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Epidemiological analysis of typhoid fever in Kelantan from a retrieved registry

Ja'afar Nuhu Ja'afar[1], Yuan Xin Goay[1], Nur Fatihah Mohammed Zaidi[1], Heng Chin Low[2], Hani Mat Hussin[3], Wan Mansor Hamzah[3], Subhash Janardhan Bhore[4], Prabha Balaram[5],Asma Ismail[1], and Kia Kien Phua[1*].

[1]Typhoid and other Enteric Diseases Cluster, Institute for Research in Molecular Medicine (INFORMM), Universiti Sains Malaysia, 11800, Penang, Malaysia.
[2]School of Mathematical Sciences, Universiti Sains Malaysia, 11800, Penang, Malaysia.
[3]Kelantan State Health Department, Kota Bharu, Kelantan, Malaysia.
[4]Department of Biotechnology, Faculty of Applied Sciences, AIMST University, Bedong-Semeling Road, 08100, Bedong, Kedah, Malaysia.
[5]QUEST International University Perak, No. 227, Plaza Teh Teng Seng, level 2, Jalan Raja PermaisuriBainum, 30250 Ipoh, Perak, Malaysia.
Email: kkphua@kb.usm.my

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ABSTRACT

Aim: Despite the endemicity of typhoid in Kelantan, epidemiological data showing typhoid association to age, sex, ethnicity and district of patients is limited. This retrospective study investigated the statistical association of these variables from a retrieved registry.
Methodology and results: Cross-tabulation using SPSS was used to analyze 1394 cases of confirmed typhoid patients admitted to various hospitals in Kelantan state over a six-year period. Fourteen age groups with a five-year range interval were generated. There was a significant association between typhoid infection and sex of subjects, whereby females were generally more susceptible than males. Ethnicity and district of typhoid patients did not show significant association.
Conclusion, significance and impact of study: The observation of an increased number of typhoid cases with a male predominance in the age group 5-14 and female predominance in the 20-60 age group calls for improved hygiene, continued public health education, together with better laboratory diagnostics to identify carriers, are some measures to control this disease.

Keywords: *Salmonella* Typhi, Kelantan, Malaysia, retrospective study, typhoid

INTRODUCTION

Typhoid fever, caused by *Salmonella enterica* subspecies *enterica* serovar Typhi (*S.* Typhi), develops following ingestion of food or water that is contaminated with 10^3-10^6 cfu/mL of *S.* Typhi (Hornick *et al.*, 1970; Levine, 2009).This human restricted pathogen has the ability to survive for several months in soil and water (Tran *et al.*, 2005). Kelantan, a North-eastern state in Peninsular Malaysia with co-ordinates 5° 25' 0" North and 101° 55' 0" East, is endemic for typhoid fever. In endemic areas, the incidence of typhoid fever peaks in the youngest age group of 1-19 years (Lin *et al.*, 2000). Malik and Malik (2001) reported from the Ministry of Health Malaysia that the "highest number of typhoid cases reported in 1998 and 1999 was from Kelantan and the majority of the patients were children". A study conducted by Choo *et al.* (1988) reported that the average age incidence of typhoid fever patients admitted to Hospital Universiti Sains Malaysia (HUSM) was 7.3 years, which was comparable to the study by Malik and Malik (2001) who reported 7.5 years from the same hospital. These data, however, contrasted with the study by Levine *et al.* (1982) in Santiago, Chile. This often cited report highlighted the well-known "4Fs" risk factors amongst Chilean people; *viz.* 1) Female, 2) Fat, 3) Fertile, and 4) Over forty years old. However, there has been no similar study conducted amongst Asian people as to whether such risk factors prevail. Because typhoid fever continues to be a serious public health problem in many developing countries, the time is now to re-examine and critique old "truths".

Epidemiological surveillance of *S.* Typhi is essential for public health management to identify origins of outbreaks, transmission patterns, and risk factors contributing to the persistence and spread of typhoid fever in this endemic area. Yap and Puthucheary (1998) cited the annual incidence of typhoid in Malaysia as 10.2-17.9 cases per 100,000 population between 1978 to 1990, and as high as 50.3 cases per 100,000 population in the state of Kelantan. However, a significant improvement was achieved in reducing the

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incidence of typhoid fever in Kelantan from 14.7 cases per 100,000 population in 2000 to 2.8 cases per 100,000 population in 2010 (Hamzah *et al.*, 2011).

