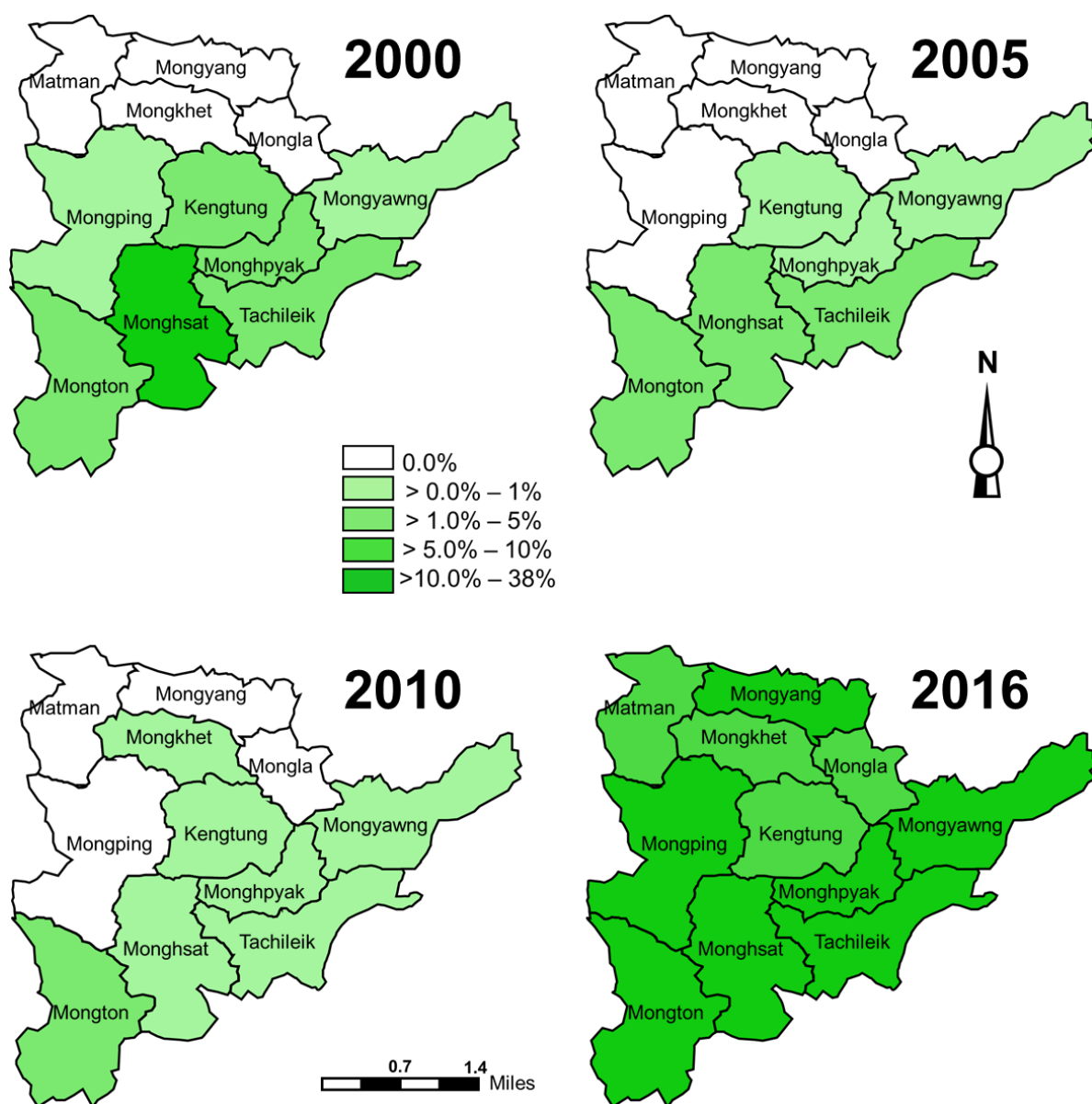
Figure 3. Annual blood examination rates (ABER) in Eastern Shan State according to township, 2000, 2005, 2010 and 2016
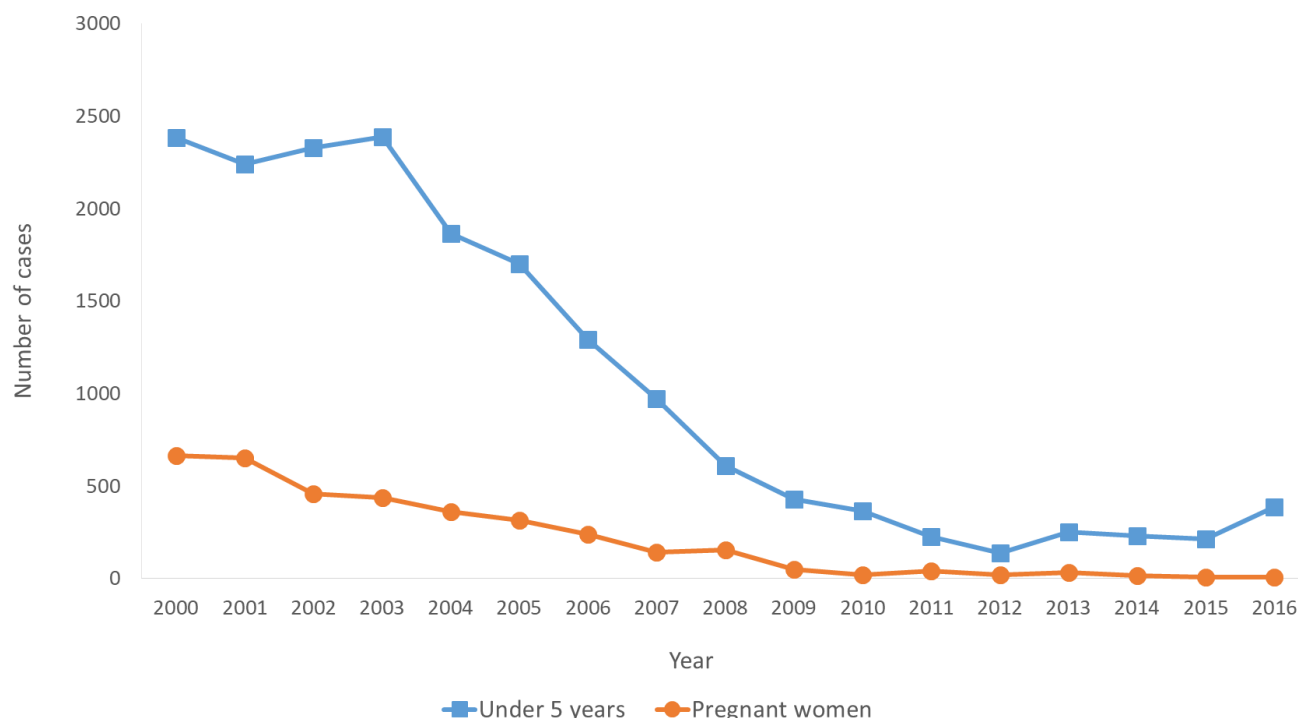
Figure 4. Number of malaria cases among children aged less than 5 years old and pregnant women in Eastern Shan State, 2000-2016

Discussion

The decreasing trends in malaria morbidity, mortality and case fatality rate in Eastern Shan State during 2000-2016 coincided with the expansion of three key interventions: the distribution of long-lasting insecticidal nets (LLINs), early malaria diagnosis and effective treatment. This finding is consistent with other studies conducted in Africa where a dramatic decline in malaria burden was due to the effective vector control measures and scaling up of artemisinin-based combination therapies (ACT) as first line anti-malarial drugs.[7-9] The increase in morbidity rates during 2012-2016 might be due to the increase in reporting rates. This finding is consistent with a study conducted in South Sudan during 2006 and 2013 where a gradual increase in the number of malaria cases was due to improvement of the surveillance system and increasing reporting rates.[10] Human migration is another possible factor that might contribute to an increasing number of cases during that period because migrant workers are highly exposed to poor housing which lack preventive measures such as LLINs.[11]

