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Polio Seroprevalence in Thailand: Assessment of Outbreak Risk by Age Cohorts

Tanapol Wangteeraprasert[1,*], Jiraphongsa C[1], Guntapong R[2], Singchai P[2], Chompook P[3], Tharmaphornpilas P[4]

1 Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, Thailand
2 National Institute of Health, Department of Medical Sciences, Ministry of Public Health, Thailand
3 Faculty of Public Health, Thammasat University, Thailand
4 Bureau of General Communicable Diseases, Department of Disease Control, Ministry of Public Health, Thailand

* Corresponding author, email address: ponthana83@hotmail.com

Abstract

We conducted a serological survey to evaluate the population's antibody level against three types of polio virus and identify high risk groups. We analyzed stored serum samples from a hepatitis immunity study conducted in 2004 on people born between 1928 and 2004. These samples were categorized into nine age cohorts and selected by random sampling. Antibody titers were tested by micro-neutralization. A protective level was defined as greater than 1:8. Protective antibody level against poliovirus and geometric mean titer (log2 reciprocal) were described by types of polio virus in the vaccine and birth cohorts. A total of 1,712 samples were tested. Protective antibody level against poliovirus type 1 was 90.9% while that of type 2 was 94.7% and type 3 was 83.9%. Means titers were 6.0 for type 1, 6.7 for type 2 and 4.9 for type 3. In the different birth cohorts, the antibody levels were the lowest against poliovirus type 2 (89.9%) in those who were born during 1955-1964. For poliovirus types 1 and 3, percentages in the 1975-1984 birth cohorts were less than 80%. Protective antibody level against the three types of poliovirus among the population in Thailand was assumed to be sufficient to generate herd immunity. People born during 1975-1984 were at risk and should be targeted for immunization if a polio outbreak occurred.

Key words: polio, sero-surveillance, immunity, population, Thailand

Introduction

Polio is a viral disease which can cause muscle weakness and paralysis.[1] The World Health Organization (WHO) concerned about the possible spread of poliovirus and supports vaccination campaigns to eliminate the disease.[2] Oral polio vaccine (OPV), also known as trivalent oral polio vaccine, is a live-attenuated vaccine that contains types 1, 2 and 3 Sabin strain poliovirus.[3] There are other types of polio vaccine available such as monovalent OPV (one type of poliovirus), bivalent OPV (two types of poliovirus) or inactivated polio vaccine (three types of killed poliovirus). Since 1977, three doses of OPV (OPV3) have been given to Thai children aged two months, four months and six months under the expanded program on immunization (EPI).[4] During 1991-1999, an additional dose of OPV (OPV4) was given to children at age two. Since 2000, the fifth dose of OPV (OPV5) were introduced to the EPI for children at age four.[5] Additionally, National Immunization Days (NIDs), began in 1995,[6,7] provided supplementary dose of polio vaccine to children under 10 and five in 2001.[7]

The last case of wild-type poliovirus (WPV) in Thailand was reported in 1998. One case of type 2 immunodeficiency associated vaccine-derived poliovirus (VDPV), a vaccine strain of poliovirus that genetically mutates to cause poliomyelitis, was identified in Thailand in 2003.[8]

In 1980, the first national vaccine coverage survey carried out by the Ministry of Public Health found that the coverage of OPV3 was 21.2%. In the most recent survey completed in 2008, OPV3 coverage was 98.7% and OPV5 coverage was 79.4%.[5]

However, even with the successful EPI and NID programs, Thailand needs to continue to monitor the polio prevention and control program closely due to possible recurrence of the disease. There have been several re-emerging and cross-border polio outbreaks in the region. In 2005, Indonesia had an outbreak of 299 polio cases after 10 polio-free years.[9] In 2010, Myanmar had one imported polio case, as did China in 2011.[10] Additionally, China, Myanmar, Cambodia, and Philippines had experienced VDPV outbreaks since 2001.[11] Such events put Thailand at risk and raised the need to ensure that Thai population had

sufficient immunity to prevent reintroduction of poliovirus.

The objectives of our study, using secondary data and samples from a serological survey conducted earlier, were to evaluate the proportion of Thai population who had a protective antibody level against the three types of poliovirus, explore the mean titers among the population in different age groups and identify population at risk.

Methods

Serum Specimens

The serum specimens tested in this study were selected from samples of the hepatitis immunity study (HIS) conducted by Ministry of Public Health, Thailand in 2004. These samples were collected from four regions in Thailand, represented by Chiang Rai, Udon Thani, Chon Buri and Nakhon Si Thammarat Provinces.[12] Samples collected from one provincial hospital and two randomly selected community hospitals in each participating province were used. Healthy children attending well-baby clinics and every patient were included in the study, except those with chronic illnesses, undergoing immunosuppressive therapy, having clinical signs or symptoms associated with human immunodeficiency virus (HIV) or immunodeficiency diseases. Serum specimens were taken from the participants, coded with a sequential number and stored in a temperature-controlled freezer at the Faculty of Medicine in Chulalongkorn University. The serum specimens were thawed to determine seroprevalence of antibodies to measles, mumps and rubella in a study by another investigating team in 2009.[13]

Serum specimens were categorized into nine birth cohorts, spanning the years from 1928 to 2004. Estimated proportion of protective antibody for each birth cohort, ranging from 0.60-0.85, were used to calculate sample size with 10% margin of error. We added 20% to the calculated sample size to compensate for attrition (Table 1). In each cohort, we randomly selected the first serum sorted by order of collection, and then selected the next serum at regular intervals. Serum with volume less than 0.35 mL were excluded and replaced by unselected samples.

Antibody Assay

Polio antibody levels were tested by micro-neutralization assay conducted at the National Institution of Health (NIH).[14] Reference strains of Sabin types 1, 2 and 3 produced by the National Institute for Biological Standard and Control, United Kingdom were used. Serial two-fold dilutions of the serum were tested up to 1:1,024. The protective levels for poliovirus types 1, 2 and 3 were those samples with antibody titer greater than 1:8.[15]

Data Analysis

Percentages of protective antibody against three types of poliovirus with 95% confidence interval (95% CI) were described for each cohort. Geometric mean titer (GMT) and 95% CI of GMT were presented as log2 reciprocal titers (log2 titer 1: 8 = 3). To obtain the average results for the total population, data was weighted by age distribution of Thai population in 2004.[16]

Ethical Consideration

The code from the HIS, the identifier for the serum samples, could not be linked to individual person. The study was reviewed and approved by the Ethical Review Committee for Research in Human Subjects, Ministry of Public Health, Thailand (20/2554).

Results

Among the 1,717 serum samples, five specimens were denatured and a total of 1,712 samples were analyzed for antibody level. Among Thai population, protective

Table 1. Stored and tested serum by birth cohorts from 4 regions in Thailand, 2004

Birth cohort	Number of stored serum	Estimated proportion of protective immunity	Calculated sample	20% plus calculated sample	Tested serum
1928-1954	840	0.70	165	198	197
1955-1964	760	0.70	165	198	198
1965-1974	789	0.60	256	307	308
1975-1979	407	0.60	256	307	303
1980-1984	396	0.60	256	307	306
1985-1989	569	0.75	128	154	154
1990-1994	649	0.85	68	82	82
1995-1999	966	0.85	68	82	82
2000-2004	850	0.85	68	82	82
Total	6,226	-	1,430	1,717	1,712

antibody level against poliovirus was 90.9% for type 1, 94.7% for type 2 and 83.9% for type 3 (Table 2). Thai people born during 2000-2004 had 100% protective antibody against all three poliovirus types. Percentages for poliovirus types 1 and 3 decreased in cohorts born before 2000. The lowest percentages were among the 1980-1984 birth cohorts for poliovirus types 1 (74.5%) and 3 (66.0%), then increased by age. People who were born after 1990 had 100% protection for poliovirus type 2, which then decreased by age. All nine birth cohorts had protective antibody against poliovirus type 2, with the lowest (89.9%) among the 1955-1964 birth cohort.

Log2 antibody titers against poliovirus were 6.0 for type 1, 6.7 for type 2 and 4.9 for type 3. The titers had a similar trend with that of the percentages of protective antibody (Table 2 and Figure 1). The highest titers were in the 2000-2004 birth cohorts. Mean titers decreased to the lowest values in the 1980-1984 birth cohorts for polio types 1 and 3, and

the 1955-1964 birth cohorts for type 2. All mean titers were higher than three (log2 titer of 1:8).