The complete eradication of typhoid fever in Kelantan remains a challenge despite extensive efforts from the state's Public Health Department. Understanding the epidemiology of an endemic disease such as typhoid fever in a given population could sometimes be complex, especially when multiple factors are involved in perpetuating the disease. Updated epidemiological databases will not only be of help to the epidemiologist and public health officers in rectifying and re-defining more sensitive and specific control measures, but will also help in elucidating and characterizing host-pathogen interactions, and provide better understanding of the disease pathogenesis at the molecular level. Furthermore, it will aid in public policy decision-making. However, accurate statistical interpretation of the available data is a pre-requisite to the above-mentioned benefits.

Under Act 342 (Prevention and Control of Infectious Diseases Act of Malaysia, 2006) of Malaysia, government hospitals, health care centers, outpatient departments and private hospitals are required to notify all cases of typhoid fever to the state's Public Health Department. Because of this legal requirement, a typhoid population-based registry was set up by the state Public Health Department, which can be used to study the association of typhoid fever with various epidemiological parameters amongst Kelantanese in the state. Several studies have been conducted on the risk factors for contracting typhoid in several countries including Malaysia (Black *et al.*, 1985; Velema *et al.*, 1997; Zain and Naing, 2002; Vollaard *et al.*, 2004; Tran *et al.*, 2005; Hosoglu *et al.*, 2006). We have identified only one study that associated incidence of typhoid to its spatial distribution in the state of Kelantan (Safian *et al.*, 2008). In Malaysia, typhoid fever affects all classes of society (Malik and Malik, 2001). However, the relationship between typhoid fever and sex, ethnicity and district of typhoid fever subjects in Kelantan have not been fully documented. In this paper, a retrospective study was carried out using the typhoid registry from the Kelantan state's Public Health Department and demographic data from the Kelantan Department of Statistics (Population and Housing Census, Malaysia 2010) to study association between typhoid fever and age, sex, ethnicity and district of infection occurrence.

MATERIALS AND METHODS

Study area

Kelantan (Figure 1), the eight largest state in the country, is located in the North-eastern part of Peninsular Malaysia. The state has a population of 1,639,000 with a population density of 109 persons per square kilometre (km^2). The state is divided into ten districts according to the Kelantan State Department of Statistics (Population and Housing Census, Malaysia 2010).

Figure 1: Ten districts in the state of Kelantan Malaysia.

Study design

From the Kelantan State's Public Health Department registry, 1394 records of confirmed typhoid fever patients admitted to various hospitals within the state from year 2004 to 2009 were retrieved. Fourteen age groups were generated, each with a five-year range interval (Figure 2).

Statistical analysis

Data retrieved were analysed by cross-tabulation using SPSS statistical package version 19 (IBM SPSS Version 19, USA) and statistical significance was defined as $p<0.05$. Associations between typhoid fever and age, sex, ethnicity, district and year of infection were determined.

RESULTS

The distribution of typhoid patients by demographic variables were Malay 98.1% (n=1367), females 50.9% (n=709) and district of Kota Bharu 71.8% (n=1001). The median age was 16 ± 16.4 years with a range 1 to 101 years. Thirteen (0.9%) patients were less than 1 year old. The overall male to female ratio was 1:1.

Association of typhoid fever between sex and age

Analysis of the fourteen age groups (Figure 2) for association between typhoid fever and sex showed a significant association ($p=0.02$). It was observed that the age group 10-14 years (n=139) had the highest number of male typhoid fever patients followed by age group 5-9 (n=129), while age group 10-14 (n=112), had more

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females. On the other hand, the 55-59 years age group had the least number of typhoid fever patients (n=19). An important observation here was the predominance of males in the age groups 5-14 and females in the age group 20-35 and 45-60 (Figure 2).

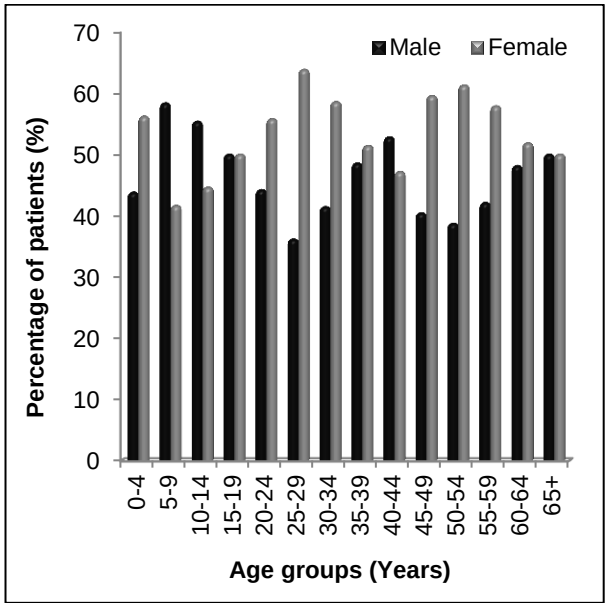

Figure 2: Percentage distribution of typhoid fever patients in Kelantan in relation to their sex and age.