Total patient attendance at a health facility due to any illness during 2000-2016 increased by 57%, whereas malaria patient attendance decreased by 77%. Therefore, reduction in malaria cases might not be due to a decrease in accessibility. However, accessibility of health services is still challenging for those who live in remote areas of the state. We observed changing patterns of malaria seasonality in 2015-2016, i.e. having two peaks of reported cases as compared with only one peak in other years which might be due to environmental factors, such as temperature and humidity which can affect vector densities. This finding is consistent with the seasonal patterns in other states/regions of Myanmar.[12] A study conducted in Burkina Faso on data recorded during 1999–2003 revealed that the highest malaria mortality was during and at the end of the wet season when the transmission intensity of malaria is at its highest.[13]

Malaria morbidity and mortality varied widely between townships. This might be due to the varying ecological conditions. Mong Tong Township retained its position as the township with the highest malaria rates for a decade. In 2000, all townships had low ABER indicating low coverage of diagnostic and treatment services. In 2016, there was improvement in case finding as ABER increased from 2.0% to 12.5% by intensification of case finding through mobile clinics, expansion of health facilities in special regions, capacity building of basic health staff and VHVs and increased reporting by NGOs.[3]

Similar to other studies conducted in Myanmar, males and adults had higher malaria incidences compared to females and other age groups, respectively, which might be due to occupation and

behavioral patterns that cause a greater exposure to vectors.[7] The proportion of malaria in children under 5 years old was fairly constant at around 10%, indicating a persistent local transmission. The number of reported malaria cases among pregnant women also decreased during the study period, which probably indicates a more effective integration of maternal and children health care and malaria programme.[2] The gender and age distribution pattern of malaria in Myanmar is different from the African settings where younger age group and pregnant women are the most affected populations.[14]

Blood examination by microscopy decreased whereas the use of RDTs increased. This could be because microscopy can be performed only at hospitals whereas RDTs can be used in all health facility levels.[4] Regarding parasite species, since bivalent RDT was used throughout 2011-2016, we can assume that the proportion of *P. vivax* increased due to the high sensitivity of *P. falciparum* to artemisinin-based combination therapy. Prior to 2011, the proportion of *P. vivax* infections was low because only monovalent RDT, which can detect only *P. falciparum*, was in use.[4] This study supports the increasing roles of VHVs and NGOs in diagnosing malaria with RDTs, treatment with artemisinin-based combination therapy and reporting in 2015-2016.

Limitations

Due to data unavailability, we could not describe the distribution of malaria by gender, age and species before 2011. Limitations in use of health facility data in assessing trends in malaria should be kept in mind, especially in terms of service utilization and completeness of reporting. However, with the available data, we could describe the trends of malaria indicators and identify differences in malaria epidemiology between townships which may be useful for better prioritization and targeting implementation.

Conclusions

The findings revealed that morbidity and mortality of malaria in Eastern Shan State decreased over the period under review. Mong Tong and Mong Hsat Townships had the highest malaria incidence. Malaria morbidity varies according to gender and age with males and those aged more than or equal 15 years old showing a higher incidence. Case detection rates increased over time in all townships due to increasing roles of village health volunteers and NGOs and introduction of rapid diagnostic tests.

Recommendations

Routine malaria surveillance should be strengthened to ensure complete and timely reporting from all health sectors including public and private health facilities, NGOs, and Ethnic Health Organizations. Transmission reduction activities such as intensification of case detection in hard-to-reach areas, early case detection, appropriate treatment and effective vector control measures should be scaled-up to be ready for malaria elimination. Strong political commitment should be maintained with adequate financial support for malaria elimination.

Suggested Citation

Thet BS, Swaddiwudhipong W, Thimasarn K, Thi A, Soe TN, Lin Z. Epidemiological trends of malaria in Eastern Shan State, Myanmar 2000-2016. OSIR. 2019 Sep;12(3): 84-92.

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Surveillance of Rotavirus Gastroenteritis (2015-2017): Epidemiology and Circulating Rotavirus Genotypes in Pre-rotavirus Vaccine Introduction Period in Myanmar

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Abstract

A hospital-based prospective active surveillance for rotavirus gastroenteritis (RVGE) was conducted among hospitalised acute gastroenteritis (AGE) patients to identify the infecting rotavirus strains and to provide epidemiological information on RVGE in Myanmar. Stool samples were collected from children less than 5 years old admitted to Yangon Children's Hospital (YCH) for AGE during January 2015 to September 2017. Collected stool samples were screened for rotavirus antigen by ELISA and genotyped by reverse transcription polymerase chain reaction (RT-PCR). Overall, 48.8% (1,167/2,393) of samples were ELISA positive for rotavirus and the most affected were children aged 6-23 months, 81.9% (956/1,167). RVGE occurred in a seasonal cycle with peak detection in the cold and dry months (November to February). As compared with non-RVGE, RVGE cases had significant higher percentage of vomiting (84.5% versus 73.0%; P<0.05), fever (80.1% versus 71.8%; P<0.05) and severe clinical scoring (79.4% versus 67.5%; P<0.05). Genotyping revealed that G9P[8] was predominant in the year 2015 (53.3%) and 2016 (30.9%), but it was replaced in 2017 by G3P[8] (58.2%). Information from this surveillance not only highlights facts for consideration of rotavirus vaccine introduction plan in pre-vaccination era, but also provides vital baseline data for post-vaccination monitoring of vaccine impact and effectiveness.

Keywords: rotavirus, gastroenteritis, pre-vaccination, Myanmar

Introduction

Acute gastroenteritis (AGE) is among the top causes of childhood mortality worldwide with rotavirus as the leading cause of severe AGE in children less than 5 years of age.[1] The annual global burden of rotavirus deaths in 2013 in this age group is estimated at 215,000 (range 197,000 – 233,000 deaths) and approximately half (49%) of these deaths occurred in India, Nigeria, Pakistan and the Democratic Republic of Congo.[2]

In order to reduce the burden and mortality of rotavirus gastroenteritis (RVGE), prevention by vaccination is considered to be critical, because it cannot be prevented with just improvements in sanitation and hygiene practices.[3] The World Health Organization (WHO) recommended that rotavirus vaccine (RV) be incorporated in the childhood immunisation programme and particularly in those

with high child mortality due to diarrhea such as Southeast Asia and Sub-Saharan Africa. Two currently available vaccines with demonstrated efficacy against severe rotavirus disease are Rotarix (GSK Bio, a monovalent vaccine containing a single G1P[8] strain) and RotaTeq (Merck, containing 4 common G types (G1–G4) and 1 common P type P[8]).[4] As of August 2018, 96 countries around the world including 46 low-income countries have introduced rotavirus vaccines in their universal immunisation programs which have demonstrated dramatic impact. According to the WHO report, there was 40% decrease in the prevalence of rotavirus in countries that introduced the vaccine and rotavirus-related child deaths was reduced from 800,000 in 1985 to 215,000 in 2016.[5]

In Myanmar, the National Health Plan (2011-2016) declared diarrhea as a high-priority childhood

disease.[6] Also Myanmar is a member of the Global Rotavirus Surveillance Network (GRSN) and has been conducting hospital-based rotavirus surveillance since 2009. This surveillance is funded by WHO. Every year, more than 80% of eligible AGE cases were enrolled and stool samples were collected and tested for rotavirus. The surveillance data revealed that the proportion of RVGE among hospitalised less than 5 years old children with diarrhea at Yangon Children's Hospital (YCH) ranged from 42% to 56% during 2009-2014 which demonstrated a high burden of the disease and called for introduction of rotavirus vaccine.[7] Before introducing vaccines into target populations, the baseline data of the epidemiology of rotavirus infection must be established. Therefore, this study was conducted to provide information on the epidemiology of rotavirus infection and circulating rotavirus genotypes to establish vital baseline, as well as determine key factors to decision makers for vaccination plan, including target population, dose scheduling and selection of appropriate vaccines in pre-vaccination era.

Methods

Study Design and Setting

A cross-sectional, active hospital-based sentinel surveillance for RVGE among children under 5 years of age was conducted at YCH from January 2015 through September 2017 according to the World Health Organization (WHO) generic protocol.[8] YCH is the largest and main tertiary care referral pediatric hospital in Yangon with a pediatric inpatient unit consisting of three wards and 1,300 beds. Approximately 10,000 to 13,000 children under 5 years of age are admitted year-round to these wards, with admissions to each ward occurring on a rotating basis.