Discussion

The protective antibody level against poliovirus among the general Thai population who had access to hospital was sufficient to prevent re-introduction of polio. However, this conclusion should be used with caution for population who lived in remote isolated areas or in areas with inadequate vaccine coverage. Additionally, this finding should not be assumed to apply to foreign migrant workers whom were not included in the study design. In other studies, protective herd immunity had been estimated between 80-86%.[15,16]

The protective proportion and mean titers of antibody among Thai people was less than those in high income countries such as Netherlands and Germany[17,18] possibly because of the interference from concurrent infections with other enterovirus or

Table 2. Protective antibody level and 95% confidence interval (95% CI) against 3 types of poliovirus by birth cohorts in Thailand, 2004

Birth cohort	Number of test	Type 1		Type 2		Type 3	
		Percent	95% CI	Percent	95% CI	Percent	95% CI
1928-1954	197	95.9	92.2-98.2	94.9	90.9-97.5	86.8	81.3-91.2
1955-1964	198	95.0	90.9-97.6	89.9	84.8-93.7	82.8	76.8-87.8
1965-1974	308	84.4	80.0-88.2	91.9	88.1-94.6	82.1	77.3-86.2
1975-1979	303	76.2	71.0-80.8	93.1	89.4-95.6	69.3	63.7-74.4
1980-1984	306	74.5	69.2-79.2	95.8	92.7-97.6	66.0	60.4-71.3
1985-1989	154	96.8	92.6-99.0	96.1	91.7-98.6	83.1	76.3-88.7
1990-1994	82	98.8	93.4-100.0	100.0	100.0-100.0	93.9	86.3-98.0
1995-1999	82	98.8	93.4-100.0	100.0	100.0-100.0	96.3	89.7-99.2
2000-2004	82	100.0	100.0-100.0	100.0	100.0-100.0	100.0	100.0-100.0
Total*	1,712	90.9*	-	94.7*	-	83.9*	-

Weighted by age distribution of Thai population in 2004 (Bureau of Policy and Strategy, Thailand)
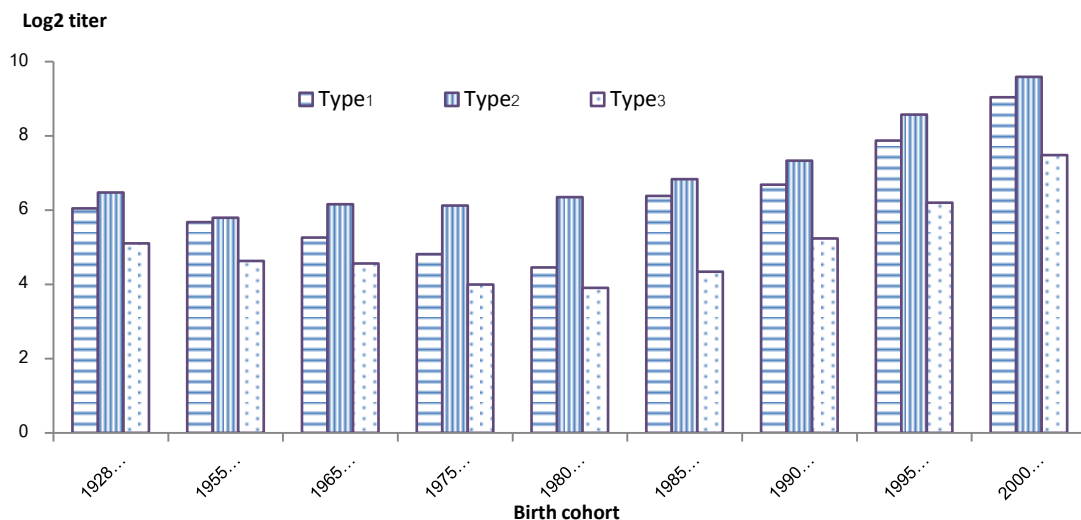

Figure 1. Mean and 95% confidence interval (95% CI) of antibody titers against 3 types of polio virus by birth cohorts in Thailand, 2004

diarrheal diseases. Moreover, higher levels of maternal antibody in low to middle income countries could interrupt increasing of immunity during childhood.[19]

The proportion of persons with protective antibody was higher in the earlier birth cohorts, presumably because these age groups had been exposed to wild poliovirus. People born during 1965-1984 had a lower protective immunity than that of other birth cohorts. This might be due to the start-up of the EPI in 1977 when not everyone received the polio vaccine, yet the circulation of wild poliovirus decreased, and thus lowering the chance of natural infection. This result was similar to the Republic of Korea's seroprevalence data which immunity is lower among middle-aged population.[20] The proportion of the population with protective antibody also increased among later birth cohorts as polio vaccination coverage increased.

Among the three types of poliovirus, type 2 had the highest percentage of protective antibody at 90-100%. This finding was similar to other studies[21,22] that showed high immunogenicity of type 2 vaccines. The high percentage of protective levels of type 2 antibodies makes infection from type 2 VDPV less likely.

The low percentage of protective antibody against poliovirus type 3 was also similar to other studies[20-22]. This might be explained by low sero-conversion rate or potency of OPV type 3.[23] Other studies had shown that the level of protective antibody against poliovirus type 3 might be lower than other types of poliovirus.[24,25]

The protective titer for poliovirus types 1 and 3 for people born during 1975-1984 was lower than 80%, which put this population at risk of a polio outbreak. This underlined the importance of rapid OPV immunization in this group if there was a wild or VDPV outbreak in the country. The person in this birth cohort should also receive OPV or IPV vaccine if plan to visit high risk countries. A pre-outbreak OPV booster might be considered as a preventive measure. However, this would need to be weighed against the risk of polio importation, outbreaks and vaccine side effects in adults, especially vaccine associated polio paralysis (VAPP). The advantage of booster doses was supported by a study in Cuba in which eight OPV doses generated immunity against poliovirus higher than six OPV doses.[26]

Following the polio eradication and endgame strategy plan 2013-2018, replacing trivalent OPV with bivalent OPV (only poliovirus types 1 and 3) in routine immunization program of Thailand was likely to have no problem from the switch because of globally eliminated wild type poliovirus type 2[27] and high immunity against poliovirus type 2 among population[26,27]. Advantages of the bivalent OPV include better immunity against poliovirus types 1 and 3, with at least 35% more effectiveness than trivalent OPV, and no VAPP from poliovirus type 2[28].

There were some limitations in this study. First, as samples were collected from only four provinces, they might not be representative of the country. However, those provinces were located in four of the Thai geographic regions, so they captured a wide range of the population. Even though the serum samples were collected more than 10 years ago, the immunity results could represent the present situation because all the subjects would have or have not received OPV before 2004 and there has been no report of polio in the country since 2003.

In conclusion, Thailand was not at risk for polio outbreak. The protective levels for poliovirus types 1, 2 and 3 antibodies among Thai population were high enough to generate herd immunity. Because of the low percentage of antibodies to types 1 and 3, persons in 1975-1984 birth cohorts should be targeted for immunization if an outbreak occurred in Thailand or those persons plan to visit high risk countries.

Acknowledgement

Suggested Citation

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References

1. Hamborsky J, Kroger A, Wolfe S, editors. Epidemiology and prevention of vaccine-preventable diseases. 13th ed. Washington D.C: Public Health Foundation; 2015. p. 297-310 [cited 2015 Feb 2].

<http://www.cdc.gov/vaccines/pubs/pinkbook/polio.html#features>.

2. Centers for Disease Control and Prevention. Updates on CDC's polio eradication efforts. 2015 Apr 10 [cited 2015 Apr 22]. <http://www.cdc.gov/polio/updates/>.

3. Centers for Disease Control and Prevention. Polio and polio vaccine. 2012 [cited 2015 Apr 7]. <www.cdc.gov/vaccines/pubs/pinkbook/downloads/17-Polio.pdf>.

4. History of immunization in Thailand. In: Chokpaiboonkit K, Trishnananda M, Chunsuttiwat S, Tharmaphornpilas P, editors. Vaccine and immunization 2007. Nonthaburi: Ministry of Public Health; 2007. p. 13-24.

5. Warinsathien P. Vaccine coverage of diphtheria, tetanus, pertussis and polio among 1-2, 2-3 and 5-6 years age. In: Tharmaphornpilas P, Ratchumroensuk A, editors. Vaccine coverage survey, Thailand 2008. Nonthaburi: Ministry of Public Health, Thailand; 2008. p. 33-8.

6. Birmingham ME, Aylward RB, Cochi SL, Hull HF. National immunization days: state of the art. J Infect Dis. 1997 Feb;175 Suppl 1:S183-8.

7. Yoocharoen P, Warinsathien P, Ratchumroensuk A, Ratchumroensuk P. Vaccination. In: Tharmaphornpilas P, editor. Polio Eradication Guideline. Nonthaburi: Ministry of Public Health, Thailand; 2005. p. 21-3.

8. World Health Organization. Polio lab network quarterly update. 2004 [cited 2015 Apr 22]. <http://www.who.int/immunization_monitoring/VolXIssue4Dec04.pdf>.

9. Resurgence of wild poliovirus type 1 transmission and consequences of importation--21 countries, 2002-2005. Morb Mortal Wkly Rep. 2006 Feb 17;55(6):145-50.

10. MacInnis L. Polio afflicts child in Myanmar, vaccinations planned. Reuters. 2011.

11. Global Polio Eradication Initiative. Circulating vaccine-derived poliovirus (cVDPV) 2000-2013. 2013 [cited 2013 May 2]. <http://www.polioeradication.org/Dataandmonitoring/Poliothisweek/Circulatingvaccinederivedpoliovirus.aspx>.