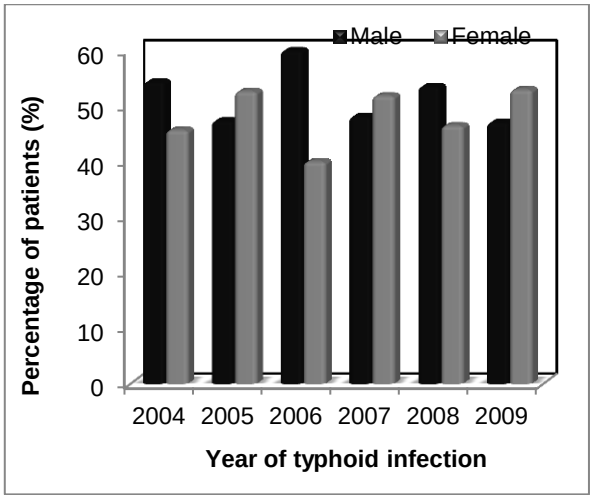

Figure 3: Percentage distribution of typhoid fever patients in Kelantan in relation to their sex and year of infection.

Association of typhoid fever between sex and year of infection

Although the number of females was higher during the outbreak in the year 2005 (n=469) and 2007 (n=70), analysis of the patient's sexin association with typhoid and year of infection (Figure 3) did not show any significant association (p=0.20).

Association of typhoid fever between districts and ethnicity of patients

Majority of typhoid fever patients in the study were Malays (n=1367). Equally, Kota Bharu having the highest number of typhoid patients (n=1001) had ethnic Malays as the majority (n=976) as shown in Table1. The statistical analysis indicate that association of ethnicity of patients in relation to typhoid infection and their districts was not significant (p=0.92).

Table 1: Number of typhoid fever patients in relation to district and ethnicity.

District	Chinese	Indian	Malay	Others
Bachok	1	0	25	0
Kota Bharu	15	4	976	6
Machang	0	0	21	0
Pasir Mas	0	0	51	0
PasirPuteh	0	0	84	0
Tanah Merah	0	0	26	0
Tumpat	0	0	108	0
GuaMusang	0	0	11	0
Kuala Krai	0	1	47	0
Jeli	0	0	16	0
Missing	0	0	2	0
Total	16	5	1367	6

DISCUSSION

In an effort to corroborate the findings of Levine *et al.* (1982) and to identify any association between typhoid fever and sex, age, ethnicity and district in the state of Kelantan, we performed a retrospective study and analyzed by cross-tabulation typhoid fever patients' data retrieved from the Kelantan state's Public Health Department registry.

Typhoid has been shown to be common among infants and young children in Southeast Asia (Choo *et al.*, 1988; Velema *et al.*, 1997; Malik and Malik, 2001; Tran *et al.*, 2005). In this study, typhoid was found in all age groups from 1-101 years old, but like other Southeast Asian countries, the age groups 5-9, 10-14 and 15-19 were more susceptible. The overall male to female ratio was 1:1, which was in agreement with that reported in the studies of Choo *et al.* (1988) and Malik and Malik (2001) for the state of Kelantan that was 1:1.1 and 1.2:1, respectively. Similar to the findings of Velema *et al.* (1997), typhoid distribution was skewed to the right. This means that children (0-4 years) and young

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adults (25-29 years) were more susceptible to typhoid fever compared to the older population. This was substantiated by the reports of other researchers from other parts of the world (excluding Southeast Asia) that showed cases of typhoid fever in these categories of age groups (Black *et al.*, 1985; Hosoglu *et al.*, 2006; Siddiqui *et al.*, 2006). Perhaps a reason for this is that the undeveloped immune system of these age groups makes them vulnerable to this enteric pathogen.

The increased cases of typhoid fever observed in 2005 (Figure 3) was due to a major typhoid outbreak (Hamzah *et al.*, 2011). It was glaringly observed that the number of females (Figure 3) was higher in both the 2005 and 2007 outbreaks (a small outbreak occurred in 2007). The cause for this is uncertain. Levine *et al.* (1982) observed that the female gender above forty years of age was more susceptible to chronic typhoid infection. In this study, the theory was upheld in almost all of the age groups (Figure 2) with regard to gender susceptibility except in age groups 5-14 and 40-44 years that had more males than females infected. Two age groups, 15-19 and 65+ (Figure 2) had equal numbers of male and female typhoid victims.