Inclusion and Exclusion Criteria for Participants

Inclusion criteria for patients eligible for enrollment were children less than 5 years of age, who presented with diarrhea (≥3 looser-than-normal stools in a 24-hour period during the illness, with onset of diarrhea ≤14 days at presentation) and treated in one of the three pediatric-medical wards of YCH.[8] Exclusion criteria was presence of either blood or mucus in the stool or failure to obtain an informed consent from parents or legal guardians of patient.

Surveillance Methods

Active case finding was conducted from every Monday to Friday during the study period in the pediatric-medical wards. Only the patients on the first post-admission day were approached. As such, children admitted on late Friday or Saturday were not recruited, and children admitted on Sunday were approached for enrollment on Monday. All hospitalized AGE patients of less than 5 years old, who met the selection criteria were enrolled in the study.

Upon enrollment, a case report form containing information on demographics, clinical history, physical examination, treatment and outcome was completed. A stool sample containing not less than 3 ml was collected within 48 hours of admission, using wide-mouth screw capped bottles. The bottles were labeled, kept below 4°C, and transported in the same day to the Virology Research Division laboratory at the Department of Medical Research, and subsequently stored at -20°C until testing was performed. Upon discharge, the date and outcome of the cases were recorded on the case report form.

Laboratory Analysis

All samples were tested for rotavirus antigen by ProSpecT™ Rotavirus ELISA kit, Oxoid, UK, according to the manufacturer's instructions. Patients with a positive test result were defined as RVGE cases. A subset of rotavirus-positive stool samples (approximately 30% of ELISA positive samples from each month) was randomly chosen for G (VP7) and P (VP4) genotyping. RNA was extracted using QIAamp Viral RNA Mini Kit (QIAGEN GmbH, Germany) and the extracted dsRNA was amplified by RT-PCR using specific oligonucleotide primers provided by the WHO Rotavirus Reference Laboratory, CMC, Vellore, India.[9]

Statistical Analysis

Data were entered into Microsoft Excel. For descriptive analyses, number and percentage were calculated and Chi-square test was performed to determine statistically significant differences between RVGE and non-RVGE groups regarding characteristics of patients, clinical presentations and outcomes. A p-value less than 0.05 was considered significant.

Ethical Consideration

This study was approved by the Ethics Review Committee, Department of Medical Research, Myanmar. Written informed consent was obtained from the parents or guardians of children prior to enrolment.

Working Definitions

Acute gastroenteritis is the sudden onset of diarrhea and/or vomiting, usually with three or more bouts of diarrhea or vomiting and diarrhea.[10] Also, the severity of the disease is assessed using Vesikari Clinical Severity Scoring System.[11]

Results

From January 2015 to September 2017, 2,939 eligible children were identified by the surveillance system. Of these, 84.8% (2,494/2,939) were enrolled and stool samples were collected from patients 95.9% (2,393/2,494). Among them, 48.8% (1,167/2,393) were
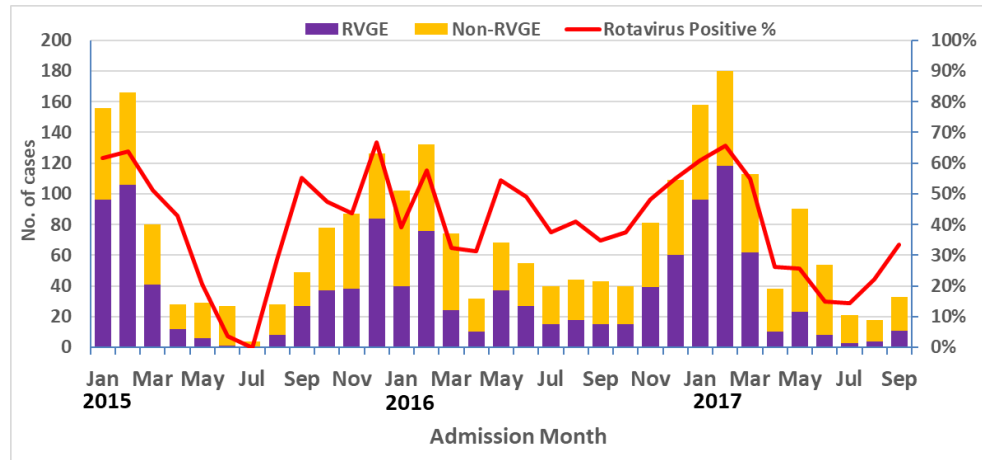
Figure 1. Number of RVGE, non-RVGE cases and percentage of rotavirus positive among hospitalized <5 years old children by month, YCH, September 2015-2017

rotavirus positive and the proportion of rotavirus positivity was 52.5% (456/868), 45.9% (376/820) and 47.5% (335/705) in 2015, 2016 and 2017 respectively. AGE cases are admitted to YCH year round, and rotavirus positivity has also been detected year round except July 2015. High numbers of AGE cases due to rotavirus were observed from November through February, which comprised 58-66% positivity of each year, and often peaked in February (Figure 1).

Table 1 compared the demographic characteristics, clinical presentations and outcome of RVGE and non-RVGE cases. Male to female ratio was 1.6:1 among both RVGE and non-RVGE cases.

The 6-23 months age group accounted for the majority (81.9%) of rotavirus cases, followed by the 0-5 months age group (9.1%) and the 24-59 months age group (9.0%). Additionally, the 6-23 months age group also had a significantly higher percentage of rotavirus positive (52.1%) compared to 0-5 months age group (34.9%) and 24-59 months age group (41.3%). Both overall and annually, nearly 60% of the RVGE cases were found among children aged less than 12 months, and over 90% among children aged less than 24 months (Table 2).

Hospitalised AGE cases commonly presented with vomiting, fever and dehydration. Among them,

vomiting (84.5% versus 73.0%; $P<0.01$), fever (80.1% versus 71.8%; $P<0.01$) and severe clinical score (79.4% versus 67.5%) were more frequently observed in RVGE compared with non-RVGE patients. Furthermore, dehydration (76.0% versus 73.4%) and hospital stay of more than 5 days (3.0% versus 2.0%) were also more frequently observed in RVGE although not statistically significant (Table 1).

Distribution of rotavirus genotypes by seasonal year (from July to June of the following year) is shown in Table 2 and Table 3. G9 was the most prevalent G genotype in 2014-2015 and 2015-2016 and accounted for 79.3% and 50.6% respectively of the genotypes. However, G3 was the most common genotype in 2016-2017 accounting for 60.0%. Regarding P genotype distribution, P[8] was consistently predominant throughout the study period accounting for 66.7%, 69.1% and 83.6% in 2014-2015, 2015-2016 and 2016-2017 respectively.

From July 2014 to June 2015, G9P[8] was predominant, and accounted for 53.3% (72/135) followed by partially typed strain 39.4% (41/135). The G9P[8] strain was still predominant in 2015-2016 and partially typed strain accounted up to 41.9% (34/81). However, the most prevalent strain changed to be G3P[8] in 2016-2017, and accounted for 58.2% (32/55).