12. Chongsrisawat V, Yoocharoen P, Theamboonlers A, Tharmaphornpilas P, Warinsathien P, Sinlaparatsamee S, et al. Hepatitis B seroprevalence in Thailand: 12 years after hepatitis B vaccine integration into the national expanded programme on immunization. Trop Med Int Health. 2006 Oct;11(10):1496-502.

13. Tharmaphornpilas P, Yoocharean P, Rasdjarmrearnsook AO, Theamboonlers A, Poovorawan Y. Seroprevalence of antibodies to measles, mumps, and rubella among Thai population: evaluation of measles/MMR immunization programme. J Health Popul Nutr. 2009 Feb;27(1):80-6.

14. World Health Organization. Manual for the virological investigation of polio. Geneva: World Health Organization; 1997 [cited 2013 May 2]. <whqlibdoc.who.int/hq/1997/WHO_EPI_GEN_97.01.pdf>.

15. Arya SC, Agarwal N. Reassessing the cutoff level for poliovirus antibody in patients after successful chemotherapy for leukemia or hematopoietic stem cell transplantation. Clin Infect Dis. 2007 Aug 1;45(3):397; author reply 398-9.

16. Thailand. Bureau of Policy and Strategy. Ministry of Public Health. Important health information. 2557.

17. Conyn-Van Spaendonck MA, de Melker HE, Abbink F, Elzinga-Gholizadea N, Kimman TG, van Loon T. Immunity to poliomyelitis in The Netherlands. Am J Epidemiol. 2001 Feb 1;153(3):207-14.

18. Diedrich S, Claus H, Schreier E. Immunity status against poliomyelitis in Germany: determination of cut-off values in International Units. BMC Infect Dis. 2002 Feb 6;2:2.

19. Sutter RW, Kew OM, Cochi SL. Poliovirus vaccine-live. In: Plotkin SA, Orenstein WA, Offit PA, editors. Vaccines. 5th ed. Philadelphia: WB Saunders; 2008. p. 631-85.

20. Kim HJ, Hwang S, Lee S, Kwon Y, Park K, Park YJ, et al. A national cross-sectional study for poliovirus seroprevalence in the Republic of Korea in 2012: implication for deficiency in immunity to polio among middle-aged people. BMC Infectious Diseases. 2015;15(164):1-7.

21. Diedrich S, Schreier E. Status of immunity against poliomyelitis. Polio serosurvey in 1993. Dtsch Med Wochenschr1995 Feb 24;120(8):239-44. German.

22. Gidding HF, Backhouse JL, Gilbert GL, Burgess MA. National serosurvey of poliovirus immunity in Australia, 1996-99. Aust N Z J Public Health. 2005 Feb;29(1):48-52.

23. Patriarca PA, Wright PF, John TJ. Factors affecting the immunogenicity of oral poliovirus vaccine in developing countries: review. Rev Infect Dis. 1991 Sep-Oct;13(5):926-39.

24. Frantzidou F, Diza E, Halkia D, Antoniadis A. A seroprevalence study of poliovirus antibody in the population of northern Greece. Clin Microbiol Infect. 2005 Jan;11(1):68-71.

25. Mastroeni I, Patti AM, Fabrizi A, Santi AL, Manduca AM, Vescia N, et al. Immunity status against poliomyelitis in persons 13-14 years old living in Rome. Vaccine. 1997 Apr-May;15(6-7):747-50.

26. Mas Lago P, Ramon Bravo J, Andrus JK, Comellas MM, Galindo MA, de Quadros CA, et al. Lessons from Cuba: mass campaign administration of trivalent oral poliovirus vaccine and seroprevalence of poliovirus neutralizing antibodies. Bull World Health Organ. 1994;72(2):221-5.

27. Apparent global interruption of wild poliovirus type 2 transmission. Morb Mortal Wkly Rep. 2001 Mar 30;50(12):222-4.

28. Sutter RW, John TJ, Jain H, Agarkhedkar S, Ramanan PV, Verma H, et al. Immunogenicity of bivalent types 1 and 3 oral poliovirus vaccine: a randomised, double-blind, controlled trial. Lancet. 2010 Nov 13;376(9753):1682-8. Epub 2010 Oct 25.

An Investigation of Human Brucellosis and Goat Farm Network Analysis in Ratchaburi Province, 2013

Thanidtha Te-chaniyom[1,*], Sinanan N[1], Watthanakul M[2], Choomkasean P[1], Chuxnum T[1], Smithsuwan P[1], Pimprapai W[3], Hinjoy S[1]

1 Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, Thailand
2 Ratchaburi Provincial Livestock Office, Department of Livestock Development, Ministry of Agriculture and Cooperatives, Thailand
3 Faculty of Veterinary Medicine, Kasetsart University, Thailand
 * Corresponding author, email address: Polarbear_pig@hotmail.com

Abstract

In April 2013, a person was confirmed to have *Brucella melitensis* in Chombueng District; and Ratchaburi Provincial Health Office notified about this patient to Bureau of Epidemiology. As the patient was a goatkeeper in a farm that had animal movement with other goat farms, active human case finding was conducted. History of goat movement among the related goat farms was explored to identify key persons for disease transmission in the network. Serum samples from 53 goatkeepers in 28 goat farms and two livestock officials who investigated the farm with confirmed case were tested for brucellosis. Only one goatkeeper was identified as a probable case, with attack rate of 1.8%. Goat serum specimens from 12 out of total 34 goat farms were tested positive for *Brucella*. In egocentric network, 44 nodes were included in the network analysis, including 34 goat farms, four slaughterhouses and six merchant's goat shelters. Visualization from network analysis was useful to identify goat farm networks at risk of disease spreading. Key person in the network with the highest degree centrality (26) and betweenness centrality (2455.462) was identified as a merchant's goat shelter with a goat tested positive for brucellosis. Hence, knowledge on brucellosis prevention and control should be disseminated among goatkeepers and merchants in that network. The information should also be used for strengthening communication between goat farmers and local livestock officials.

Key words: outbreak, investigation, brucellosis, Ratchaburi Province, goat farm network

Introduction

Brucellosis is a disease caused by *Brucella* spp.[1] which is a facultative intracellular Gram-negative cocco-bacillus.[2] *Brucella melitensis* is the most important zoonosis among *Brucella* spp. as it is the most common species found in goats and the most virulent to humans.[1,3] Brucellosis poses severe economic losses in affected goat farms.[4] The cost for controlling brucellosis in a herd of 60 goats in Thailand was estimated at 7,000 USD[5], and loss of work productivity due to prolonged illness can lead to socioeconomic problems as well.[1]

In April 2013, Ratchaburi Provincial Health Office notified Bureau of Epidemiology of a confirmed brucellosis case. The case was a 66-year-old male goat farmer with diabetes mellitus. He was admitted on 4 Apr 2013 due to intermittent fever, weight loss about five kilograms and myalgia since 2012. On 5 Apr 2013, laboratory testing of his specimen reported gram-negative coccobacilli and he was confirmed to have *Brucella melitensis* by hemoculture on 25 Apr 2013. He had a goat farm since 2012 and recently imported

new goats into his farm from many sources. In 2012, one goat in his farm aborted and that goat was sent back to the originating farm. He often exposed to secretions and placentas while assisting goats giving birth. Furthermore, goats in his farm showed positive results of *Brucella* infection during April 2013. Hence, in May 2013, Bureau of Epidemiology set up a team to conduct an investigation.

Objectives of the investigation were to verify the diagnosis and the outbreak, describe the network of goat farms, identify key persons for disease transmission in the network, and provide recommendations for prevention and control.

Methods

Ratchaburi Province locates in the central region of Thailand, approximately 100 kilometers south of Bangkok. Nine out of total 10 districts have goat farms. It is also one of the provinces where Department of Livestock Development has set up the laboratory surveillance and the monitoring program for brucellosis in goats. The farms in Chombeung and

Saun Pheung Districts which had live goat movement with the confirmed case's farm (index farm) were included in the study. A cross-sectional study was conducted with sampling by snowball technique from the index farm in Chombeung District.

Active Case Finding in Humans

The investigation team reviewed medical records of human brucellosis cases who received treatment during 1 Jan to 24 Apr 2013 in the hospital where the confirmed case admitted. A probable case was defined as a goatkeeper in the network who had fever or intermittent fever, with at least two out of five following symptoms: headache, myalgia, arthralgia, night sweat or orchitis, and positive result for brucellosis using parallel testing by rose bengal test (RBT) and enzyme-linked immunosorbent assay (ELISA). A confirmed case was a probable case who was tested positive for *Brucella* spp by hemoculture.

A questionnaire was used as a tool for face-to-face interview about demographic information, date of onset, clinical signs and risk activities. Serum specimens of goatkeepers from related goat farms that had goat movement with the index farm and livestock officials who investigated in the index farm were collected as well. The specimens were sent to the Department of Medical Sciences for IgM and IgG antibodies testing by RBT and ELISA.

Active Case Finding in Animals

Serum specimens were also collected from goats in the related farms and tested with RBT at Central Veterinary Research and Development Center. Information on herd size and history of brucellosis, sharing goats and movement of goats since 2012, was retrieved as well. A positive farm was defined as a goat farm in the network which had at least one goat tested positive by RBT and reported by Provincial Livestock Office during August 2012 to May 2013. The status of *Brucella* infected goat farms was obtained from database of the routine sero-survey conducted by local livestock offices.