In this study, Malays were the majority ethnic group in Kelantan (Table 1). As ascertained by the report of Safian *et al.* (2008) that "In terms of racial distribution, the majority of the population in Kelantan are Malays, comprising 96.2% of the total population, compared to 5.35% Chinese and 0.33% Indians". Hence, no statistically significant association between ethnic group and typhoid could be ascertained (p=0.92). Levine (2009) reported living condition as the probable precipitating factor for susceptibility to typhoid fever rather than race. However, genetic disposition has been proposed as a predisposing factor to typhoid response, such as seen in Javanese population of Indonesia that have a more severe clinical syndrome compared to other population (Levine, 2009; Bhuvanendran *et al.*, 2011).

The majority of typhoid cases were reported in the capital, Kota Bharu (Table 1). This could be linked to the relatively higher population density in capital cities as is seen in other parts of the world. Hamzah *et al.* (2011) made a similar observation where they found 30-40% of typhoid cases in the state occurred in Kota Bharu.

The lingering incidence of typhoid fever in Kelantan State could largely be attributed to poor environmental sanitation, poor follow-up management of typhoid cases, low success rate of identification of carriers, and unhygienic food handling, which are known to be among the major contributory factors of typhoid's resistance (Hamzah *et al.*, 2011). As previously reported by Soon *et al.* (2011) that, "most of the implicated food settings occurred in schools' and academic institutions' food preparation premises and inappropriate food handling practices, meals prepared too early and kept at ambient temperature until served and unhygienic practices were the causes of food poisoning cases". More so, lack of strict control over erecting food stalls in Kelantan (Malik and Malik, 2001; Hamzah *et al.*, 2011) could have increased the chances of transmitting *S.* Typhi through asymptomatic infected individuals (carriers) serving as food handlers since the bacteria could be transmitted from their biological fluids through food and drink handled by them (Center for Disease Control, 2005). In addition, consumption of contaminated raw milk products, flavoured drinks and ice creams have been implicated in the transmission of typhoid fever (Stevenson, 1935).

CONCLUSION

Young children and females commonly considered susceptible for typhoid fever have a statistical significant association in this study, which is in concordance with the findings of the World Health Organization (WHO) in other parts of Asia. With regard to the well-known "4Fs" alliteration "Female, Fat, Fertile and Forty", suggesting susceptibility to chronic typhoid infection being more in women than men, and the significance of age, pregnancy and obesity favouring this infection, this study showed more females to males for most age-matched groups in the population. However, typhoid infection was highest in male young children aged between 10-14 years old. In addition, by inference, since the ratio of females to males is more in the age groups 20-59, it can be hypothesised that fertile females are more susceptible to typhoid infection. More so, obesity that is linked to cholecystitis (Stevenson, 1935) and greater chance of *S.* Typhi's sequestration in the gallbladder may in fact be a predisposing factor for the typhoid carrier state.

From previous observations and findings of other researchers, it is tempting to hypothesise that indiscriminate eating behaviour of children and young adults in Kelantan could be a risk factor in their continuous susceptibility to typhoid fever. As such, improved hygiene and continuous health education to the public should further decrease the number of typhoid cases in the state.Furthermore, since the typhoid bacterium is human specific, and thus only humans are carriers of the disease, the development of better laboratory diagnostic tests to identify asymptomatic carriers, such as the thermostabilised PCR for *S*. Typhi (Ismail *et al.*, 2007) could be the Archile's heel in efforts to eradicating the disease.

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REFERENCES

Black, R. E., Cisneros, L., Levine, M. M., Banfi, A., Lobos, H. and Rodriguez, H. (1985). Case-control study to identify risk factors for paediatric endemic typhoid fever in Santiago, Chile. *Bulletin of the World Health Organization* **63(5), 899-904.**

Bhuvanendran, S., Hussin, H. M., Meran, L. P., Anthony, A. A., Zhang, L., Burch, L. H., Phua, K. K., Ismail, A. and Balaram, P. (2011). Toll-like receptor 4 Asp299Gly and Thr399Ile polymorphisms and typhoid susceptibility in Asian Malay population in Malaysia. *Microbes and Infection* **13, 844-851.**

Center for Disease Control (CDC) (2005). Typhoid fever: frequently asked questions. Department of Health and Human Services, Centers for Disease Control and Prevention.