Discussion

The percentage of rotavirus positivity ranged from 46% to 53% in the present study during 2015-2017, highlighting that RVGE burden is persistent in Myanmar when compared to the previous data of 42-56% during 2009-2014.[7] This proportion was also similar to that of the neighboring countries; 53% in Kolkata in 2011-2013, and 42% in Bangladesh in 2008-2012.[10,13] According to the WHO's rotavirus surveillance network data, the median rotavirus detection in the Southeast Asian Region was 35% in 2012-2013 with Myanmar having the highest proportion at 47%.[14] This study additionally demonstrated that rotavirus infection has a strong seasonal peak in colder, drier months as seen in other Asian countries.[15]

Table 1. Characteristics, clinical presentations and outcome of hospitalised children with rotavirus gastroenteritis and non-rotavirus gastroenteritis, September 2015-2017 (n=2,393)

Characteristics	RVGE (%) n=1,167 (48.8%)	Non RVGE (%) n=1,226 (51.2%)	P value
Sex			
Male	721 (61.8%)	753 (61.4%)	0.86
Female	446 (38.2%)	473 (38.6%)	
Age in months			
0-5 months	106 (9.1%)	198 (16.2%)	
6-23 months	956 (81.9%)	879 (71.6%)	<0.01
24-59 months	105 (9.0%)	149 (12.2%)	
Clinical Symptoms			
Vomiting	986 (84.5%)	895 (73.0%)	<0.01
Fever	935 (80.1%)	880 (71.8%)	<0.01
Dehydration	887 (76.0%)	900 (73.4%)	0.14
Vesikari Clinical Score			
Mild (<7)	24 (2.1%)	26 (2.1%)	
Moderate (7-10)	216 (18.5%)	373 (30.4%)	<0.01
Severe (≥11)	927 (79.4%)	827 (67.5%)	
Hospital Stay			
<2 days	93 (8.0%)	123 (10.0%)	
2-5 days	1,039 (89.0%)	1,079 (88.0%)	0.06
>5 days	35 (3.0%)	24 (2.0%)	
Outcome			
Recovery	1,167 (100.0%)	1,225 (99.9%)	0.49
Expired	0	1 (0.1%)	

This study showed male predominance in both RVGE and non-RVGE groups which is in accordance with the findings of other studies, such as in Lahore, where 60% of enrolled children were male, and Uganda, where 61% of children were male.[16,17] The factors underlying this difference are poorly understood and further study is warranted. Regarding the age distribution of RVGE patients, the highest proportion of rotavirus positive was among children 6-23 months of age and more than 90% of the cases had rotavirus infection by their second birthday. These results are in line with previous studies conducted prior to vaccine introduction in other countries.[18] Thus, the WHO's recommended dose schedule is applicable in Myanmar.[19]

Regarding the clinical presentations, vomiting, fever and severe clinical score were found to be significantly associated with rotavirus positivity. This finding is also in line with the findings of other studies where RVGE cases presented with more severe clinical manifestations compared to rotavirus negative cases.[20] Of enrolled children, only one patient, a 7-month-old male admitted in April 2016 who presented with high fever, severe dehydration and shock, and tested rotavirus negative, expired.

This study identified a different profile of genotype distribution by seasonal years. G9P[8] was predominant in 2014-2015 and continued its predominance in the following year 2015-2016. However in 2016-2017, G9P[8] disappeared and G3P[8] replaced it as the most predominant strain. In the previous study during 2009-2014, G12P[8] predominated consecutively for 3 years from 2009-2012, and then the predominant strain changed to

Table 2. Distribution of rotavirus G genotypes by seasonal year, September 2015-2017

Genotype	G1 (%)	G2 (%)	G3 (%)	G9 (%)	G12 (%)	Mixed (%)	UT (%)
2014-2015 (n=135)	2.2	3.0	0	79.3	0	2.2	13.3
2015-2016 (n=81)	13.6	2.5	4.9	50.6	2.5	4.9	21.0
2016-2017 (n=55)	7.3	12.7	60.0	0	0	18.2	1.8

G2P[4] in 2012-2013 and again to G1P[8] in 2013-2014. This changing pattern is in agreement with the WHO's genotype distribution reported both globally and regionally with higher resemblance to regionally reported strains.[21] From 2009-2011, the globally dominant genotype was G1P[8], although the G12P[8] strain emerged in Southeast Asian Region starting from 2010. The dominant strain globally as well as regionally in 2013 and 2014 was G1P[8] and G9P[8] respectively.[15,20,22,23] Diversity of circulating rotavirus strains is reported regardless of vaccine use.[24] Enhanced surveillance is needed from the perspective of devising future vaccine strategies and monitoring

strain specific vaccine effectiveness.

Limitations

This analysis was subject to limitations. This was a hospital based surveillance and conducted at one site only up to 2017, although YCH is the largest children's hospital and the major pediatric referral centre and its patients are drawn not only from urban and rural areas of Yangon Region, but also from other States and Regions especially from the lower part of Myanmar, and likely captures the epidemiological profile of a large portion of our population of interest.

Table 3. Distribution of rotavirus P genotypes by seasonal year, September 2015-2017

Genotype	P[4] (%)	P[6] (%)	P[8] (%)	Mixed (%)	UT (%)
2014-2015 (n=135)	1.5	3.7	66.7	4.5	23.6
2015-2016 (n=81)	0	1.2	69.2	0	29.6
2016-2017 (n=55)	0	9.1	83.7	3.6	3.6

Conclusions

The RVGE burden in Myanmar urges consideration of introducing rotavirus vaccine. The high proportion of RVGE is in children less than 5 years hospitalized with AGE, and the diversity of circulating genotypes and epidemiological patterns reported in this study provide vital inputs for vaccine programmers in planning vaccine introduction and monitoring vaccine impact and effectiveness in post-vaccine introduction period. As the GRSN recommendation, surveillance should be carried out continuously to assess disease trends over time, to monitor circulating genotypes after vaccine introduction and to serve as a platform for vaccine effectiveness and safety evaluation.

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Prevalence and Associated Factors of Neonatal Microcephaly in Thailand, 2014-2018

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Abstract

Microcephaly became of high concern after Zika outbreaks occurred worldwide. An estimation of its prevalence is crucial for public health preparedness and response. The objectives of this study were to estimate the prevalence of neonatal microcephaly in Thailand during 2014-2018, describe its epidemiological characteristics, and identify associated factors. This study was a cross-sectional study using data from the Health Data Center, Ministry of Public Health, Thailand. Neonatal microcephaly, as defined in this study, is a condition where a newborn has a head circumference (HC) less than the 3rd percentile of the International Fetal and Newborn Growth Consortium for the 21st Century standard head circumference charts for term newborn, and Fenton's growth charts for preterm newborn by gestational age and gender. Univariate and multivariate analysis were performed to identify associated factors. During 2014-2018, 121,448 newborns were identified and the prevalence of neonatal microcephaly was 14.5%. There were 9,871 boys and 7,687 girls. Multivariate analysis showed that small for gestational age (adjusted odds ratio (Adjusted OR) 5.34, 95% confidence interval (CI) 3.24, 8.81), birth length less than the 10th percentile (Adjusted OR 2.92, 95% CI 1.36, 6.29), elderly pregnancy (Adjusted OR 1.84, 95% CI 1.07, 3.18), and primigravida (Adjusted OR 2.01, 95% CI 1.37, 2.95) were significantly associated with neonatal microcephaly. The prevalence of neonatal microcephaly in Thailand was higher than expected. The international head circumference chart may not be suitable for Thai newborns suggesting that a head circumference growth standard for Thai newborns is needed.

Keywords: prevalence, neonatal, microcephaly, Thailand

Introduction

Neonatal microcephaly is a condition where a newborn is born with a smaller than normal head, which is defined as a head circumference less than 2 standard deviations (SD) below the mean, or the 3rd percentile, compared with other newborns of the same gestational age and gender using a standard reference population.[1-3] Up to now, the cause of microcephaly remains unclear. Apart from a genetic predisposition, the most common causes are infection and exposure to toxic chemicals during pregnancy.[1,3] Newborn with microcephaly may have a normal development, delayed development or, in severe cases, die soon after birth.[1-4] The data from Latin America and the Caribbean showed that microcephaly can

cause a loss of almost 30 disability-adjusted life years per case and an expenditure of over US$ 91,100 per patient-years.[5] The prevalence of microcephaly varies by region. It ranges from 20-120 cases per 100,000 live births in the United States, around 55 cases per 100,000 live births in Australia, 15.3 per 100,000 live births in Europe, and 4.36 per 100,000 live births in Thailand.[1,6-8]

The global concern of microcephaly rose in 2016 after the global Zika virus infection epidemic.[9] The increasing rate of congenital microcephaly in Brazil and potential association between microcephaly and other central nervous system abnormalities and Zika virus infection from 17 countries were reported to the World Health Organization (WHO) in 2015.[9]

Consequently, WHO declared that the cluster of microcephaly cases and other neurological disorders constituted a Public Health Emergency of International Concern.[10] Furthermore, a case-control study from Brazil confirmed an association between microcephaly and Zika virus infection.[11] Thailand was one of the 17 affected countries. In 2016, the Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health (MoPH), Thailand reported more than 1,000 cases of Zika virus infection from many parts of the country, and two confirmed Zika-related microcephaly cases.[12]

Estimating the prevalence of microcephaly after the Zika virus epidemic is crucial for improvement of public health preparedness and response. Moreover, knowing the epidemiological characteristics of microcephaly in Thailand are vital for clinical management and development of clinical guidelines. Head circumference plays an important role in screening for genetic disorders, brain or neurological development abnormalities, and microcephaly. Measurement of head circumference is non-invasive, easy to perform and inexpensive.[13] However, the head circumference of a newborn requires proper standardization before it can be used as an indicator as it has been reported to be associated with many factors such as birth weight and length, maternal race, maternal age, maternal weight, maternal height, and parity.[14-21]

The objectives of this study were to estimate the prevalence of neonatal microcephaly in Thailand during 2014-2018, describe its epidemiological characteristics and identify associated factors.