Network Analysis

Network analysis is a tool that can be used to describe linkages between different particular members, including directions, locations and frequencies of activities.[6] Information from network analysis is usually presented in nodes (units of interest) and ties (relationships between each node).[7] This method helps to visualize directions of connections between individuals. Moreover, visual presentations of network analysis can describe important nodes within the network, providing a range calculated from the number or the frequency of linkages and activities.[6]

Quantitative measurements for relationship, including degree centrality and betweenness centrality, can provide relative values of each node.[7] Degree centrality is measured from number of ties related to each node. Non-direction is the total number of paths while direction includes number of in-degree and out-degree paths. Betweenness centrality is a ratio measurement on sum of the shortest path of each pair of nodes.[7] An egocentric network emphasizes interactions or activities related to each particular node.[8]

Partial network analysis was explored from the index farm to other nodes within the study area. Egocentric analysis from the index farm was performed to represent the linkage between nodes and identify the highest centrality node within the network. Network visualization included graphical depictions and network measurement related to degree centrality and betweenness centrality, which were calculated by UCINET 6 program.[9] A node with high value of betweenness centrality means that this node is a high representative of the middle node in this pathway.

Results

Total 34 goat farms were found to have linkage with the index farm in Chombeung and Suan Pheuang Districts.

Active Case finding in Humans

Medical records review in the hospital did not identify new human cases. Total 55 human serum samples were collected, including 53 goatkeepers from 28 goat farms and two livestock officials who investigated the index farm. There were 22 females and 33 males. Median age was 47 years, with age range of 15-67 years old. Out of 53 goatkeepers, 46 were from 25 goat farms in Chombueng District while seven were from three goat farms in Saun Pheung District. Only one goatkeeper was identified as a probable case, with attack rate of 1.8%.

Active Case finding in Animals

Out of total 34 goat farms, 29 farms were located at Chombueng District and five were in Saun Pheung District. Goats from 12 goat farms were tested positive for *Brucella*, including 2 farms identified during August to December 2012 and 10 farms during January to May 2013.

Network Analysis

The egocentric network analysis revealed that total 89 nodes had linkage with the index farm, including 34 goat farms, four slaughterhouses, six merchant's

goat shelters and 45 other locations. Information of 34 goat farms was matched with *Brucella* sero-positive results of goats from Provincial Livestock Office.

Network Visualization

The egocentric network showed relation among goat farms with brucellosis, neighboring farms and merchant's goat shelters during January to May 2013 (Figure 1). After we explored the *Brucella* infection status of goat farms, we found that the merchant's goat shelter A had a goat with brucellosis since August 2012, followed by identification of brucellosis in other farms that received the goats from the merchant's goat shelter A in December 2012, March and April 2013 (Figure 2).
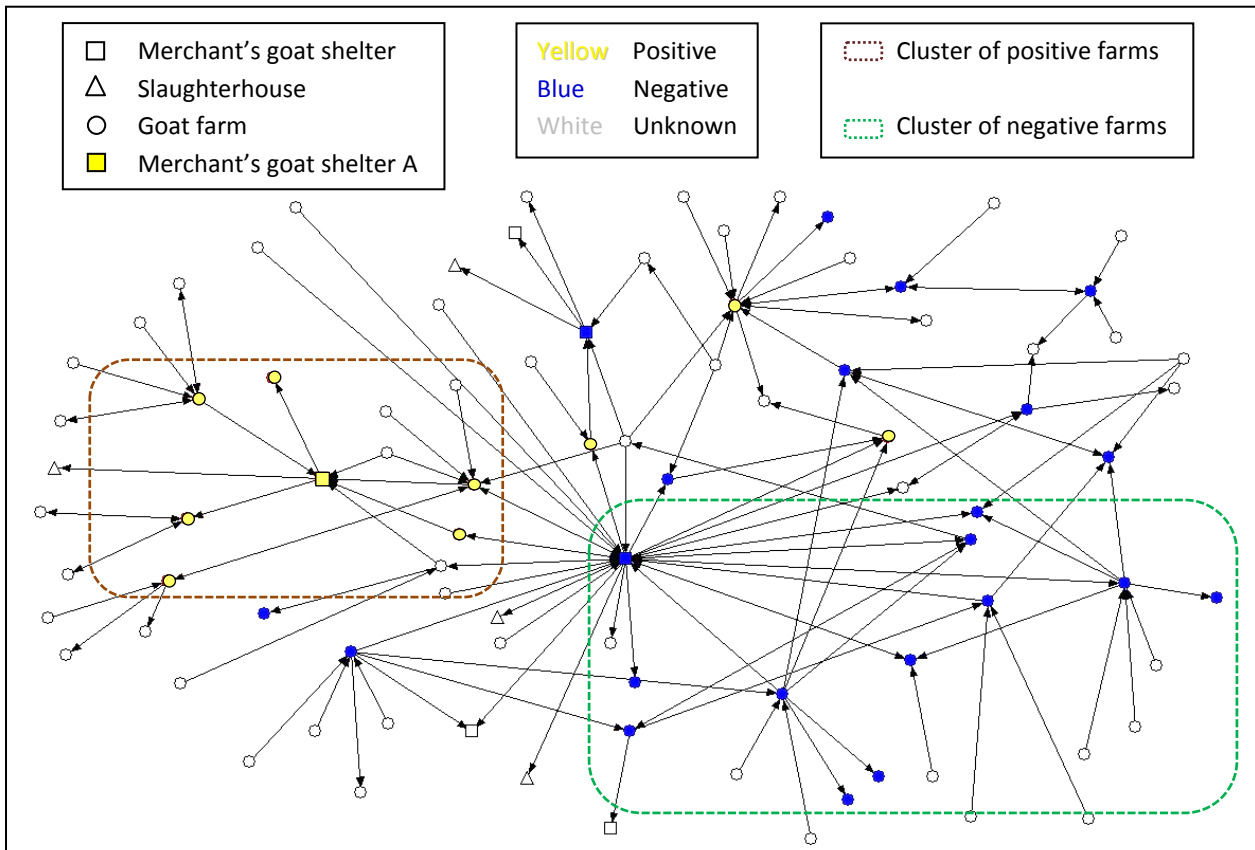

Figure 1. Network analysis of *Brucella* infection in 44 locations related to the first confirmed case's farm, Chombeung and Saun Pheung Districts, Ratchaburi Province, Thailand, 2013
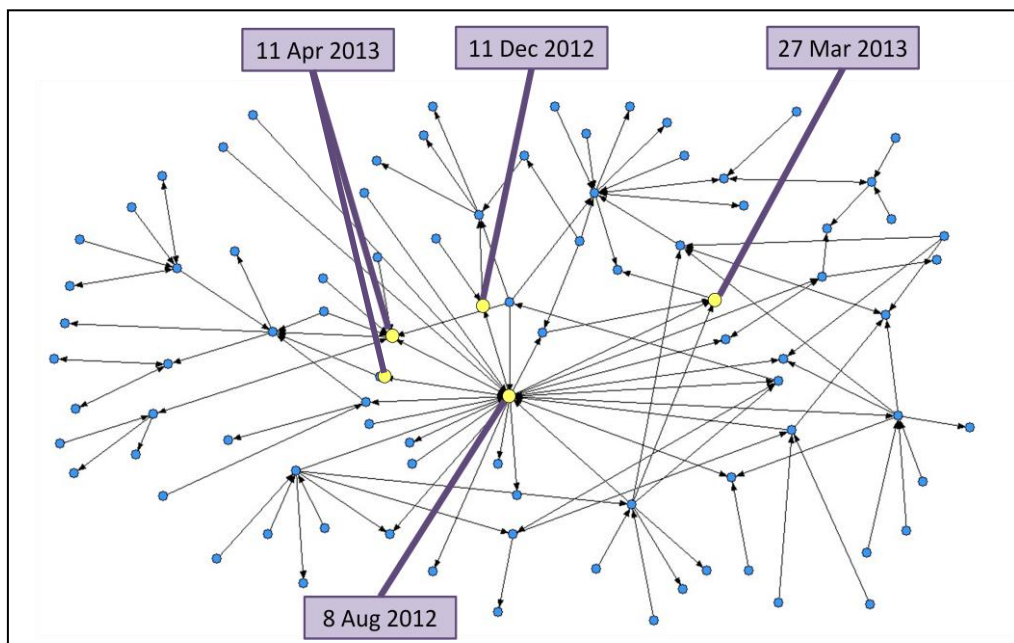

Figure 2. Network analysis of farms with goat positive for brucellosis (yellow circles), stating date of diagnosis, Chombeung and Saun Pheung Districts, Ratchaburi Province, Thailand, 2013

Arrow that pointed towards the node means goat movement into the farm, in-degree, while arrow pointed out of the node states goat movement out of the farm, out-degree. In egocentric network analysis, the highest degree centrality was 26 both in and out degree while the smallest was one tie (Figure 3). Our results revealed a node with highest value for both degree centrality (26) (Figure 3) and betweenness centrality (2455.462) (Figure 4), which was merchant's goat shelter A where goats were raised temporarily for trade. After a goat in the merchant's goat shelter A had brucellosis, the disease later spread to other farms that received the goats from the merchant's goat shelter A, which led to extensive spread of *Brucella* infection in the network.