Choo, K. E., Razif, A., Ariffin, W. A., Sephia, M. and Gururaj, A. (1988). Typhoid fever in hospitalized children in Kelantan, Malaysia. *Annals of Tropical Paediatrics* **8, 207-212.**

Hamzah, W. M., Nor, M. F. and Husin, H. M. (2011) Kelantan typhoid initiative: Lessons learnt. *Malaysian Journal of Public Health Medicine* **11(Suppl 3), 6.**

Hornick, R. B., Greisman, S. E., Woodward, T. E., DuPont, H. L., Dawkins, A. T. and Snyder, M. J. (1970). Typhoid fever: Pathogenesis and immunologic control. *The New England Journal of Medicine* **283(13), 686-746.**

Hosoglu, S., Celen, M. K., Geyik, M. F., Akalin, S., Ayaz, C., Acemoglu, H. and Loeb, M. (2006). Risk factors for typhoid among adult patients in Diyarbakir, Turkey. *Epidemiology and Infection* **134, 612-616.**

IBM SPSS Statistics Statistical Package. Version 19, USA.

Ismail, A., Ravichandran, M. and Ismail, A. (2007). Amplification of ST50gene using dry-reagent-based PCR for the detection of *Salmonella* Typhi. *Diagnostic Microbiology and Infectious Diseases* **5, 373-377.**

Levine, M. M. (2009). Typhoid fever. *In:* Bacterial Infections of Human. Evans, A. S. and Brachman, P. S. (eds.). 4th edn. Springer Science, New York. **pp. 913-937.**

Levine, M. M., Black, R. E. and Lanata, C. (1982). Precise estimation of the numbers of chronic carriers of *Salmonella* Typhi in Santiago, Chile, an endemic area.*Journal of Infectious Diseases* **146, 724-726.**

Lin, F. Y., Vo, A. H., Phan, V. B., Nguyen, T. T., Bryla, D., Tran, C. T., Ha, B. K., Dang, D. T. and Robbins, J. B. (2000). The epidemiology of typhoid fever in the Dong Thap province, Mekong Delta region of Vietnam. *American Journal of Tropical Medicine and Hygiene* **62, 644-648.**

Malik, A. S. and Malik, R. H. (2001). Typhoid fever in Malaysian children. *Medical Journal of Malaysia* **56(4), 478-490.**

Population and housing census, Malaysia (Census 2010). Population distribution and basic demographic characteristic report. Available from www.statistics.gov.my. Accessed on 9th May 2012.

Safian, N., Shah, S. A., Idrus, S. and Hamzah, W. M. (2008). Cluster analysis of typhoid cases in Kota Bharu, Kelantan, Malaysia. *Medical Journal of Indonesia* **7(3), 175-182.**

Siddiqui, F. J., Rabbani, F., Hasan, R., Nizami, S. Q. and Bhutta, Z. A. (2006). Typhoid fever in children: Some epidemiological considerations from Karachi, Pakistan. *International Journal of Infectious Diseases* **10, 215-222.**

Soon, J. M., Singh, H. and Baines, R. (2011). Foodborne diseases in Malaysia: A review *Food Control* **22, 823-830.**

Stevenson, H. (1935). The role of chronic cholecystitis in the production of indigestion. *The Ulster Medical Journal* **4(4), 211-214.**

Tran, H. H., Bjune, G., Nguyen, B. M., Rottingen, J. A., Grais, R. F. and Guerin, P. J. (2005). Risk factors associated with typhoid fever in Son La province, northern Vietnam. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **99, 819-826.**

Velema, P. J., van Wijnen, G., Bult, P., van Naerssen, T. and Jota, S. (1997). Typhoid fever in Ujung Pandang, Indonesia–high-risk groups and high-risk behaviours.*Tropical Medicine and International Health* **2(11), 1088-1094.**

Vollaard, A. M., Ali, S., van Asten, H. A. G. H., Widjaja, S., Visser, L. G., Surjadi, C. and van Dissel, J. T. (2004). Risk factors for typhoid and paratyphoid fever in Jakarta, Indonesia. *Journal of American Medical Association* **291(21), 2607-2615.**

Yap, Y. F. and Puthucheary, S. D. (1998). Typhoid fever in children-a retrospective study of 54 cases from Malaysia.*Singapore Medical Journal* **39 (6), 260-262.**

Zain, M. M. and Naing, N. N. (2002). Sociodemographic characteristics of food handlers and their knowledge, attitude and practice towards food sanitation: A preliminary report. *Southeast Asian Journal of Tropical Medicine and Public Health* **33(2), 410-417.**

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