Methods

This was a cross-sectional study. The study population was all newborns who received a medical service in public hospitals under the jurisdiction of the Thai MoPH and other hospitals that sent their service data to the MoPH from 1 Jan 2014 to 31 Dec 2018. We excluded newborns who had no data on head circumference or gestational age.

The national health database from the Health Data Center, Thai MoPH, was used as the data source for this study. This database was established in 2012 and achieved nationwide coverage in 2014. The aim of this database is to collect health information among care seekers who received a medical service in public hospitals under the Thai MoPH for health strategic management and health policy planning.[22] The

database contains data from 1,076 public hospitals and 378 private hospitals throughout the country.[23]

The definition of neonatal microcephaly is a newborn with a head circumference less than the 3rd percentile when compared to a reference population of newborns with the same gestational age and gender. According to the Royal College of Pediatricians of Thailand, a newborn's head circumference should be measured within three days of birth and compared with the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH 21st) standard head circumference charts for term newborns, and Fenton's growth chart for preterm infants.[24-26] Microcephaly was determined based on these reference charts and the prevalence is shown as a proportion with 95% confidence interval (CI).

Independent variables were neonatal factors (gender, birth weight, and length) and maternal factors (age, weight, height, nationality, gravida, and living in a Zika virus infected area). Birth weight was compared with standard references (INTERGROWTH 21st for term newborn, and Fenton growth chart for preterm infants) and classified as small for gestational age (a newborn who has a birth weight below the 10th percentile of the expected weight for their age and gender), appropriate for gestational age (a newborn who has birth weight between the 10th – 90th percentile of expected weight for their age and gender), and large for gestational age (a newborn with weight more than the 90th percentile of expected weight for their age and gender).[27] Similarly, birth length was classified as less than 10th percentile or more than or equal to 10th percentile.

There was a study showed that an advance maternal age (≥35 years) have a relationship with pregnancy outcome so maternal age was divided into less than 35 years or more than or equal to35 years.[28] Maternal weight and height were used to calculate body mass index (<18.5 kg/m^2= underweight; 18.5–22.9 kg/m^2= normal range; 23–24.9 kg/m^2= overweight; ≥25 kg/m^2= obesity).[29,30] In previous study, mother with short stature (<145 cm) was a risk factor of microcephaly so mother's height was grouped into less than 145cm and more than or equal to 145cm.[19] First gravida showed a relationship with newborn head size so gravidity was classified into two groups: primigravida and multigravida.[15] The residential address (province) of the mother and year of delivery were used to classify the mother as living in a Zika transmitted area or non-Zika transmitted area based on reports from the Bureau of Vector Borne Diseases, Department of Disease Control, Thai MoPH.[31] Any

province that had a confirmed case of Zika virus infection was categorized as being a Zika transmitted area from that year on.

Univariate analysis of independent variables associated with microcephaly was performed using Chi-square tests. Variables with a P-value less than 0.2 were included in a multiple logistic regression. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated to assess the statistical association.

Results

During Jan 2014 – Dec 2018, a total of 2,335,320 newborns in Thailand were recorded in the Health Data Center database. Among these, 134,004 (5.7%) had head circumference recorded, of which 121,448 (90.6%) also recorded the gestational age. The prevalence of neonatal microcephaly, normal head size, and macrocephaly are shown in Table 1. There were 17,558 newborns (14.5%, 95% CI 14.3, 14.7%) with microcephaly.

Table 1. Prevalence of neonatal microcephaly, normal head size, and macrocephaly, Thailand, 2014-2016

Year	2014	2015	2016	2017	2018	Total
Microcephaly	2,700	3,565	5,717	2,415	3,161	17,558
Prevalence of microcephaly (%)	14.0	14.9	16.0	15.8	11.6	14.5
95% Confidence interval	13.5 - 14.5	14.5 - 15.7	15.6 - 16.6	15.2 - 16.3	11.3 - 12.0	14.3 - 14.7
Macrocephaly	1,958	1,925	2,324	865	1,298	8,370
Prevalence of macrocephaly (%)	10.1	8.1	6.5	5.6	4.8	6.9
95% Confidence interval	9.7 - 10.6	7.7 - 8.4	6.3 - 6.8	5.3 - 6.0	4.5 - 5.0	6.8 - 7.0
Normal head size	14,679	18,416	27,678	12,042	22,705	95,520
Total	19,337	23,906	35,719	15,322	27,164	121,448

In addition, 8,370 newborns (6.9%, 95% CI 6.8, 7.0%) had macrocephaly. The prevalence of neonatal microcephaly increased between 2014 and 2016, peaking (16.0%) in 2016 and then decreased over the next two years. The prevalence of neonatal microcephaly before (2014-2015) and after the Zika virus outbreak (2016-2018) were 14.5% and 14.4% (P-value 0.82), respectively. The epidemiological characteristics of newborns and their mother in this study are illustrated in Table 2. Most newborns with microcephaly were boys (56.2%). Most newborns had an appropriate weight for their gestational age (63.4% for those with microcephaly and 85.8% for those with normal head size). Approximately 86.3% and 97.6% of newborns had a length more than or equal to 10th percentile for the microcephaly and normal head size groups, respectively. The microcephaly condition was more likely among boys than girls, small for their gestational age and having a length less than 10th percentile were positively associated with microcephaly, in univariate analyses.

For maternal characteristics, most mothers were aged less than 35 years (98.2% in the microcephaly group and 97.6% in the normal head size group). The majority of mothers in both groups had a normal body mass index. However, microcephaly was more likely if the mother was underweight (OR 1.23, 95% CI 1.16, 1.29) or obese (OR 1.09, 95% CI 1.04, 1.14). The height of majority of mothers in both groups were higher than 145 cm. Most (51.4%) were Thai nationals but mothers who were born in other countries were less likely to have a newborn with microcephaly (OR 0.47, 95% CI 0.42, 0.53). Multigravida was slightly more common for both groups and was protective for microcephaly. More than 50% of mothers in both groups lived in Zika transmission areas, although this was not a risk factor for microcephaly.

Results of the multiple logistic regression analysis is shown in Table 3. Factors significantly associated with microcephaly were birth weight, birth length, maternal age, and gravidity. Newborns whose weights were small for their gestational age were 5.34 times (95% CI 3.24, 8.81) more likely to have microcephaly. Newborns who had a birth length less than 10th percentile were 2.92 times (95% CI 1.36, 6.29) more likely to have microcephaly. Concerning maternal factors, mothers aged 35 years or more were more likely to have newborns with microcephaly (Adjusted OR 1.84, 95% CI 1.07, 3.18) and being primigravida also increased the risk of microcephaly (Adjusted OR 2.01, 95% CI 1.37, 2.95).