Discussion

From our investigation, the index case was not included as a new case, as his onset was before 1 Jan 2013. Therefore, one probable case of human brucellosis was identified in Chombeung District, Ratchaburi Province during 2013. The attack rate of probable human case from was only 1.8% which was different from other studies e.g. the one conducted in Petchabun Province with attack rate of 10.3% (4/39).[4] This was probably due to intensive brucellosis control and management activities that have been conducting in the province since 2003 after a human brucellosis outbreak occurred.[5]
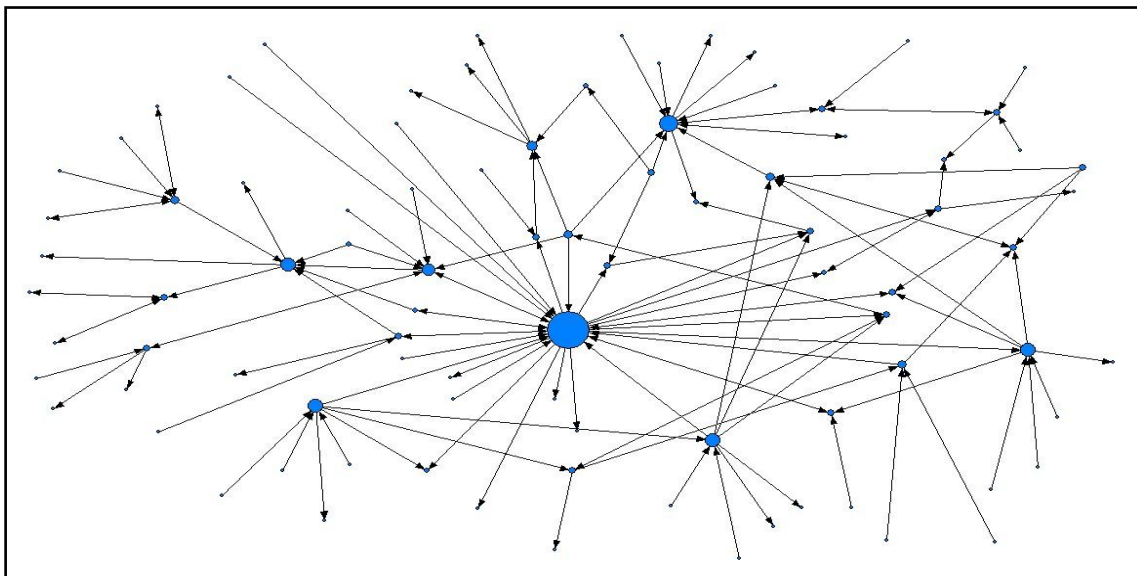
Remark: Size represents degree value.

Figure 3. Network analysis showing degree centrality of 44 locations related to the index farm, Chombeung and Saun Pheung Districts, Ratchaburi Province, Thailand, 2013
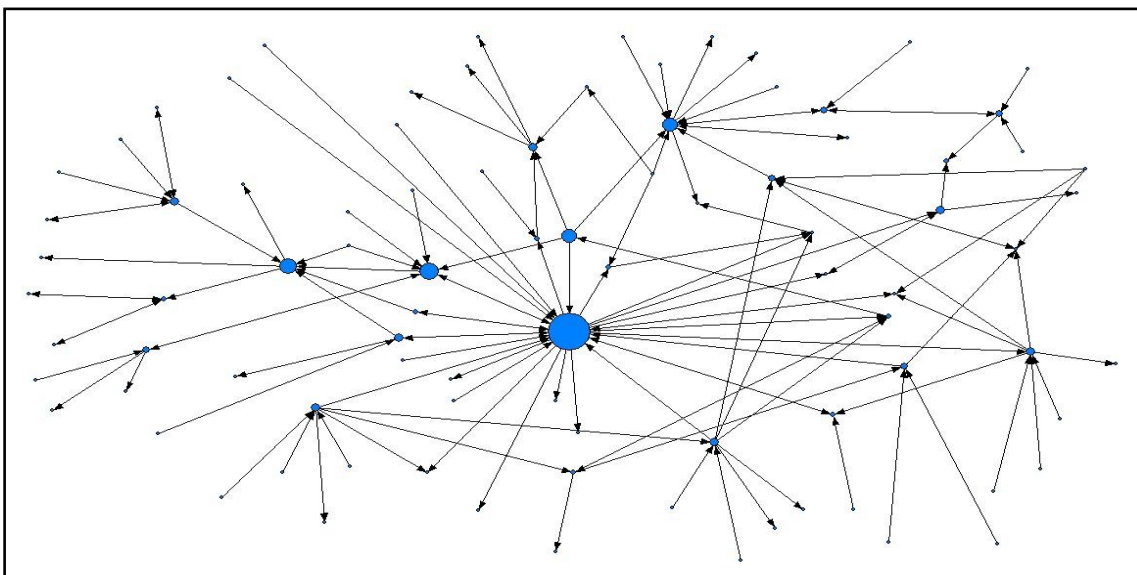
Remark: Size represents degree value.

Figure 4. Network analysis showing betweenness centrality of 44 locations related to the index farm, Chombeung and Saun Pheung Districts, Ratchaburi Province, Thailand, 2013

Some inappropriate methods of farm management were identified in the study. The most inappropriate one was selling infected goats to other farms. This goat-share practice could cause the spread of brucellosis between farms in the network.[1,10] Some farms imported new goats with unknown infection status from other provinces, and thus increase the risk of disease transmission among goats and further spreading to goatkeepers[11].

Goatkeepers and people who exposed to infected goats can then be infected with brucellosis as well. Hence, health knowledge on brucellosis should be distributed among goatkeepers and merchants in the network, and collaboration between goat keepers and livestock officials should be strengthened.

In this study, we demonstrated the use of network analysis to visualize the linkage among the nodes with goat movement. The nodes with high betweenness centrality and degree centrality are the key persons that should be under attention as these nodes can spread the disease to other connected nodes in the network. Thus, in case of limited resources are available, disease control and prevention should be mainly focused on the key persons.[12]

Limitations

This investigation might be subjected to selection bias as some farms that were not referred by the goatkeepers could not include in the study. There might also be information bias due to long incubation period of brucellosis[2,13].

In addition, this study covered only a partial network with egocentric data started at the index farm in Chombeung District and expanded to other nodes in Saun Pheung District. However, we did not include other nodes outside of these two districts.

Although this study revealed the direction of goat movement, frequency between each node was not explored. Moreover, as this study was focused on the herd level, the source of the disease could not be precisely concluded as some farms had introduced goats from many sources.

Conclusion

A probable human brucellosis case was found in the goat farm network of Chombeung and Saun Pheung Districts. Egocentric network started from the index farm and linked with other farms through live goat movement. A key person in the network was identified as a merchant's goat shelter A. Visualization from network analysis was important to identify network and key persons for disease control and prevention. Our recommendations included knowledge distribution among goatkeepers and merchants who were key persons for disease transmission in that network, and strengthening communication between goat farmers and local livestock officials.

Suggested Citation

Te-chaniyom T, Sinanan N, Watthanakul M, Choomkasean P, Chuxnum T, Smithsuwan P, et al. An outbreak of human brucellosis and goat farm network analysis in Ratchaburi Province, 2013. OSIR. 2015 Jun;8(2):7-12.
<http://www.osirjournal.net/issue.php?id=80>.

References

1. Corbel MJ. Brucellosis in humans and animals. Geneva: World Health Organization; 2006.

2. Elzer PH, Hagius SD, Davis DS, DelVecchio VG, Enright FM. Characterization of the caprine model for ruminant brucellosis. Vet Microbiol. 2002 Dec 20;90(1-4):425-31.

3. Ekgatat M. Brucellosis and diagnosis in Thailand. Bangkok: National Institute of Animal Health; 2009.

4. Wongphruksasoong V, Santayakorn S, Sitthi W, Chuxnum T, Doung-ngern P, Pipatjaturon N, et al. Investigation of brucellosis case and death in Chondaen District, Phetchabun Province, Thailand, December 2009. Weekly Epidemiological Surveillance Report. 2010; 41(34): 539-44.

5. Laosiritaworn Y, Hinjoy S, Chuxnum T, Vagus A, Choomkasien P. Re-emerging Human Brucellosis, Thailand 2003. Bulletin of the Department of Medical Services. 2007;32(4):415-23.

6. Benton DC, Fernández Fernández MP. Social network analysis: a tool for the identification of next generation trainers. Collegian. 2014 Dec;21(4):311-8.

7. Penghirun K. Risk factors of foot and mouth disease occurrence on social network of smallholder dairy farmers, Nongpho Dairy Co-Operative Ltd. (Under the Royal Patronage) [thesis]. Nakhon Phathom: Kasetsart; 2013.