Table 2. Univariate analysis of epidemiological characteristic and microcephaly among Thai newborn, 2014-2018

	Microcephaly		Normal head size		Odds Ratio	95% CI		P- value
	n	%	n	%		Lower	Upper	
Neonatal factors								
Gender (n= 113,078)								
Boy	9,871	56.2	48,908	51.2	1.22	1.18	1.26	<0.001
Girl	7,687	43.8	46,612	48.8	ref.			
Weight (n= 113,042)								
SGA	6,341	36.1	5,974	6.3	7.82	7.51	8.14	<0.001
AGA	11,128	63.4	81,942	85.8	ref.			
LGA	81	0.5	7,576	7.9	0.08	0.06	0.10	<0.001
Length (by Age and Gender) (n= 112,938)								
<10th percentile	2,401	13.7	2,319	2.4	6.38	6.01	6.77	<0.001
≥10th percentile	15,110	86.3	93,108	97.6	ref.			
Maternal factors								
Age (year) (n= 14,788)								
≥35	43	1.8	295	2.4	0.75	0.54	1.03	0.08
<35	2,355	98.2	12,095	97.6	ref.			
BMI (Kg/m2) (n= 80,506)								
Underweight	2,543	19.1	11,207	16.7	1.23	1.16	1.29	<0.001
Normal range	4,679	35.1	25,280	37.6	ref.			
Overweight	1,521	11.4	7,890	11.7	1.04	0.98	1.11	0.21
Obesity	4,596	34.5	22,790	33.9	1.09	1.04	1.14	<0.001
Height (centimeters) (n= 81,265)								
<145	60	0.4	353	0.5	0.86	0.65	1.12	0.26
≥145	13,407	99.6	67,445	99.5	ref.			
Nationality (n= 13,798)								
Myanmar	310	14.2	1,752	15.1	0.70	0.61	0.80	<0.001
Laos	131	6.0	624	5.4	0.83	0.68	1.01	0.06
Cambodia	84	3.8	341	2.9	0.97	0.76	1.24	0.80
Other	536	24.5	4,476	38.5	0.47	0.42	0.53	<0.001
Thai	1,124	51.4	4,420	38.1	ref.			
Gravida (n= 82,559)								
1	6,192	47.9	29,402	42.2	1.26	1.21	1.31	<0.001
>1	6,723	52.1	40,242	57.8	ref.			
Zika transmission area (n= 73,718)								
yes	6,527	57.8	35,834	57.4	1.02	0.98	1.06	0.44
no	4,766	42.2	26,591	42.6	ref.			

BMI: body mass index. AGA appropriate for gestational age. LGA: large for gestational age. SGA: small for gestational age. CI: confidence interval. ref: reference group.

Discussion

In this study, the definition of neonatal microcephaly is a newborn who had head circumference of less than the 3rd percentile of standard head circumference by age and gender.[24] This means that in a fictional but normal population the expected prevalence of neonatal microcephaly will be around 3%. The prevalence of neonatal microcephaly in this study was 14.5% or 14,457 per 100,000 live births which is much higher than a previous study (4.36 cases per 100,000

live-births).[8] The higher prevalence when compared with previous study was possibly from the different methods. In this study, we used head circumference compared with a standard reference population to identify microcephaly cases. However, in the previous Thai study, they used diagnosis code (ICD-10-CM = Q02) to identify microcephaly cases. The definition of Q02 is a congenital or acquired developmental disorder in which the circumference of the head is smaller than normal for the person's age and gender. It is the result of brain developmental delay.[32] Some

103

newborns with a small head but with normal brain development may not be diagnosed with microcephaly. In 2017, the Thai Bureau of Epidemiology, conducted a microcephaly reporting system evaluation using the national health database as a reporting system. They found that only 8 out of 5,796 (0.14%) newborns who had a head circumference smaller than the 3rd percentile of the standard reference population were reported as microcephaly.[33] It is likely that using clinical diagnosis, recorded as ICD-10-Q02, may result in an underreporting of the magnitude of microcephaly.

Table 3. Multivariate analysis of epidemiological characteristic and microcephaly among Thai newborn, 2014-2018 (n=1,009)

Variables	Adjusted Odds Ratio	95% CI		P-value
		Lower	Upper	
Neonatal factors				
Gender				
Boy	1.03	0.72	1.49	0.87
Girl	ref.			
Weight				
SGA	5.34	3.24	8.81	<0.001
AGA	ref.			
LGA	0.41	0.13	1.36	0.15
Length (by Age and Gender)				
<10th percentile	2.92	1.36	6.29	0.01
≥10th percentile	ref.			
Maternal factors				
Age (year)				
≥35	1.84	1.07	3.18	0.03
<35	ref.			
BMI (Kg/m^2)				
Underweight	0.63	0.12	3.22	0.58
Normal range	ref.			
Overweight	1.22	0.74	2.03	0.44
Obesity	0.67	0.42	1.08	0.10
Nationality				
Myanmar	1.38	0.13	14.07	0.79
Laos	1.77	0.17	18.71	0.63
Cambodia	2.22	0.21	23.00	0.50
Other	0.40	0.03	5.11	0.48
Thai	ref.			
Gravida				
1	2.01	1.37	2.95	<0.001
>1	ref.			

BMI: body mass index. AGA appropriate for gestational age. LGA: large for gestational age. SGA: small for gestational age. CI: confidence interval. ref: reference group.

Another reason for the high prevalence of microcephaly in this study may be due to the use of an international standard reference population which did not include countries from South East Asia where Thailand is located. A number of studies from countries in South East Asia mentioned that international standard growth curves may not be suitable for their newborns.[19,34-36] When they made their own standard reference charts for head circumference based on their newborn data and

compared this with the international standard reference charts, they found that standard head circumferences in their countries were smaller than international standard head circumferences. We compared the 3rd percentile of head circumference of the population in this study with the standard international reference charts (INTERGROWTH 21st for term newborn, and Fenton growth chart for preterm infants) as shown in Table 4. We found that the 3rd percentile of head circumference in this population was smaller than the 3rd percentile of international standard head circumference. Therefore,

the high prevalence of microcephaly in our study is likely due to misclassification using the international standard head circumference, which may not be applicable in Thailand, and higher than the actual proportion. According to the national guideline, a newborn with microcephaly is one of the criteria to initiate congenital Zika syndrome investigation, which is costly.[24] Diagnosing microcephaly using international standard head circumference may result in unnecessary investigations and costs. Therefore, a local standard head circumference chart appropriate to Thai newborns is needed.

Table 4. The 3rd percentile comparison of standard reference and study population

GA	Male			Female		
	Standard 3rd percentile	3rd percentile in this study	n	Standard 3rd percentile	3rd percentile in this study	n
28	23	23	33	22.2	23	24
29	24	23	41	23	25	42
30	25	26	118	24	24.5	91
31	25.9	26.6	119	25	26	102
32	26.8	26.2	174	26	27	170
33	27.5	28	349	27	27	346
34	28.2	28	796	28	28	739
35	29	29	1,432	29	28	1,252
36	30	29	2,027	29.5	29	1,782
37	30.7	30	6,849	30.4	30	6,084
38	31.2	30	14,314	30.9	30	13,415
39	31.7	30	18,836	31.3	30	18,423
40	32.2	30	15,250	31.7	30	14,483
41	32.6	31	1,650	32.1	30	1,579
42	33	31	248	32.4	30	191
43	34	30	65	33	30	60
44	34.5	30	125	34	29.6	120

The prevalence of microcephaly increased between 2014 and 2016, peaking in 2016 (following the Zika virus outbreak in Thailand) then decreased. However, the difference in prevalence of neonatal microcephaly was not significant when we compared before and after Zika virus outbreak time periods. Although the association between Zika virus infection and microcephaly was confirmed in other countries, there was no association between mother's history of living in Zika transmission areas and microcephaly among newborns in this study.[11] However, our study had limited ability to verify the association between Zika infection and microcephaly in Thailand due to the low proportion of people who underwent specific Zika infection investigations among all microcephaly cases

diagnosed using international standard head circumference charts.

In this study, maternal weight and body mass index did not show an association with microcephaly, a result similar to previous studies.[37-39] Some studied showed that the weight-related factor was maternal gestational weight gain.[38,40] Unfortunately, gestational weight gain data is not recorded in the national health database.

There was a report about complication during pregnancy in advanced maternal age (≥35 years).[19] Since parity is not included in the national health database, we used gravidity as a proxy. In this study, a primigravida woman was twice as likely to deliver a

newborn with microcephaly than multigravida women. The results of this study are similar to the result of a previous study by Shajari et al where the mean neonatal head circumference in the first parity group was smaller than the multiparity group. [15] The result may be explained by low birth weight. Terán et al found that a newborn with the first parity had a higher risk of low birth weight than a newborn with multiparity.[41] The explanation of low birth weight may come from poor uterine blood perfusion in primiparous mothers, which reduces the supply of oxygen and nutrients to the fetus.[42] In addition, newborns delivered in primigravida elderly mothers were likely to have small head circumference.

The strength of this study is the database. This study used data from the Health Data Center, which included data from 1,454 hospitals throughout Thailand. Since 2014, around 69% of live births in Thailand are included in this database.[43]

However, as this study used secondary data, we were unable to impute incomplete or missing data of crucial variables, such as head circumference (>95% were missing) and gestational age of the newborns, from the original data sources. This also prevent us from improving the representativeness of the group included in the multivariate analysis of our study, as a large proportion of records were excluded from the model due to missing data in one or more selected variables. Some head circumference measurements might have round-off errors which may have affected the results. However, due to the nature of secondary data analysis, we did not have a chance to validate all measurements. Moreover, some potential associated factors such as gestational weight gain, nutrition during pregnancy, socioeconomic status, environmental, and lifestyle factors (stress, smoking and alcohol use) were not available.

We recommend that a standard reference anthropometric chart for Thai newborns be developed to support health care providers to make proper diagnoses, investigations, and treatment of neonatal microcephaly. Health care facilities should ensure completeness and accuracy of the data before sending reports to the central level. The study on possible associated factors such as gestational weight gain, nutrition during pregnancy, socioeconomic status, environmental, and lifestyle factors (stress, smoking and alcohol use) should be considered.

Suggested Citation

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A Report of Effective Intervention Strategies Conducted by Non-Health Sectors

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Abstract

Non-communicable diseases (NCDs) are the main leading cause of global mortality. Several causes of NCDs emerge from social and commercial determinants of health. Many of these causes cannot be tackled by the health sector alone. Most of data in this report were collected from the preparatory meeting of the Prince Mahidol Award Conference (PMAC) 2019, under the theme 'Political Economy of NCDs: A Whole Society Approach' with the main objective to accelerate implementation of NCDs prevention and control around the world. This paper concluded examples of NCD interventions that were presented at the conference. The article demonstrates how the non-health sectors can take a pivotal role in NCDs prevention. The key non-health sectors include, but are not limited to, the Ministry of Finance, private enterprises, communities and media. Public policies such as taxation on unhealthy commodities like alcohol, tobacco, and sugar sweetened beverages, helps reduce consumption of these products. Company's voluntary policy to provide a lactation room in the workplace presents a strong vision of balancing company profits and well-being of the employees. Community intervention helps engage all relevant stakeholders to take part in NCDs prevention. The role of media is one of the powerful strategies to raise awareness in the population. These exemplified interventions have established ideas on how multi-sectoral actions are one of the key players that help topple down NCDs crisis in Thailand.

Keywords: non-communicable diseases, intervention, non-health sectors, Thailand

Introduction

Non-communicable diseases (NCDs) are one of the greatest public health challenges nowadays. NCDs, including cardiovascular diseases (CVDs), cancer, diabetes, chronic respiratory diseases and mental health, are the main leading causes of death worldwide. Recent data from World Health Organization (WHO) reported that NCDs accounted for 41 million deaths or 71% of global mortality. Importantly, more than three quarters of these deaths occurred in low- and middle-income countries (LMICs).[1] Moreover, NCDs caused a 75% loss of global gross domestic product (GDP) in 2010. It is also expected that in the near future, LMICs will share larger global burden of NCDs due to fast economic and population growth.[2]

Potential causes of NCDs are complex with many factors involved. One of the main causes of NCDs is related to the conditions in which people are born, grow, live, and work, also known as social

determinants of health.[3] People born in low socio-economic status mostly face greater NCDs risks including alcohol and tobacco consumption, and unhealthy diet.[4] Another factor that contributes to NCDs which has been wildly discussed is commercial determinants of health, the conditions that closely link with rapid globalization. The term, commercial determinants of health, is defined as *'the strategies and approaches used by the private sector to promote products and choices that are detrimental to health'*.[5] Aggressive marketing by tobacco, alcohol and ultra-processed food industries have contributed to the increasing demand among the consumers and the change of people's behaviours towards unhealthy lifestyle.[6]

Many NCDs causes are preventable by concerted effort from all sectors.[7] This idea is confirmed by the agreement of the member states in the United Nations General Assembly (UNGA) in 2011, which urged all member states to 'engage non-health actors

Table 1. Excise tax rates for alcohol, Thailand, 2017[15]

Type of alcohol	Ad valorem rate (%)	Specific rate (Baht/litre of pure alcohol content)
1. Beer	22	430
2. Wine		
2.1 Wine with retail price less than 1,000 Baht	0	1500
2.2 Wine with retail price above 1,000 Baht	10	1500
3. White spirit	2	155
4. Spirit	20	255

Table 2. Excise tax rates for tobacco, Thailand, 2017[15]

Type of tobacco	Ad valorem rate (%)	Specific rate Baht	Unit
1. Tobacco			
1.1 Cigarette with retail price less than 60 Baht per package	20	1.20	Baht/roll of cigarette
1.2 Cigarette with retail price above 60 Baht per package	40	1.20	Baht/roll of cigarette
2. Cigar	10	1.20	Baht/gram
3. Roll-your-own cigarettes	10	1.20	Baht/gram

and key stakeholders, where appropriate, including the private sector and civil society, in collaborative partnerships to promote health and to reduce non-communicable disease risk factors through building community capacity in promoting healthy diets and lifestyles'.[8] The functions of non-health sectors vary in nature. They may influence NCDs prevention in a positive way such as promoting sport and fitness while some may decelerate the process of NCDs (such as the campaigns against alcohol and tobacco).[9]

Despite an emphasis on the engagement of non-health sectors in the control measures of NCDs, it still lacks tangible examples of how non-health sectors can have seminal roles in addressing NCDs crisis. This article, therefore, aimed to provide examples of NCDs prevention interventions carried out by non-health sectors in Thailand. Most of the information reported in this article was presented in the side meeting of the Prince Mahidol Award Conference (PMAC) on 30 January 2018 (as a preparatory meeting for PMAC 2019) and in the main conference of PMAC 2019. The meeting brought many NCDs champions all over Thailand to share their knowledge, experiences and successful (or unsuccessful) stories related to NCDs prevention in the fields. The meeting participants included representatives from the Ministry of Public Health, Ministry of Finance, Department of Public Relation, private companies, and academics.

The following discussion highlights how NCDs prevention can be accelerated by non-health sectors: (i) taxation policy, (ii) voluntary lactation policy in workplace, (iii) community health promotion intervention and, (iv) media advocacy: media for health.

Taxation Policy

Fiscal policy is an economic tool used for many purposes including raising revenue, redistributing resources and changing population behaviour.[10] Taxation is also part of the fiscal policy, which has been used to promote health for the population for many decades. Products that are mainly the target of taxation are tobacco, alcohol, and sugar sweetened beverages (SSBs).[11,12] The WHO has identified taxation as one of the 'best-buy' strategies for NCDs prevention. The best-buy strategies mean measures that are cost-effective with favourable health outcomes.[13] Theoretically, taxes always influence people's purchasing behaviour.[14]

Thailand has just reformed the excise tax structure for alcohol, tobacco, and SSBs in September 2017. The Excise Department has worked closely with Ministry of Public Health, academics and non-governmental organization (NGOs) to gather related evidence on feasibility and impact of taxation. The main aim of tax restructuring was to reduce the consumption of unhealthy commodities in the

population. Alcohol tax rate is now proportionate to alcohol content. Tobacco tax rate has grown double from 20% to 40% since 2019. The tax rate for SSBs also varies according to the products' sugar content. Any SSBs containing more than 6 grams of sugar per 100 millilitres will be taxed for 0-14% for ad valorem and 0.1-1 Baht (approximately US$ 0.003-0.03) per litre for a specific rate of sugar content. The specific tax rates will be increased after 2 years of a grace period to a maximum of 5 Baht per litre for fruit and vegetable juice, soda, and carbonated drinks and of 44 Baht per litre for beverage concentrates by 2023 and onwards.[15] Table 1-3 present the excise tax rates for tobacco, alcohol and SSBs based on the Excise Tax Act B.E. 2560.