8. Valente TW. Social network and health: models, methods, and applications. New York: Oxford University Press; 2010.

9. Borgatti SP, Everett MG, Freeman LC. Ucinet for Windows: software for social network analysis. Harvard, MA: Analytic Technologies. 2002 [cited 2015 Feb 2]. <https://sites.google.com/site/ucinetsoftware/home>.

10. Suddee W. Prevalence and fisk factors associated with *Brucella* spp. infection in meat goats and quantitative release assessment of *Brucella* spp. into Chainat Province by live meat goats importation [thesis]. Nakhon Phathom: Kasetsart; 2011.

11. Mikolon AB, Gardner IA, Hernandez De Anda J, Hietala SK. Risk factors for brucellosis seropositivity of goat herds in the Mexicali Valley of Baja California, Mexico. Prev Vet Med. 1998 Dec 1;37(1-4):185-95.

12. Nöremark M, Håkansson N, Lewerin SS, Lindberg A, Jonsson A. Network analysis of cattle and pig movements in Sweden: measures relevant for disease control and risk based surveillance. Prev Vet Med. 2011 May 1;99(2-4):78-90. Epub 2011 Feb 1.

13. Brucellosis in human and animals: WHO guidance. Geneva: World Health Organization; 2005.

Severe Complicated Malaria in High Risk Areas of Mon State, Myanmar, 2006-2012

Nyi Nyi Lwin[1,*], Kyaw TT[2], Hlaing T[2], Satimai W[3], Niramitsantipong A[3]

1 Yangon Regional Health Department, Ministry of Health, Myanmar
2 National Malaria Control Program, Nay Pyi Taw, Ministry of Health, Myanmar
3 Bureau of Vector Borne Disease Control, Department of Disease Control, Ministry of Public Health, Thailand

* Corresponding author, email address: mr.nyinyilwin007@gmail.com

Abstract

Cases of severe complicated malaria in Myanmar had declined during 2006-2012, yet some townships in the southeastern part continued to report poor outcome of malaria patients in spite of applying similar interventions as other high-risk areas. The purpose of this paper was to understand the reasons behind the poor malaria outcome of some townships in Mon State. We described trends and distribution of severe complicated malaria cases in 2006-2012. During 2006-2012, Yae Township contributed one-third to half of all severe complicated malaria cases in Mon State every year. In 2012, more than 25% of confirmed malaria cases were reported from high risk areas, including Beelin, Kyaikhto, Thaton and Yae Townships. Among these townships, Yae and Kyaikhto reported higher proportion of severe complicated malaria cases among under five children and pregnant women in 2012. In addition, fewer number of malaria cases was detected by village health volunteers than basic health staff in these townships, which might be due to inaccessibility to health services. Strengthening surveillance system and community-based malaria control program in Yae and Kyaikhto might reduce severe complicated malaria in these areas.

Key words: severe complicated malaria, Mon State, micro-stratification, Myanmar

Introduction

Of 10 countries with ongoing malaria transmission in Southeast Asia, incidence of confirmed malaria cases decreased to 75% or more in five countries (Bangladesh, Bhutan, Democratic People's Republic of Korea, Nepal and Sri Lanka) between 2000 and 2012. It was projected that by 2015, incidence of malaria cases would decrease to more than 75% in Thailand and Timor-Leste, and 50-75% in India. However, incidence trends in Indonesia and Myanmar were obscured by changes in diagnostic or reporting practices.[1]

Among six Mekong countries, the malaria burden was the highest in Myanmar.[2,3] Malaria has been a major public health problem in Myanmar due to climatic and ecological changes, population migration, development of multidrug resistant *P. falciparum* parasites and insecticides resistant vectors, and changes in behavior of malaria vectors.[4] During 2012 in Myanmar, total number of confirmed malaria cases was 375,503 (annual parasite index 7.7 per 1,000 population) and number of total malaria deaths was 403 (0.8 per 100,000 population). Cases of severe complicated malaria were significantly decreased from 10,160 in 2008 to 4,160 in 2012.[5]

As credible evidences of artemisinin resistant malaria was reported in all townships in Mon State[6-8], immediate and multifaceted response was necessary in these areas. Interventions for malaria control in Mon State included vector control activities and utilization of community-based volunteers for malaria diagnosis and treatment in hard-to-reach areas in the state. Despite these interventions, some areas continued to report severe complicated malaria.[9] Furthermore, limited data were available to describe the occurrence and reasons for severe complicated malaria in the state.[10] The primary objective of this paper was to review malaria surveillance and describe trends and distribution of severe complicated malaria cases in 2006-2012 in Mon State. This study was conducted in order to understand the reasons behind the poor malaria outcome in some townships of Mon State despite similar interventions were implemented across the high-risk townships in the state.

Methods

Data Collection and Analysis

We conducted a descriptive study using different sources of surveillance data in all 10 townships of

Mon State during 2006-2012, including Mawlamyine, Kyaikhto, Beelin, Thaton, Kyaikmayaw, Mudon, Paung, Chaungzon, Thanbyuzayat and Yae Townships (Table 1).

Table 1. Data sources for malaria in Mon State, Myanmar, 2006-2012

Source	Data	Time period
Vector Borne Disease Control (VBDC), Mon State	Annual report for malaria	2006-2012
National Malaria Control Program (NMCP), Nay Pyi Taw*	Surveillance data	2006-2012
Mon State Health Department	State health profile and baseline data	2012
UNICEF and Global Fund	Microstratification maps and data	2011

Data reported from the partner agencies were included.

The annual report for malaria morbidity, mortality and geographic distribution data in 2006-2012 were obtained from Vector Borne Disease Control (VBDC), Mon State and National Malaria Control Program (NMCP), Nay Pyi Daw. Data from these two sources in 2012 were compared to extract volunteer activities in different townships.

In this report, a case of severe complicated malaria was defined as a person who was showing one or more of the following clinical criteria: altered or decreased consciousness; convulsion; persistent vomiting; inability to sit, stand or walk unaided; hyperpyrexia (39°C or more, with dry skin); severe anemia (hematocrit below 20% or hemoglobin level less than 6g/dl); and organ failure.[11]

Trends for severe complicated malaria cases and malaria deaths, and distribution by townships of severe complicated malaria cases were described. In addition, the distribution was also described by risk groups, townships and types of person who reported the cases (basic health staff - BHS or village health volunteer - VHV) to identify whether this might help explaining the differences.

Micro-stratification maps and data were collected by UNICEF and Global Fund during 2011 in Mon State to inform strategic use of resources in more focused and efficient ways. In this study, the micro-stratification maps of townships were merged into the state micro-stratification map using ArcGIS software.

Results

Mon State is a long narrow coastal state situated at the southeastern part of Myanmar (Figure 1). Mon

State has a population of 2.1 million distributed in 10 townships. Most of the Mon people worked as rubber tappers, forest-goers and farmers.[12]
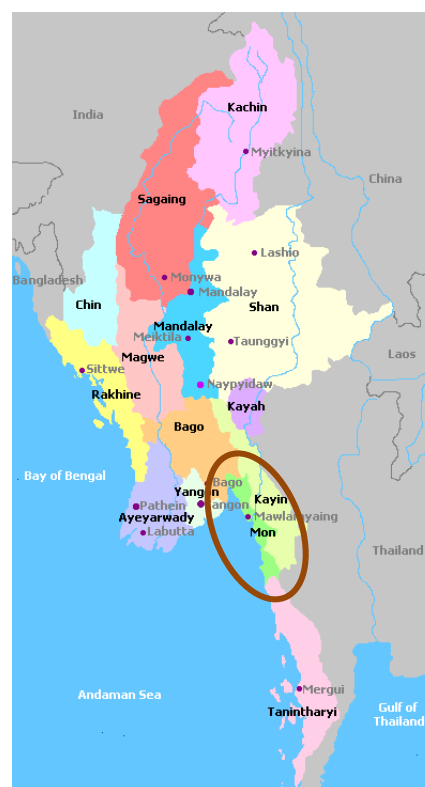

Figure 1. Map of Myanmar, showing Mon State

For both surveillance systems of VBDC and NMCP, the most basic reporting unit was the sub-center where a midwife was responsible for 5-10 villages, with support of VHV. The paper-based surveillance system was utilized to submit case registers and line-listing forms of malaria cases from the rural health center to township level. Township medical official, the focal administrative person in township, checked completeness and consistency of data manually for program management in township level. The township medical official then sent the data to the state level where the data were compiled, analyzed and submitted again to NMCP.[9]

The VBDC surveillance system covered all out-patients and in-patients with malaria from all townships in Mon State. Data in the VBDC surveillance system included a line-listing of individual patient's clinical and demographic information. Information with a limited number of malaria indicators, including number of malaria out-patient and in-patient, was also collected monthly through health management information system (HMIS), which was not considered sufficient to support VBDC with the information needed to manage the program.[13]

Micro-stratification was conducted by BHS in rural areas who are taught about the criteria and trained to

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identify and map out the villages within high, moderate and low risk areas. Each village in every township was classified as malarious (Stratum 1), potentially malarious (Stratum 2) or non-malarious (Stratum 3). Stratum 1 villages were further categorized into high (1A), moderate (1B) and low (1C) risk areas. Main parameters for stratification were presence of indigenous cases, type of vectors found and ecological features favorable for malaria. Supporting parameters for stratification included distance from forest and the nearest health care facility.[14]

According to the micro-stratification data, four townships (Beelin, Kyaikhto, Thaton and Yae) were designated as high risk or Stratum 1A areas (Figure 2). Although only 10% of the population lived in these four townships during 2012 (Table 2), over one-quarter of the reported malaria confirmed cases were from those areas. Although Mawlamyine, the capital city of Mon State, was stratified as risk-free for malaria, 2.6% (458) of malaria confirmed cases were reported in 2012.