The reformed excise tax structure echoes the important role of the Department of Excise in health promotion. Chaiyasong et al. suggested that the consumption behaviour of the Thai population is likely to be changed after the tax reformulation. Prices of beer, white spirit, and spirit are estimated to increase by 3.5%, 18.0%, and 0.2%, respectively. Alcohol consumption is projected to reduce by 2.8% or 10.4 million litres equivalent.[16] Price of SSBs is likely to increase by 12.5% and several SSBs products are aiming to reduce sugar content.[17] Consequently, there will be more revenue from tobacco and alcohol taxes dedicated to health promotion activities through the Thai Health Promotion Foundation (ThaiHealth).[18] In

2017, over US$ 129 million fund from excise tax were spent on NCDs campaigns.[19] Over the past 15 years, the collective efforts of the ThaiHealth and relevant partners have contributed to better health outcomes, reduction of tobacco and alcohol consumption, and increase in moderate-intensity exercise.[19]

Voluntary Lactation Policy in Workplace

Breastfeeding is confirmed by many studies as one of the most effective strategies to prevent the babies against obesity, diabetes, and cancer as well as to provide effective immunisation.[20] The WHO has recommended all mothers to exclusively breastfeed their babies for minimum six months as breastfeeding can benefit both mothers and babies.[13] However, as more women are now in the labour market, it is difficult for many employed mothers to continue breastfeed up to six months. One of key facilitating factors for breastfeeding is arranging breastfeeding-friendly environment in the workplace.[21,22]

One of the companies presented in the PMAC provided a showcase on how breastfeeding can be implemented in the workplace. The company has fully endorsed breastfeeding-friendly workplace policy since 2011 with strong support from the Department of Labour Protection and Welfare. The company also works closely with nearby health centres and the Thai Breastfeeding Centre Foundation in many activities, such as providing breastfeeding

Table 3. Excise tax rates for sugar sweetened beverages (SSBs), Thailand, 2017[15]

Type of beverages	Ad valorem rate (%)	Sugar content (gram/100 ml.)	Specific rate, based on sugar content (Baht/Litre)			
			16/09/2017 - 30/09/2019	1/10/2019 - 30/09/2021	1/10/2021 - 30/09/2023	1/10/2023 - 30/09/2025
1. Soda, no sugar added	14	-	-	-	-	-
2. Carbonated soft drink with added sugar or other sweeteners or flavour	14	≤6	0.0	0.0	0.0	0.0
		>6-8	0.1	0.1	0.3	1.0
		>8-10	0.3	0.3	1.0	3.0
		>10-14	0.5	1.0	3.0	5.0
		>14-18	1.0	3.0	5.0	5.0
		>18	1.0	5.0	5.0	5.0
3. Fruit juice and vegetable juice	10	≤6	0.0	0.0	0.0	0.0
		>6-8	0.1	0.1	0.3	1.0
		>8-10	0.3	0.3	1.0	3.0
		>10-14	0.5	1.0	3.0	5.0
		>14-18	1.0	3.0	5.0	5.0
		>18	1.0	5.0	5.0	5.0
4. Beverage concentrates	0	≤6	0.0	0.0	0.0	0.0
		>6-8	0.1	0.1	0.3	1.0
		>8-10	0.3	0.3	1.0	3.0
		>10-14	0.5	1.0	3.0	5.0
		>14-18	1.0	3.0	5.0	5.0
		>18	1.0	5.0	5.0	5.0

information to and arranging breastfeeding training for mothers. Besides, the company does not allow formula companies to intervene with breastfeeding process.

The key successes from this practical intervention are attributed to the vision and leadership of employers and the close collaboration with other partners. However, challenges still exist, especially for the incoherence between WHO breastfeeding recommendation and the Thai law. According to the Labour Protection Act B.E. 2541, a mother is allowed to have 90 days for maternity leave, in which a mother will get fully paid from her employer and the Social Welfare Fund.[23] This means most mothers likely return to work before completing the 6-months exclusive breastfeeding period.

The case study above attests that leadership and vision of the employers are indispensable to the success of NCDs prevention measures.[24] Tubsart et al. also confirmed that having lactation room policy in the workplace is feasible given the support of the employers. The support can be in many forms, such as setting policy agenda, granting budgets, and disseminating information on breastfeeding.[25] The balancing of the company profit and quality of life of employees is clearly seen from this case study. However, transferring this practice to other workplaces is doubtful. As mentioned earlier, one of the most powerful factors for success breastfeeding policy in workplaces is the support from employers.[26] In reality, not all workplaces have the employers who are such supportive.[27] Therefore, campaigns to raise awareness and support positive attitudes of breastfeeding among employers with extensive support from the authorities (such as Ministry of Labour and Ministry of Public Health) are necessary to expand the implementation of this policy to a wider scale.[25,28]

Community Health Promotion Intervention

A case study was presented regarding Mueang Ang Thong Municipal Office, Mueang District, Ang Thong Province where NCDs prevention programs originated by the local residents. The municipality has set the city strategy as 'Promote good health and prevent all risk factors for all populations in all age groups in the community'. Many activities have been instigated, creating self-help groups for physical activities among the elderly, and raising awareness of NCDs through local wisdom such as local songs and lullabies. The city also links these activities with tourism business. The local dances of the elderly are also used to attract revenue from the city guests. The contributory factor for this success is due to adequate financial support from the community itself in addition to extra-revenue from the business sector in the area and the ThaiHealth. Moreover, schools and monasteries have engaged in the campaigns.

The story above is comparable to 'the North Karelia' project in Finland, which was introduced in the early 1970s. The main objective of the project was to reduce the increasing prevalence of CVDs. The intervention was based on the practical idea of life-style modification and environment, together with the community participation.[29] After four decades of the project operation, it is found that the coronary artery disease mortality reduced substantially by 84%.[30,31]

It is worth noting how Mueang Ang Thong gains strong support from the communities. One of the key explanations is the utilisation of local culture and tradition to NCDs prevention campaigns.[31] This, among other things, makes the local residents conform to the campaigns and agree to change their behaviours.

Media Advocacy: Media for Health

Media advocacy is not generally mentioned in the public health field. However, it is very useful to promote behavioural changes among various sectors of the society.[32,33] The Thai Public Broadcasting Service (Thai PBS) is a public media institution in Thailand. Thai PBS is established under the Thai Public Broadcasting Service Act, B.E. 2551. Its legal body is a state agency that does not belong to the Government. Its institutional mission is to provide and inform the public with diverse educational and entertainment programs while strictly abiding to the code of media ethics.[34]

Since 2018, the Thai PBS has committed to broadcast campaigns to create healthy environment and promote healthy behaviour of populations through three main communication channels: on air, online and on ground. The reported content is adapted to meet the nowadays audiences' favours while still keeping the main ideas of NCDs prevention. Therefore, it is not exaggerating to mention that the Thai PBS is serving as 'media for health' in the Thai society; and indeed, the country needs more and more media for health in light of the rising trend of NCDs in the modern world.

Remaining Challenges and the Way Forward

Several examples were illustrated on how various sectors beyond the health field could play seminal role in NCDs prevention. However, one of the key challenges is how to monitor and evaluate the success of these programs while taking into account the fact that behavioural changes need time and are multi-faceted.[35] Innovative means of monitoring and evaluation are required and these are critical tasks for modern-day academia. Though the aforementioned examples are mainly from the non-health sectors, it does not mean that the role of the government can be neglected. All of the above examples cannot be successful without continuing support from the state; and this support must be seamlessly linked at all levels.

Conclusions

This article presented four examples of NCDs prevention strategies which are managed by non-health sectors. As root causes of NCDs involve various social determinants of health, which cannot be addressed solely by the health sector. The role of media, communities and private sectors in NCDs prevention could not be ignored. Without seamless collaborations between the health and non-health sectors, the quest towards the world free of preventable NCDs is still a long way to go.

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