From 2006 to 2012, trends of both severe complicated malaria cases and malaria deaths decreased in Mon State (Figure 3). Many severe and complicated malaria cases were admitted and many malaria

deaths were reported in Yae and Kyaikhto compared with other high risk townships. Each year, cases of severe complicated malaria from Yae Township contributed one-third to one-half of the reported cases.

In 2012, Yae, Kyaikhto and Mawlamyine Townships reported higher proportion of severe complicated malaria cases among all ages (Figure 4). Although high number of confirmed malaria cases among under five children was reported in Thaton Township, there was no severe complicated malaria in this high risk population during 2012. Pregnant women with malaria were mostly from Yae Township followed by Thaton, Thanbyuzayat and Beelin. However, among these pregnant women, higher proportion of complications was observed in Kyaikhto (100%), Beelin (20%) and Yae (11%) (Table 3).

Majority of confirmed malaria cases in 2012 were out-patients (93%). Community-based malaria case detection by VHV contributed 45% of all cases detected. Out-patient malaria cases detected by VHV were the highest in Beelin and Thaton while the detection by VHV was much lower than diagnosed by BHS in Kyaikhto and Yae, implying that activities of VHV were likely to be weaker in Kyaikhto and Yae Townships (Figure 5).
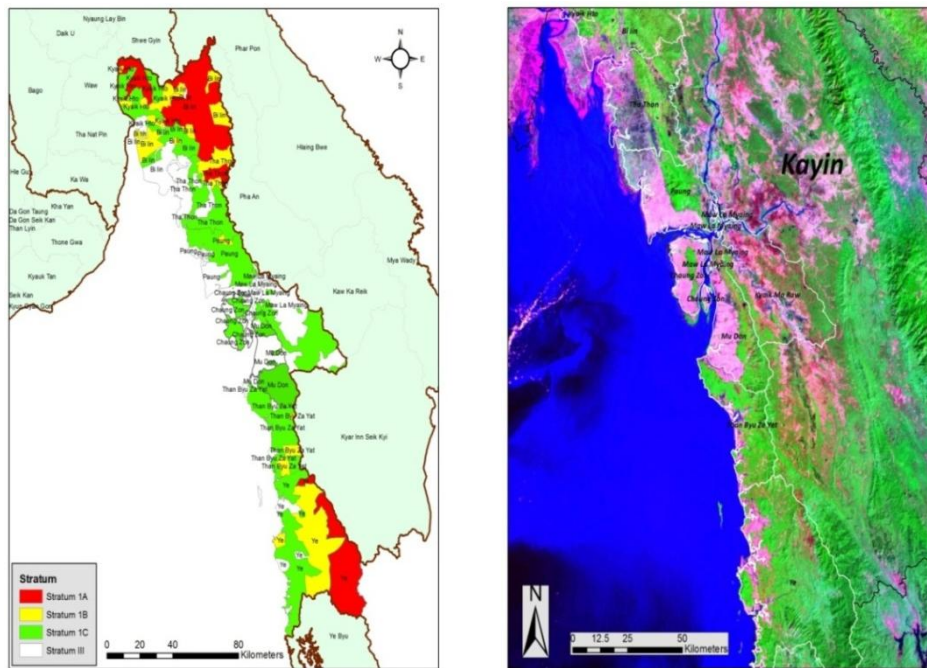

Figure 2. Maps on micro-stratification and vegetation of Mon state, Myanmar, 2011

Table 2. Number of villages and population in high and moderate risk areas of Mon State, Myanmar, 2012

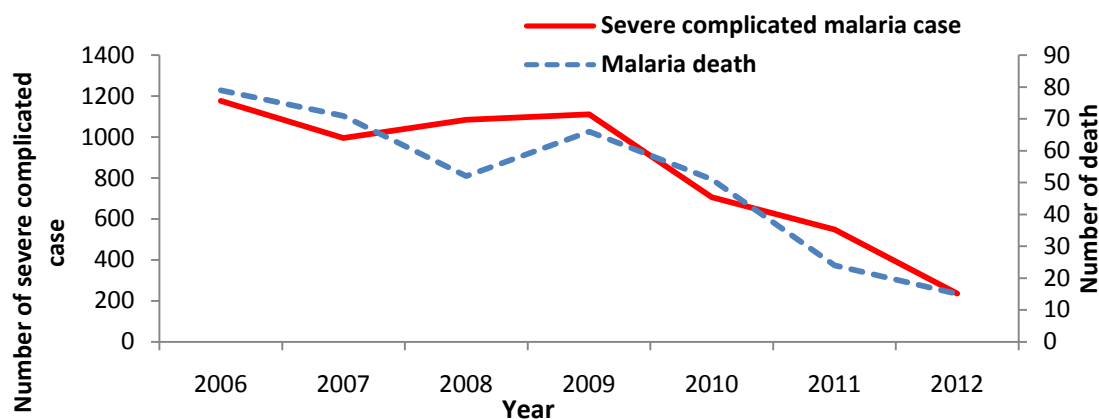| Risk	Variable	Township			
		Beelin	Kyaikhto	Thaton	Yae
High	Village	85	26	11	15
	Population	37,710	13,617	5,117	6,244
Moderate	Village	48	30	44	63
	Population	39,545	23,082	26,608	58,020

Figure 3. Trends of severe complicated malaria cases and malaria deaths in Mon State, Myanmar, 2006-2012
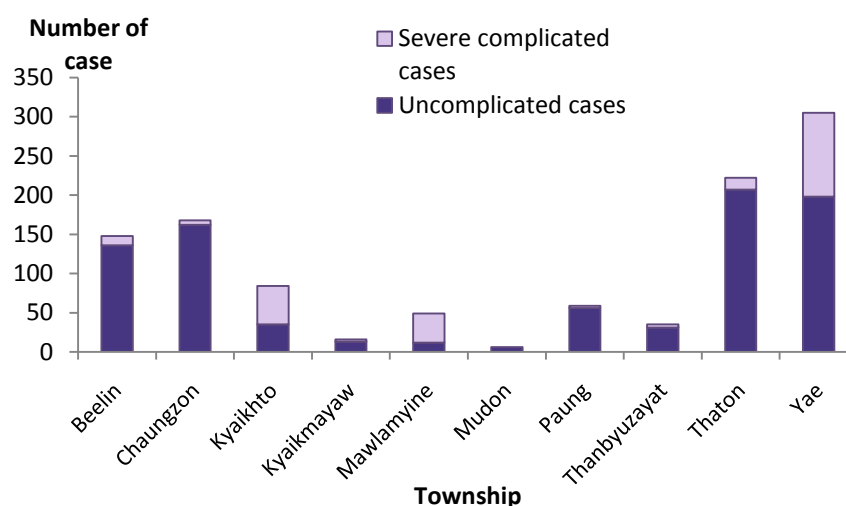

Figure 4. Township-wise distribution of uncomplicated and severe complicated malaria cases in Mon State, Myanmar, 2012

Discussion

Micro-stratification is useful to allocate available limited resources effectively and strategically according to levels of micro-stratification. The risk map will be an important planning tool in township as well as state, regional and central levels. Based on the risk map, a micro-plan is prepared at township level which includes a supply/logistics plan of diagnostic, treatment and preventative equipment, a training plan for BHS and VHV prioritizing the high risk areas, and a targeted program communication

Table 3. Number of total in-patient malaria cases and severe complicated malaria cases by different groups in Mon State, Myanmar, 2012

| Township	In-patient			< 5 years			Pregnancy		
	Number of malaria	Number of severe complicated malaria	Percent	Number of malaria	Number of severe complicated malaria	Percent	Number of malaria	Number of severe complicated malaria	Percent
Beelin	148	12	8.1	73	1	1.4	5	1	20
Chaungzon	168	6	3.6	21	0	0	1	0	0
Kyaikhto	84	49	58.3	74	8	10.8	1	1	100
Kyaikmayaw	16	3	18.8	40	0	0	2	0	0
Mawlamyine	49	37	75.5	132	0	0	1	0	0
Mudon	6	0	0	9	0	0	1	0	0
Paung	59	3	5.1	58	0	0	0	0	0
Thanbyuzayat	35	4	11.4	64	0	0	6	0	0
Thaton	222	15	6.8	110	0	0	8	0	0
Yae	305	107	35.1	159	24	15.1	18	2	11.1
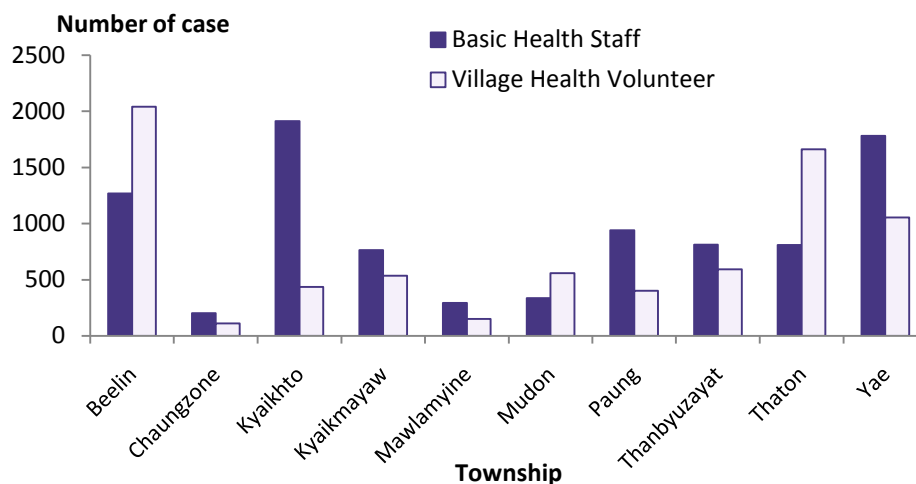
Figure 5. Number of out-patient malaria cases detected by basic health staff and village health volunteers by townships in Mon State, Myanmar, 2012

plan. Insecticide-treated bed nets provision and insecticide impregnation activities can be also strategically planned, based on the risk map. However, our finding of consistent high number of severe complicated malaria cases among high risk groups in Yae, Kyaikhto and Mawlamyine Townships during 2012 when compared with other townships with high malaria transmission suggested that micro-stratification method might not be sufficient to allocate resources in Mon State.

The routine malaria surveillance system which reported data on malaria deaths and severe complicated malaria cases from in-patient health facilities showed unambiguity about the figures of severe complicated malaria. Limited accessibility to public health care facilities in areas of political instability in Yae Township was likely to render delay in seeking medical care since a major cause for developing severe complicated malaria was due to missed or delayed diagnosis.[15-17]

The high number of reported severe complicated malaria cases and malaria deaths in Yae and Kyaikhto was likely due to delayed diagnosis and referral. Hence, the community-based malaria control program in these townships should be strengthened to reduce severe complicated malaria.

However, very few severe and complicated malaria cases were identified in Thaton Township, with no severe and complicated malaria among pregnant women and under five children, although there were many cases of confirmed malaria. It might be related with higher case detection by VHV in Thaton Township, and thus, could prevent occurrence of severe and complicated malaria and deaths.

Despite higher number of confirmed malaria cases reported from Beelin and Thaton Townships, earlier

case detection and treatment among persons living in remote areas helped prevent severe malaria.[17] The lower case detection by VHV in Yae and Kyaikhto might be due to a problem in systematic recruitment of VHV in remote areas of these townships, leading to some villages without any VHV. Furthermore, some VHV did not work well due to lack of motivation and supportive supervision by BHS while BHS were overburdened with heavy workload of numerous activities across different health programs.[18] Another explanation might be due to less effective surveillance system for reporting of malaria cases in Yae and Kyaikhto Townships. Therefore, further studies were suggested to explore the causes of different case detection of malaria cases by VHV among these townships.

Although the capital city, Mawlamyine, was being micro-stratified as a no-risk area, our data showed high number of severe complicated malaria in the hospital, which might be the referral cases from other townships. Drawbacks of the malaria surveillance system in Myanmar were that patients' current residence reported by BHS might be the location of treatment taken, not their permanent residence[13], and unavailability of data from the private sector might lead to underestimation or misinterpretation of the data.

Limitations

This study was subjected to several limitations. Firstly, as the routine malaria surveillance data in Myanmar did not include patients' occupational status (for example, migrant workers) and actual residency status, we could not accurately describe the role of migrant workers in malaria epidemiology of Myanmar.

The official population in Mon State was stated as three million in 2008 and 1.9 million in 2009. Due to unreliable information on number of population, we reported number of cases as trend, instead of rate. This might mask some trends due to denominator population change.

Furthermore, our analysis was limited to only severe complicated cases. Despite that, analysis of trend in this study included a long time period (2006-2012) during which the malaria case detection was more specific, with rolling rapid diagnostic tests out. Lastly, 2012 data were passively reported and thus, our results might be subjected to reporting bias, which would be beneficial from validation of reporting checks.

Public Health Actions and Recommendations

Risk mapping of the townships should be updated again in 2014, thereby township-wise and health center-wise micro-planning for malaria control activities could be done according to the updated micro-stratification areas. Micro-planning means bottom-up planning on malaria control activities, starting from village level through sub-center, Rural Health Center to township level according to their needs. With the updated micro-stratification, health managers could identify the prioritized areas for resources allocation and vector control activities.

In addition, strengthening of community-based malaria services in Yae and Kyaikhto Townships was needed by means of providing incentives and supportive supervision to VHV by BHS for early detection of more cases in rural areas and preventing severe complicated malaria. Drug adherence according to the national guidelines by BHS and VHV in the rural areas should be explored for prevention of drug resistant malaria and severe complicated malaria. Even in low malaria burden areas such as Mudon and Chaungzon Townships, surveillance systems should be strengthened as well in order to prevent spread of drug resistant malaria since all areas in Mon State were regarded as Tier 1 areas.[19] Moreover, the routine surveillance data should include occupation status of the patients. Information on patients' permanent residence, instead of location of treatment provided, would be advantageous to more effectively plan malaria control activities.

Acknowledgement

Suggested Citation

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References

1. World Health Organization. World malaria report 2013. Geneva: World Health Organization; 2013. p.57.

2. President's Malaria Initiative. Malaria operation plan FY 2013 for Greater Mekong Subregion [cited 2014 Feb 4]. <http://www.pmi.gov/docs/default-source/default-document-library/malaria-operational-plans/fy13/mekong_mop_fy13.pdf?sfvrsn=8>.

3. World Health Organization - Mekong Malaria Programme. Strategic plan to strengthen malaria control and elimination in the Greater Mekong Subregion: 2010-2014. 2009 [cited 2014 Feb 4]. <http://whothailand.healthrepository.org/bitstream/123456789/696/1/Strategic%20Plan%20to%20Strengthen%20Malaria%20Control%20and%20Elimination%20in%20the%20Greater%20Mekong%20Subregion%20%2020102014.pdf>.

4. Myanmar. Ministry of Health. Health in Myanmar, 2013.

5. Myanmar. Department of Health. Ministry of Health. Surveillance data from National Malaria Control Program, 2006-2012.

6. Myanmar. Department of Medical Research, Lower Myanmar. Ministry of Health. Potential spread of artemisinin resistant malaria to other parts of Myanmar. 2013.

7. World Health Organization. Proposal for National Malaria Control Program including artemisinin resistance containment. Yangon: World Health Organization, Myanmar; 2012.

8. World Health Organization. External evaluation of National Malaria Control Program, Myanmar. New Delhi: World Health Organization Regional Office of South East Asia; 2013.

9. Myanmar. Department of Health. Ministry of Health. Annual report from Mon State Vector Borne Disease Control Program. Mawlamyine: Mon State Health Department; 2012.

10. Win H. Malaria situation in Mon State, 1978-1982. Yangon Institute of Medicine. 1985. p.83.

11. World Health Organization. Guidelines for diagnosis and management of malaria in Myanmar. 2011. p. 9-17.

12. Myanmar. Department of Health. Ministry of Health. Mon State health profile. 2013.

13. Myanmar. Department of Health. Ministry of Health. Monitoring and evaluation plan for malaria prevention and control, 2010-2015. Nay Pyi Taw: National Malaria Control Program; 2012. p. 10-12.

14. Japan International Cooperation Agency and United Nations Children's Fund. Malaria risk micro-stratification in UNICEF 80 townships: No publication year. p. i-v.

15. Pasvol G. The treatment of complicated and severe malaria. Br Med Bull. 2006 Feb 22;75-6:29-47. Print 2005 [cited 2014 Feb 4]. <http://www.bmb.oxfordjournals.org/content/75-76/1/29>.

16. Ejov MN, Tun T, Aung S, Lwin S, Sein K. Hospital-based study of severe malaria and associated deaths in Myanmar. Bull World Health Organ. 1999;77(4):310-4 [cited 2014 Feb 4]. <http://www.who.int/bulletin/archives/77(4)310.pdf>.

17. Kheang ST, Duong S, Olkkonen A. Increasing access to early malaria diagnosis and prompted treatment in remote Cambodian villages. Am J Public Health. 2011 Dec;101(12):e6-8. Epub 2011 Oct 20.

18. World Health Organization. Report of the first annual meeting for Myanmar artemisinin resistant containment (MARC). Nay Pyi Taw: Ministry of Health; 2012.

19. World Health Organization. Global plan for artemisinin resistance containment. Geneva: World Health Organization; 2011. p.29-31.